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Editorial

Dear Readers,

Greetings of the Season!

It is a moment of happiness to recall that Indian Journal of Pharmacy Practice (ijopp) was launched during the APTI convention 2008 and we have successfully completed two years.

In these two years, we were able to publish some quality research articles, review articles, short communications and case reports with your contribution and support. Although, there have been some hiccups, slowly things are falling in place.

We have received both 'Bouquets' and 'Brickbats' during these two years! We have taken note of all the feedback and trying to implement things in the best possible way.

Also, we are very happy to inform you that APTI is conferring award for the two best research papers published in ijopp during 2009-2010 in order to encourage good research and publications in the field Pharmacy Practice.

We appeal to all the colleges offering Pharmacy Practice and Pharm.D/Post Baccalaureate courses to subscribe the journal.

Anticipating your support and encouragement as always.

Dr. Shobha Rani R Hiremath

Editor-in-Chief

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An Overview on Paclitaxel in Advanced Chemotherapy

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ABSTRACT

Paclitaxel is a new cytotoxic agent that has demonstrated significant activity in advanced ovarian, breast, lung, head and neck cancer. The chemotherapy remains problematic and ineffective because of the problems of poor efficacy, parasite resistance, high toxicity, high cost and unavailability of drug in larger hospital. Therefore there is an urgent need for review drug therapy and efficacious of paclitaxel. We developed a search engine to find any literature about pharmacokinetic parameters of paclitaxel and its drug treatment in DOAJ database, Science Direct, and PubMed using the key phrases paclitaxel; drug therapy; adverse drug reactions and pharmacokinetics. Our results shows that efficacy, neurotoxicity and application of paclitaxel. Hence our review concludes that, about the importance and implementation of therapeutic drug monitoring in individualization of chemotherapy in various cancer patients.

Key-words: Paclitaxel, Pharmacokinetic, Cancer, Chemotherapy

INTRODUCTION

During the screening programmes of natural products in the 1960s, the National Cancer Institute (NCI), identified crude extract of the bark of the pacific yew tree, Taxus brevifolia, which was found to have active against several murine tumors. In 1971 Wall and Wani of research triangle institute north Carolina identified paclitaxel (taxol,NSC,1259730) as the active ingredient of bark.[1] In a 1979 study of paclitaxel, unique mechanism of action, Horwtiz and associates[2-3] noted that the drug prevented the cells from dividing by promoting the assembly of microtubules without inhibiting their disassembly. In 1983 the national cancer institute began toxicological studies of paclitaxel and initiated clinical phase 1 trials. Progress of these trials was hampered by hypersensitivity reactions (HSRs). This led to the premature closure of some phase 1 studies.

The next major step in paclitaxel's development was the recognition of its activity against ovarian cancer, which led to further clinical evaluation of this agent in other tumor types. Responses in approximately 30% of ovarian carcinoma patients were reported in 1989.[4] Clinical studies at the university of Texas M.D. Anderson cancer center led to the recognition in 1991 that paclitaxel had activity against breast carcinoma and in 1992 against non-small bronchial carcinoma.[5- 6] Even as evidence of paclitaxel's activity increased, its rapid clinical development was prevented by a persistent supply shortage, since paclitaxel could not be supplied by either a totally synthetic or a semi synthetic process.

The structures of paclitaxel and docetaxel are provided in figure 1. The chemical name of paclitaxel is 5β,20 Epoxy-1,2α,4,7β,10β,13α-hexahydroxytax-11-en-9-one 4, 10-diacetate 2-benzoate 13-ester with (2R,3S)-N-benzoyl-3-phenyl isoserine, paclitaxel is a white to off-white crystalline powder; the marked product is clear colourless to slightly yellow viscous solution . Paclitaxel chemical formula is C40H5O11 and it has a molecular weight of 853.9. It is highly lipophilic and melts at around 216-217 C. Paclitaxel is insoluble in water, slightly soluble in octanol and propylene glycol, sparingly soluble in t-butanol and soluble in cremophor EL. Paclitaxel is freely soluble in dimethylacetamide.

PHARMACOLOGY OF PACLITAXEL

The preclinical and toxicology studies of paclitaxel were well underway in the late 1970s and early 1980s there was little knowledge of the pharmacology of paclitaxel until the late 1980s and early 1990s. The most commonly cited reasons for the delay in paclitaxel's clinical development of appropriate analytical assays as well as the relative insensitivity of the available analytical methods at the time in measuring concentration ranges in tested small animals.[1-2]

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MECHANISM OF ACTION

Microtubules are long, hollow cylinders comprising 13 protofilaments aligned along the axis of a cylinder. The microtubules are assembled from tubulin, a 100, 000 molecular weight proteins. The microtubules are in a dynamic equilibrium with soluble tubulin dimmers. Tubulin has two sub unit; α and β, similar but distinct acidic polypeptides. Each subunit has a molecular weight of 50,000.[7-3]

The vinca alkaloid (vincristine, vinblastine and vindesine) bind to specific sites on tubulin and prevents its polymerization to microtubules leading to the disruption of the mitotic spindle.[7-3] In contrast, paclitaxel alters the normal equilibrium in favor of the microtubule, thus lowering the critical concentration of tubulin required to form microtubules. In the absent of guanosine 5"-triphosphate (GTP), a cofactor usually required for *invitro* microtubule polymerization, paclitaxel enhances tubulin polymerization.[2-8] Although cold and calcium chloride normally disrupt microtubules, this effect is not observed in microtubules assembled in the presence of paclitaxel. Paclitaxel binds specifically and reversibly to microtubules (usually the β subunit to a single set of high-affinity binding sites). Drug such as colchicines, which depolymerization microtubules, eliminates paclitaxel binding, thus corroborating the microtubules as essential in paclitaxel's mechanism of action.[2-8]

PHARMACOKINETICS

Paclitaxel from plasma was determined to be biphasic with linear pharmacokinetic behavior. These early studies, however, used variable infusion schedules of the drug with[1-6] and 24h infusions, and were hampered by suboptimal analytical techniques. Hamel et al.[8] found the alpha (α) and beta (β) half-lives to be 0.045 and 0.75h, respectively, with paclitaxel bolus intravenous administration in rabbits. Other early phase studies concurred with biexponential elimination, most of which were administered with 6 or 24 h infusions.[9-11] Linear kinetics was assumed, as clearance seemed independent of dose, especially with 24-h infusion schedules.[7,12,13]

Elimination of paclitaxel has been found to have a three-phase elimination curve and non-linear pharmacokinetic behaviour, particularly with shorter infusions. Typical values reported for the α, β, and gamma (γ) half-lives are 0.19h (range 0.01 - 0. 40), 1.90 h (range 0.50 -2.80), and 20, 70 h (range 4.00-65.00), respectively.[7] Paclitaxel exhibits non-linear pharmacokinetics in that it has a disproportionate increase in the maximal plasma concentration (Cmax) and area under the concentration curve (AUC) as the dose increased, suggesting saturation of elimination at higher concentrations of paclitaxel. [14-15] Several studies with paclitaxel given as a 6-h infusion have documented non-linear pharmacokinetics with doses higher than 250mg/m2.[16-17] while other believe that a lesser dose of 135mg/m2 is the critical threshold for non-linear kinetics. Similar findings were noted with 3-h infusion scheduled and in pharmacokinetics studies in children that found nonlinear disappearance of paclitaxel with saturation of elimination pathways and tissue distribution.[7,22,24] It has been shown in Table: 1.

The non-linear pharmacokinetics behavior of paclitaxel with shorter administration scheduled is as expected with saturable tissue distribution and drug elimination processes.[14-15] In such situations, plasma drug concentrations and Cmax are generally higher than with longer infusion scheduled and signify reaching or exceeding the Michaelis-Menton constant. As paclitaxel Cmax and AUC disproportionately increase with the dose of drug administered, saturation must occur during drug elimination, though saturable tissue distribution cannot be ruled out[9-22] implications of saturable non-linear model includes relative saturation of paclitaxel binding sites at lower Cmax, more effective binding of paclitaxel with shorter infusion scheduled compared with longer schedules, and the potential for plateau of response to the drugs as dose and concentrations increases . Such implications have likely prompted the migration toward shorter infusion scheduled and lower drug dosage.

Paclitaxel is bound to proteins in plasma, tissues, and tubulins. Estimates of magnitude of protein binding reach as high as 98% with equilibrium dialysis and ultracentrifugation studies.[10, 17] Supporting extensive drug binding *invivo*, total volumes of distribution have been reported as significantly larger than that of total body water ranging from 50L/m2 to over 650L/m2depending on infusion arrangement.[16,17,12,13] In addition, paclitaxel has an affinity for distribution in specific tissues types. Kidney, lungs, spleen, and third space fluid, including ascites and pleural fluid, have been found to have the highest tissue concentrations.[17,24] Most impressive though is the high distribution is found in liver and tumour tissues, as studied by Fugita et al. Though paclitaxel is known to distribute to body fluids, this is not the case with cerebrospinal fluid. Similarly, tumour sanctuary sites, including testes and brain, do not have detectable paclitaxel levels.[24]

Despite paclitaxel being highly bound in plasma and in tissues, elimination occurs readily and correlates with its own low and reversible binding affinity. The major route of elimination is biliary excretion. Walle et al. and Monasarrat et al demonstrated one – fifth of the dose of paclitaxel is recovered from bile within 24 h after administration. Paclitaxel metabolites are also measurable in bile which account for the majority of drug elimination from the body. Metabolite concentrations far exceed paclitaxel parent compound concentration in bile if measured *in vivo*. In humans, renal excretion and other extra hepatic excretion mechanisms account for less than 10% of elimination.[9,10, 17] This is not to imply that paclitaxel can be administered in standard doses to patients with chronic renal failure. The literature would suggest that there is a modest suppression of cytochrome p 450 activity in patients with chronic renal failure; unfortunately no clinical studies have examined. The impact of renal failure on paclitaxel pharmacokinetics. In vitro evidence would suggest that the dose of paclitaxel should be reduce in patients with chronic renal failure. Jiko et al Studied paclitaxel metabolism in rats who were treated with a 5/6 partial nephrectomy and found that the clearance of paclitaxel was reduced by 34% in the rats with renal failure with compared to controlled rats. For patients with liver dysfunction there are a few clinical studies that can provide guidance with respect to dosing. Fennelly et al[18, 19] showed that patients with either elevated liver enzymes or elevated total bilirubin are more likely to develop myelosupression with paclitaxel treatment than those patients who have neither abnormality. As such, it is prudent that dose reduction be considered for those individuals with hyperbilirubinemia and /or increased liver transaminases.[20,21]

PHARMACODYNAMICS

The most concerning side effects of paclitaxel are myelosupression, particularly neutropenia, and neuropathy. Gianni et al.[22] studied paclitaxel in 30 patients with varying doses and infusion schedules. A comparision between a 135 or 175mg / m2 dose given by a 3-or 24h infusion versus a 225mg / m2 dose by a 3h infusion was made neutropenia was the most significant toxicity. A correlation was observed between paclitaxel concentration above 0.05µmol/L and neutropenia but no relationship was noted with paclitaxel AUC or peak Cmax concentrations. Similarly, Huizing et al.[7] studied paclitaxel in 18 heavily platinum pre-treated ovarian cancer patients. Women were treated with paclitaxel 135 or 175 mg/m2 on a 3h or 24-h infusion schedule. A relationship was again found between neutropenia and the duration that paclitaxel exceeding a certain concentration threshold; in this study the dose threshold was 0.1µmol/L. There was no relationship between AUC or Cmax and toxicity.

To address this surprising finding, Henningsson et al.[23] went on to study paclitaxel pharmacodynamic in a slightly larger group of 45 patients. Here, they found the free paclitaxel drug concentrations were a slightly better predictor than total paclitaxel concentrations for toxicity but did not improve measure of goodness of fit in their pharmacodynamic model.

Two studies suggested a trend for increased neurotoxicity with increased paclitaxel AUC.[7,24] The first was a phase 1 study in children with solid tumors using paclitaxel in dose range of 200 -420 mg/m^2. Sonnichsen et al.[24] observed a trend for higher paclitaxel AUCs in children with neurologic toxicity compared to children without toxicity. In children with neurotoxicity, paclitaxel AUC was 54µmol/L h compared to 30µmol/ L h in those without neurotoxicity (p=0.062). The second study by Huizing et.al.[7] treated breast cancer patients with paclitaxel and observed those who developed neurotoxicity also had higher AUCs. In contrast, a study non-small cell lung cancer by Rowinsky et.al.[25] failed to show an association of paclitaxel concentration at the end of infusion and neurotoxicity.

METABOLISM AND METABOLITES

Paclitaxel metabolism is primarily through oxidative metabolism and biliary excretion, only 5-10% of paclitaxel is renally eliminated.[9] Monsarrat et.al.[28,26] were one of the first groups to examine hepatic metabolism and biliary excretion of paclitaxel, first in rats and then in humans. They identified nine metabolites in rats and five metabolites in a human patient who had external biliary drainage. Interstingly, all metabolites were hydroxylated though obvious significant differences exist in the site of hydroxylation and metabolite proportions found in bile. The predominant major human metabolite discovered was 6α-hydroxy paclitaxel. This metabolite was not formed in rats and is modified from paclitaxel via stereo specific hydroxylation at the 6-position on the taxane ring as determined by nuclear magnetic resonance (NMR).[27]

PACLITAXEL PHARMACOGENETICS

The liver primarily metabolizes paclitaxel with three major metabolites being formed; 6α-hydroxypaclitaxel, 3-p-hydroxypaclitaxel, and 6α, 3-p-dihxydroxy paclitaxel. It is widely accepted that cytochrome P450 sub families play major roles in paclitaxel metabolism most notably the 2c and

3A subfamilies. Recently, polymorphic variants of cytochrome 2C and 3A have discovered. Effects of these polymorphisms are currently being studied and clinical trials are underway to determine whether there is correlation between variants, clinical efficacy and toxicity.

CYP2C8:

The CYP2C8 subfamily is arguably the most important enzyme in paclitaxel metabolism with general acceptance. This subfamily is responsible for metabolism of paclitaxel to its primary metabolite, 6α-hydroxypaclitaxel.[27-29] In turn, paclitaxel metabolism is a useful indicator of CYP2C8[30]. Dai et.al.[51] Recently discovered that genetic polyporphisms in CYP2C8 affects its activity. In this study, the CYP2C8 gene was sequenced from a bank of 72 different human lymphoblastoid cell lines representing African, Caucasian, and Asian ethnic groups. Two variant alleles of CYP2C8 were discovered, CYP2C8*2 and CYP2C8*3. The variants are formed due to substitution in the coding sequence. CYP2C8*2 results from a substitution at position 269 in exon 5 of phenylalanine for isoleucine while CYP2C8* has two substitutions: at position 139 of exon 5 of lysine for arginine and at position 299 of exon 5 of arginine for lysine.[31]

CYP 3A4:

CYP 3A4 is the most abundant p450 enzyme in the liver and small intestine and accounts for 30-60% of all the p450 enzymes.[32,33] In early studies, CYP3A4 was implicated to be involved with paclitaxel metabolism thought at the time, metabolites were not identified ; Harris et.al[34] showed anti-CYP3A4 antibodies reduced formation of paclitaxel metabolite while steroids were found to induce CYP3A4 resulting in an increase in paclitaxel metabolism.[35] There is general acceptance that CYP3A4 metabolism has significant inter-individual variation. Genetic polymorphisms have been found in CYP3A4 with over 30 single nucleotide polymorphism (SNP).

Lamba et.al.[36] while analyzing 179 samples, found[28] SNP, none of which showed low CYP3A4 expression or function. In fact, most CYP3A4 SNPs have yet to demonstrate clinical effects as they usually appear as heterozygous alleles and are synonymous in that they do not change the amino acid sequence. The most abundant variant, CYP3A4*1B, has an allele frequency as high as 0.45 in African –Americans, but is absent in Asians. There are links between CYP3A4 promoter region variability and prostate cancer and leukemia. For example, Rebbec at al determined CYP3A4 genotypes in 230 Caucasian males with prostate cancer. A new variant was found containing an A-G mutation in a CYP3A4 promoter region. The polymorphism correlated with higher stage and Gleason grade and was believed to be related to higher baseline testosterone levels as a result of increased CYP3A4 activity. Spurdle et.al.[37] have studied the CYP3A4*1B polymorphism but found no significance with association or risk of breast or ovarian cancer.

CYP 3A5:

CYP3A5, in individuals that express it, is the second most abundant of in the CYP3A sub family. Investigations have found distinct difference between it and CYP3A4 although coding sequence DNA is about 88% homologous . CYP3A5 and CYP3A4 have overlapping functions in terms of substrate specifity, a finding almost certainly causing significant difficulties in determining the true functions of these enzymes. Interestingly, CYP3A5 is not present in all humans and seems to have a specific age and racial distribution, being more prevalent in younger individuals and Africans-Americans. It is said to be present in only about 10-30% of the population as a whole but if expressed can be up to 50% of hepatic CYP3A content and as such likely contributes to differences in CYP3A related metabolism. An allelic variant of CYP3A5 has been identified with a point mutation that, in an unconfirmed report, appears to produce an unstable protein without enzymatic activity. Further studies have found an arginine to glycine polymorphism at position[44] of the promoter region to CYP3A5 results in a defective CYP3A5*variant.[38- 40] Additional polymorphisms with ethnic variants have been noted.

P-GLYCOPROTEIN (PGP):

P-glycoprotein is a transmembrane transporter found in the intestinal epithelium, liver and kidney, responsible for cellular efflux of products of metabolism and drugs. Genetic polymorphisms have been found in MDRI as well as the multi-drug resistance proteins –associated proteins (MRPs) 1and 2. Mixed results have been found while investigating MDR and MRP polymorphisms and effects variants have on function, though consensue is building that genotype may be responsible for inter – individual differences in oral drug absorption. For example Kim et al. found altered protein function in a MDR1 SNP with single amino acid change in exon 21 (Ala 893Ser). The Ser 893 variant resulted in up regulated efflux of digoxin compared to the Ala 893 variant.[41] Different studies of paclitaxel have been shown in table 2.

APPLICATIONS OF PACLITAXEL

Paclitaxel in Breast Carcinoma:

The initial report of paclitaxel's activity in breast cancer, by Holmes et.al.[5] noted an objective response rate of 56% (12% CR and 44% PR: 95% cl , 35-76%) in 25 patients with metastatic breast carcinoma that had failed to respond to only one prior chemotherapy regimen, either adjuvant to surgery or for metastatic disease. To confirm paclitaxel's activity in breast cancer, investigators at Memorial Solan-Kettering cancer center[43] conducted a phase II trial of 250 mg/m2 paclitaxel as a 24h infusion and filgrastim, 5mg/kg/day subcuteously on day 3, continuing until recovery of neutropenia . These patients either had received no prior chemotherapy or had received adjuvant chemotherapy only. An overall response rate of 62% (95%CL, 43-80%) was noted in 26 patients.

Paclitaxel Combination Chemotherapy for Breast Cancer:

As with the combination of paclitaxel and cisplatin, paclitaxel plus doxorubicin appears to have sequence dependence. In the initial combination trial performed at M.D Anderson, paclitaxel was given over 24h, followed by doxorubicin over 48h, with cardiac monitoring by telemetry and 72-h Holter monitoring. Filgrastim, 5mg/mg subcutaneously, was administered on days 5 through 19. The planned schedule was 60 mg /m2 doxorubicin with escalating paclitaxel doses of 125, 150, 180, and 210mg/m2. The DLT of grade 3 stottitis or myelosupression associated with fever occurred in the first three patients treated at the starting dose. The MTD os this scheduled was actually 125mg/m2 of paclitaxel and 48mg/m2 of doxorubicin, with dose reduction in 22% of treatments because of stomatitis and fever. Of the ten patients treated, eight attained PRs and one had a Cr9.

Paclitaxel in Other Cancer:

A phase II study of paclitaxel, 200mg/m2over 24 h every 3 weeks, conducted at M.D Anderson cancer center demonstrated a response rate of 24% (one CR, five PRs) in 25 evaluable patients with non-small-cell bronchial carcinoma who had not received prior chemotherapy. An additional seven patients (28%) attained minor response. The median duration of response was 27 weeks (range, 12 weeks to >54 weeks). The overall median survival for all patients was 40 weeks. CR was observed in a patient with adenocarcinoma; however responses were also observed in large cell and squamous cell carcinomas [6]. Chang et al. reported a randomized study of paclitaxel, merbarone, or piroxantrone for patients with metastatic (stage IV) non –small cell lung cancer; patients received paclitaxel ,250mg/m^2 as a 24-h infusion every three weeks . Similar to the aforementioned M.D.Anderson study, paclitaxel produced a 20.8% response rate (5 of 24 patients), with a medium survival of 24.1weeks. The response rates for merbarone and piroxantrone were 5.7% and 2.3% respectively. Applications has been shown in figure.1.

Current trials are examining the role of paclitaxel in carcinoma of the gastro intestinal tract, prostate, and bladder, endometrial carcinomas and sarcomas, and lymphomas. Pediatric phase I studies are being completed as well as examining the use of paclitaxel in patients with impaired hepatic functions.

Mechanism of resistance

Multidrug resistance (MDR) phenotype related to overproduction of p-glycoprotein. This membrane glycoprotein acts as an energy-dependent drug efflux pump to maintain intracellular drug concentrations below cytotoxic levels. 15 A highly resistant cell line (J774.2/ Taxol) selected with paclitaxel from the murine tumor J774.2 cells displays the MDR phenotype with the amplification of p-glycoproteins.

CONCLUSION

In conclusion, the population pharmacokinetics model predicted neutropenia and thrombocytopenia after administration of paclitaxel in patients with ovarian cancer. Paclitaxel tc > 0.05 was found to be a good predictive marker for severe neutropenia and clinical outcome. This review aims to shed importance and implementation of therapeutic drug monitoring in individualization of chemotherapy in various cancer patients.

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Health screening services: An Overview

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INTRODUCTION

World health organization (WHO) defines health as a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity. Over the years, WHO has taken forward the debate and has revised its definition of health as "health is the extent to which an individual or group is able. on one hand, to realize aspirations and satisfy needs and on the other hand to change or cope with the environment. Health is therefore, seen as a resource for everyday life, not an object of living. It is a positive concept emphasizing social and personal resources as well as physical capacities. There is no single definition that unifies the perceptions about health. Our understanding of it depends on the many different contexts in which life is lived and health is perceived. Health is a human right and access to health care including essential medicines is derived right. Health is essential for sustainable economic and social development. Health is thus a very precious resource. Everyday, individuals exposed to various toxic substances over a period of time result in chronic diseases. The individual's health deteriorates by aging process, which sometimes is symptomatic or asymptomatic. Exacerbation of the disease leads to complications, which can be reversible or irreversible at times. So health screening will help to detect early health status of individual. The health deteriorates over a period of time sometimes, which cannot show sign and symptoms.

Screening refers to examination of a group of usually asymptomatic individuals to detect those with a high probability of having a given disease, typically by means of an inexpensive diagnostic test. These screening tests are used to detect a disease when there is little or no evidence that an individual has a suspected disease. In some cases, screening may be confused with monitoring; however, monitoring refers to the act of observation and in some cases intervention-generally referring to monitoring of a condition after diagnosis to assess and improve outcomes.

Services refer to help or assistance by health professionals for people at risk, who will get benefited on his/her health status. At many situations these services will not be provided. Health care professionals that include physician, pharmacist, nurses, physiotherapist, dentist, health educators etc can provide health-screening services. The prerequisite for providing health care services is that he/she should be qualified enough and trained adequately before implementation of health screenings.

Health screening services are the services provided by the health care professionals to screen the health status of individuals with or without positive sign and symptoms. Health screening plays an important role in detecting traces of illness in its early stages. It is suitable for everyone and not just for high-risk individuals or top executives. Early detection can make a difference between relatively simple courses of treatment or life-threatening complications requiring lengthy and expensive hospital stays. Early diagnosis has always a better chance for cure. The screening tests are used to try to detect a disease when there is little or no evidence that a person has a suspected disease. For example, measuring blood pressure helps to identify one of the risks of heart disease. These screening tests are performed on people who may show no symptoms of heart disease, as a tool to detect a potentially harmful and evolving condition. The assessments can help to identify early signs of a disease and to provide you with an evaluation of your overall current state of health. Health screening services can be provided at hospital, clinical and community pharmacies or any other suitable setting (hospital, community pharmacy) by health professionals or trained technicians, which fulfill the minimum requirements.

Benefits of health screening

As you reach certain age groups, it is important to remember for health screening check up in order to maintain your optimum health. Health screenings save lives by early detection of conditions such as hypertension or elevated blood sugar and can help prevent serious diseases like

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diabetes and heart disease that kill thousands of people every year. The benefits of ongoing health screening services revolve around prevention and early detection. It is important for health issues such as diabetes, cholesterol, lung function or other health related conditions, which could adversely affect our lives. Many cases of disease exist and remain undiagnosed that seriously affect our quality of life. Many of these conditions can be corrected or improved through a simple course of treatment if once it has been discovered by health screening. The aim of health screening is that the prevention is better than cure. Health screening is viewed as an ongoing health management's process but not as a medical examination. The majority of people screened require no further advice or treatment. So, one of the additional benefits of a health screen is peace of mind and reassurance. According to US government reports, regular screening can reduce deaths from colorectal cancer by 30%, cervical cancer by up to 90%, and breast cancer by 15-30% among women over age 40, as well as identifying controllable risk factors for preventable diseases such as diabetes and heart disease.

The prevalence and incidence of diabetes and cardiac diseases are increasing drastically over past years. Largest number of diabetic subjects of the world is in India and being termed as diabetes capital of the world. This number is expected to rise to 69.9 million by 2025.[13]

Around the world, people were suffering from chronic diseases specifically diabetes and hypertension who remain undiagnosed. In some poorer countries, 80% to 90% of people with diabetes are undiagnosed; while even in high-income countries 30% may be undiagnosed.[14]

People often have chronic diseases for a long time before it is diagnosed. For many people, the diagnosis comes when they make contact with the health system for other reasons for example when admitted or visited to hospital with minor illness or injuries. The longer, people are undiagnosed, the more likely it is the complication of the disease. Health Screening Services contributes to economic burden of the patient by early diagnosis and prevention.

Advantages of health screening

Health screenings are convenient (readily available), affordable (inexpensive), comprehensive, very reliable with few false negatives and flexible. Also it is painless, non-invasive and inexpensive tests. For most people, a health screen will give them peace of mind and in addition to screening tests based on your current health situation, your doctor will talk to you about your risk factors and lifestyle modifications, helping you design a program for improving your health and lowering your risk factors through healthy habits. Health screening is quick and easy. You can have your weight, blood pressure and blood sugar checked in just a few minutes by health professionals. It doesn't hurt, and it takes no special preparation. Health screenings can educate you on the simple changes to your lifestyle that keep you in good health.

A standard health screen comprises of:

- Blood pressure measurement
- Total blood Cholesterol measurements
- Blood glucose measurement
- Body mass index measurement
- % Body fat measurement
- Lung function test
- Height & weight measurements
- Health education materials
- Provision of lifestyle advice and dietary advice and advice on risk factors
- Smoking cessation support
- Regular support, follow up and contact with the patient

Based on composition of Health screen, it is classified into three types. They are standard health screen, premium health screen, and executive health screen. This health screen consists of the following such as

Standard Health Screen Include:

- Consultation with health professional
- Blood glucose test (marker for diabetes)
- Blood cholesterol test (total Cholesterol level)
- Blood pressure measurement and evaluation
- Body mass indexing (measures height weight ratio)
- Cardiac risk assessment
- Comprehensive urine analysis (tests for elevation of protein, blood etc in urine)

Premium health screen includes:

- Consultation with health professional

- Blood glucose test (marker for diabetes)
- Blood cholesterol test (total Cholesterol level)
- Blood pressure measurement and evaluation
- Body mass indexing (measures height weight ratio)
- Cardiac risk assessment
- Pulmonary function tests (lung capacity, and screens for possible disease)
- Liver function tests (for abnormal liver function)
- Comprehensive urine analysis (tests for protein, blood in the urine and possible kidney disease infection)

Executive health screen includes:

- Comprehensive one to one consultation
- Blood glucose test (marker for diabetes)
- Blood cholesterol test (total Cholesterol levels)
- Blood pressure measurement and evaluation
- Body mass indexing (measures height and weight ratio)
- 12 lead ECG (measures the electrical conduction of the heart)
- Cardiac risk assessment
- Renal profile (blood test to check kidney functions)
- Bone profile (blood test for measure calcium, phosphate)
- Full blood count (measures red cells, white cells, hemoglobin etc.)
- Ferritin blood test (can detect hereditary conditions such as haemochromatosis)
- Pulmonary function tests (lung capacity, and screens for possible disease)
- Liver function tests (for abnormal liver function)
- Comprehensive urine analysis (tests for protein, blood in the urine and possible kidney disease infection)
- Healthy body fat % range

All types of health screen have common advice and patient information leaflet on the following health topic.

Weight loss

Smoking cessation

Cardiac health

Stress management

Nutrition

Cancer awareness

Osteoporosis

Prerequisites and procedures for provision of health screening services

The prerequisites are

- Competency of staff
- Quality assurance programme
- Maintenance of equipments
- Keeping up to date with new developments

Procedures involving patients require strict adherence to health and safety standards for the safety of both the patients and the staff. Hygienic methods of obtaining specimens, provisions of seating for patients who may feel faint during or after blood sampling are considered. Basic first aid techniques and safety procedures concerning 'sharps' all need to be in place. A suitable place for counseling patients is essential and some primary care groups for providing funding for building counseling areas in pharmacies.

It is vital that the results of appropriate health screening test are recorded in patients computerized medication records. The results of all the diagnostic tests carried out in pharmacies could be entered on a 'smartcard' that is retained by the patient for future reference. Such a system would put patients in control of their own records. Alternatively or as well as authorized health care professionals who are caring for that patient could transmit the results via an Internet or some other suitable means to some secure site of central patients' records that is only assessable. However it may be such that the public will wish to pay for the health screening services themselves or employers may regard it as a good investment on behalf of their staff.

Health Screening Services in India: pharmacist engages few community pharmacies and hospitals in providing these services. Past one decade many pharmacies started providing these services. Some hospitals like Sahyadri Hospital, Pune JSS Hospital, Mysore KLE Hospital, Belgaum providing these services. Community pharmacies in metro cities like

Mysore, Belgaum, Bangalore, Kozhikode, Goa, Pune started these services. Many pharmacies started providing heatlh-screening services after their training on different days and time. Also the education regulation of D Pharm 1991 also influenced by introducing Hospital, Community, Clinical, health education into the curriculum.

Health Screening in Community Pharmacies

The role and responsibility of community pharmacist is expanded to provide health-screening services to the local community. This can be carried out in few minutes to hours depending upon the type of screening measurements. Monitoring health in this way allows you to make diet and lifestyle changes to significantly reduce the risk of diseases like heart attack, stroke, diabetes and cancer. Community pharmacists should be integrated into national and local strategies aimed at tackling obesity, blood pressure etc. Community pharmacies are the first point of contact for minor illnesses. In recent years community pharmacies are offering more services for communities. Community pharmacy has been increasing its involvement in health promotion, especially information provision and screening, over the past decade.

Oral health screening for children

Primary care professionals or other appropriately trained professionals, can perform an oral health screening of the lips, tongue, teeth, gums, inside of the cheeks, and roof of the mouth to identify oral disease, especially tooth decay or other oral conditions (for example delayed tooth eruption or premature tooth loss, abscesses or trauma) and to provide guidance for management. An oral health screening takes only 2 or 3 minutes to complete.

A dental chair is not needed to perform an oral health screening. For infants and children under age 3, the professional and the parent should sit face to face with their knees touching, with the child placed in the professionals and the parents lap.

Pharmacists in health screening services

Pharmacists play an important role in provision of Health Screening Services, as he is part of health care team. Pharmacists who are involved in providing HSS should have all the pre-requisites discussed above and also require adequate infrastructure and facilities. The HSS can be provided at community, hospital, clinical, industrial pharmacy set-up, as it is easily accessible for needy people.

The outcomes of health screening services are

- Early detection/diagnosis and prevention of disease
- Reduced risk factors
- Improved quality of life
- Maintain good health and well-being
- Reduce cost and future complex problems

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Recent Advances in Management of Acute Diarrhoea in Children

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INTRODUCTION

Diarrhoea is most common health problem in children, especially those between 6 months and 2 years of age or under the age of 5 years. It is also common in babies under 6 months who are drinking cow's milk or infant feeding formulae. Frequent passing of normal stools is not diarrhoea. Babies who are breastfed often have stools that are soft; this is not diarrhoea. Diarrhoea is the number of stools normally passed in a day varies with the diet and the age of the child. In diarrhoea, stools contain more water than normal — they are often called loose or watery stools. They may also contain blood, in which case the diarrhoea is called dysentery. Diarrhoea remains the second leading cause of death among children under five globally. Nearly one in five child deaths – about 1.5 million each year is due to diarrhoea. It kills more young children than AIDS, malaria and measles combined[1].

Diarrhoea is more prevalent in the developing world due, in large part, to the lack of safe drinking water, sanitation and hygiene, as well as poorer overall health and nutritional status. According to the latest available figures, an estimated 2.5 billion people lack improved sanitation facilities, and nearly one billion people do not have access to safe drinking water. These unsanitary environments allow diarrhoea causing pathogens to spread more easily. Diarrhoea's status as the second leading killer of children under five is an alarming reminder of the exceptional vulnerability of children in developing countries. Saving the lives of millions of children at risk of death from diarrhoea is possible with a comprehensive strategy that ensures all children in need receive critical prevention and treatment measures[2].

In India the situation is going positively to achieve the child mortality related to MDG (millennium development goals). The data related to reducing under five mortality rate (U5MR) from 125 deaths per thousand live births in 1988-92 to 42 in 2015. The U5MR has decreased during the period 1998-2002 to 98 per thousand live births. The infant mortality rate (IMR) has also come down from 80 per thousand live births in 1990 to 60 per thousand in 2003 in contrast with Global data. There has been steady decline in the infant mortality rate from 92 per thousand live births in 1991 to 52 per thousand in 2003, under five child mortality rate has come down from 151 in 1990 to 78 per thousand in 2003.[3] In 2006, for the first time, the number of children in the world dying before their fifth birthday fell below 10 million to 9.7 million[4]. More than 70 percent of almost 11 million child deaths every year are attributable to six causes: diarrhoea, malaria, neonatal infection, pneumonia, preterm delivery or lack of oxygen at birth. The major cause of death among children under five in developing countries in the year 2002 was diarrhoea accounting for 15% deaths.[5]

The latest UNICEF report says, 5,000 kids die daily under the age of five in India mainly due to preventable diseases. Diarrhoea is one of the main reasons which accounts for 10 to 20% of deaths in children of 0-5 years.

Diarrhoea:

Diagnosis is based on clinical symptoms, including the extent of dehydration, the type of diarrhoea exhibited, whether blood is visible in the stool, and the duration of the diarrhoea episode. Treatment regimens differ based on the outcomes of this clinical assessment. Microbiological culture and microscopy are not necessary to diagnose diarrhoea and initiate treatment, even in high-income countries, although these tools can help identify specific pathogens for outbreak investigations[6]. It is important that caregivers recognize the symptoms that require immediate attention from appropriate health personnel, including trained community health workers. These symptoms include dehydration, blood in the stool, profuse and persistent diarrhoea and repeated vomiting.

There are three main forms of acute childhood diarrhoea, all of which are potentially life-threatening and require different treatment courses:

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♦ Acute **watery diarrhoea**: This is associated with significant fluid loss and rapid dehydration in an infected individual. It usually lasts for several hours or days. The pathogens that generally cause acute watery diarrhoea include *V. cholerae* or *E. coli* bacteria, as well as rotavirus.

♦ **Bloody diarrhoea:** This is marked by visible blood in the stools. It is associated with intestinal damage and nutrient losses in an infected individual. The most common cause of bloody diarrhoea is Shigella. It is also known as dysentery.

♦ **Persistent diarrhoea**: This is an episode of diarrhoea, with or without blood that lasts at least 14 days. Undernourished children and those with other illnesses, such as AIDS, are more likely to develop persistent diarrhoea. Diarrhoea, in turn, tends to worsen their condition.

The children are more vulnerable to diarrhoea than adults. Children are also at greater risk than adults of life-threatening dehydration since water constitutes a greater proportion of children's body weight. Young children use more water over the course of a day given their higher metabolic rates, and their kidneys are less able to conserve water compared to older children and adults.[7]

TREATMENT:

The diarrhoea can be treated by replacing the loss of fluids by Oral Re-hydration Solution along with zinc sulphate tablets. The diarrhoea causes the dehydration, the dehydration usually occurs when the output of water and salts is greater than the input. The more diarrhoea stools a child passes, the more water and salts he/she loses. Dehydration can also be caused by a lot of vomiting, which often accompanies diarrhoea. Dehydration occurs faster in infants and young children, in hot climates and when there is fever.

The treatment package focuses on two main elements, as outlined in a 2004 joint statement from UNICEF and WHO: 1) fluid replacement to prevent dehydration and 2) zinc treatment. Oral re-hydration therapy – which has been heralded as one of the most important medical advances of the 20th century is the cornerstone of fluid replacement. New aspects of this approach include low osmolarity oral re-hydration salts (ORS), which are more effective at replacing fluids than the original ORS formulation. The zinc treatment decreases diarrhoea severity and duration. Important additional components of the package are continued feeding, including breastfeeding, during diarrhoea episodes and the use of appropriate fluids available in the home if ORS are not available, along with increased fluids in general.[8]

Oral Re-hydration Solution is a mixture of clean water, salt and sugar, can be prepared and administered at home. It is estimated that this simple but effective solution has saved 40 million children's lives since it was first introduced in India in 1971.[9]

Zinc supplementation can reduce the duration of a diarrhoeal episode by 25 percent and is associated with a reduction in

Common ORS Available in Market

Name	Weight	Price	Manufacturer
Walyte	21g/litre	Rs. 11.25	Wallace
Elect ORS	21g/litre	Rs. 13.50	Piramal HC
Electrokind	21.5g/litre	Rs. 12.00	FDC
Genlyte	21.5g/litre	Rs. 13.00	Cadila

Note: The ORS is also available in smaller packs to dissolve in 200ml of water. The WHO standard formula: 20.5g for 1000 ml. The commercial products have different weights because of use of other excipients.

Zinc Sulphate Available in Market

Name	Price/No. Of Tablets	Manufacturer
Z & D DT 20	Rs. 22.00/ 7 Tablets	Dr. Reddy ' s

Note: Commercially Zinc tablets are not readily available

History:

The ancient Indian physician Sushruta date back over 2500 years used to treat acute diarrhoea with rice water, coconut juice, and carrot soup. However, this knowledge did not carry over to the Western world. The dehydration was found to be the major cause of death, secondary to the 1829 cholera pandemic in Russia and Western Europe. In 1831, William Brooke O'Shaughnessy noted the loss of water and salt in the stool of cholera patients and prescribed intravenous fluid therapy (IV) to compensate. The results were remarkable, as patients who were on the brink of death from dehydration recovered. The mortality rate of cholera dropped from 70% to 40% with the use of hypertonic IV solutions.[11] IV fluid replacement became entrenched as the standard of care for moderate /severe dehydration for over a hundred years. ORT replaced it with the support of several independent key advocates that ultimately convinced the medical community of the efficacy of ORT.[12]

In the late 1950s, ORT was prescribed by Dr. Hemendra Nath Chatterjee in India for cholera patients. Although his findings predate physiological studies, his results failed to gain credibility and recognition because they did not provide scientific controls and detailed analysis.[13] Credit for discovery that in the presence of glucose, sodium and chloride became absorbable during diarrhoea (in cholera patients) is typically ascribed to Dr. Robert A. Phillips. However, early attempts to translate this observation into an effective oral re-hydration solution failed, due to incorrect solution formula and inadequate methodology.[12]

In the early 1960s, biochemist Robert K. Crane discovered the sodium-glucose co-transport as the mechanism for intestinal glucose absorption[14]. Around the same time, others showed that the intestinal mucosa was not disrupted in cholera, as previously thought. These findings were confirmed in human experiments, where it was first shown that a glucose-saline oral therapy solution administered in quantities matching measured diarrhoea volumes was effective in significantly decreasing the necessity for IV fluids by 70-80%. These results helped establish the physiological basis for the use of ORT in clinical medicine[11].

Between 1980 and 2006, ORT decreased the number of worldwide deaths from 5 million a year to 3 million a year[13]. Death from diarrhoea was the leading cause of infant mortality in the developing world until ORT was introduced.[19]

Zinc Sulphate Available in Market			
Content		Concentration in mmol/l	
Sodium Chloride	2.6 g	Na^+	75
Potassium Chloride	1.5 g	K^+	20
Tri sodium Citrate	2.9 g	Cl^-	65
Glucose (anhydrous)	13.5 g	Glucose	75
		Citrate	10
Total Osmolarity = 245 mOsm/l			

A combined analysis of studies with low osmolarity ORS has revealed that stool volume is reduced by 20% and incidence of vomiting by 30%. The WHO/UNICEF have recommended replacement of standard (310 mOsm/l) ORS formula by the new mOsm/l .[15] The development of this improved new formula for ORS with reduced levels of glucose and salt shortens the duration of diarrhoea and the need for unscheduled intravenous fluids.[16]

ORT is not designed to stop diarrhoea, but to restore and maintain hydration, electrolyte and pH balance until diarrhoea ceases, mostly spontaneously. It is the best and not a second choice approach to intra venous hydration. Oral re-hydration salts (ORS) make a special drink that consists of a combination of dry salts. When properly mixed with safe water, the ORS drink can help re-hydrate the body when a lot of fluid has been lost due to diarrhoea. A child with diarrhoea should never be given any tablets, antibiotics or other medicines unless these have been prescribed by a medical professional or a trained health worker. The best treatment for diarrhoea is to drink lots of liquids and oral re-hydration salts (ORS) properly mixed with water.

Approximate Amount of ORS Required in the First 4 Hours[17]						
Age	Less than 4 Months	4-11 Months	12-23 Months	2-4 years	5-14 years	15 years or older
Weight	Less than 5 kg	5-7.9 kg	8-10.9 kg	11-15.9 kg	16-29.9 kg	30 kg or more
ORS solution in ml	200-400	400-600	600-800	800-1200	1200-2200	2200-4000

The studies have shown that children receiving zinc experience a decrease in the severity of their diarrhoea episodes. A ten-day course has proven to provide a prophylactic protection against future bouts of diarrhoea for two to three months after the episode. The combined recommendation of zinc and ORS is a safe, effective and inexpensive diarrhoea treatment for children in the developing world. The only known side effect of zinc use is vomiting, which is rarely reported and is typically attributed to a metallic taste in the zinc. Use of high quality zinc products easily averts this side effect.

Based on WHO/UNICEF recommendation and realising the role of zinc in the management of diarrhoea, the Government of India has already issued new guidelines for the treatment of diarrhoea in children in 2007. The new recommendation includes Zinc in addition to ORS:[18]

♦ Use of 20 mg zinc sulphate dispersible tablets for use in childhood diarrhoea.

♦ Children aged 2 months to 6 months to be advised ½ tablets (10 mg) per day dissolved in breast milk. Those older than 6 months are advised to take 1 tablet a day dissolved in breast milk or water.

♦ The tablets are to be taken for 14 days beginning from the day the child sought care.'

Counselling to Mother: As the mother's role is very critical in the management of diarrhoea in children, it is essential that they should be properly counselled on the safe and effective use of ORS. It is necessary to ensure the mother that ORS does not reduce the diarrhoea but helps in treating diarrhoea and the diarrhoea will stop automatically.

1. Wash your hands thoroughly with soap and water.

2. Pour all ORS powder from a packet into a clean container.

3. Measure one litre of clean drinking water (freshly boiled and cooled drinking water) and pour into the container in which you poured ORS, if you have ORS packets for ½ litre of water then take ½ litre water.

4. Stir until all the powder in the container has been mixed with water and none remain at the bottom of the container.

5. Taste ORS solution before giving it to the child, it should taste like tears – neither too sweet nor too salty. If it tastes too sweat or too salty then throw away the solution and prepare ORS solution again.

6. Do not use ORS already prepared with water after one day (after 24 hours). Prepare a fresh solution.

7. Continue feeding including breast feeding the child. Starving a child who has diarrhoea can cause malnutrition or make it worse.

8. When to return to the clinic:

If a child passes many stools, is very thirsty, or has sunken eyes, the child probably is dehydrated. The child may need more treatment than the mother can give at home. The child should be taken to the doctor or hospital.

CONCLUSION:

Though India's progress towards child mortality related Millennium Development Goals is significant, still a lot to be done. Even now 5000 kids die every day due to preventable and treatable conditions. Diarrhoea continues to be a major contributing factor for childhood mortality.

The WHO/UNICEF and Government of India recommend the use of ORS and Zinc in the treatment of childhood diarrhoea. While ORS prevents dehydration and loss of electrolytes, the zinc sulphate tablets decrease the duration and severity of the diarrhoea. The ORS is readily available in the market but Zinc sulphate is not. Even the label of Zinc Sulphate tablet has a warning "WARNING – To be sold by retail on the prescription of a Registered Medical Practitioner only". The Government of India has already made it clear that Zinc Sulphate does not fall under schedule H and is a OTC drug. This warning may discourage the people to use Zinc Sulphate. The Government of India must promote, through various means, the use of ORS together with Zinc for effective treatment of childhood diarrhoea, which would go in a long way reducing diarrhoea related deaths in children.

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Antibiotic Prescribing Pattern in Department of Dermatology of a Teaching Hospital in Tamil Nadu

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ABSTRACT

The present study was undertaken to study the prescribing behavior of clinicians in treating identified bacterial infection, cost of treatment, prescription error and patient counseling to improve the use of medicine from the patient view point. 132 patients with bacterial skin infections were selected from both out patients and inpatients at the time of ward round on daily basis, done in the department of Dermatology at RMMC & Hospital Annamalainagar, T.N, India and subjected for analysis according to the WHO/DSPRUD Indicators. It was observed that maximum number of cases (29.97) were in male patients between the age group of 20-39 years. **S**econdary infection was found most common (56.82%) and oral antibiotics were highly prescribed (66.18%) than topical antibiotic (23.04%). Most commonly used topical antibiotic was mupirocin (11.52%) while highly prescribed oral antibiotic was ampicillin (26.70%) and prescribing of parenteral preparation was rare. It was found that the total number of patients completely cured were 96 (11.36%). Among Prescription error occurred during practice it was observed that medication related error was more (43.28%) than duration related error (29.85%). During the follow up period it was found that counseling was effective in imparting the knowledge of time of medication (80%) and the importance of duration of treatment (90%). The WHO is advocating the promotion of rational use of drug by promoting the implementation of standard treatment guideline and essential drugs. The development and implementation of treatment guideline is a multidisciplinary activity of the health care team in which Pharmacist can play an active role.

Key words: Rational drug use, antibiotic, medication error, skin infection,

INTRODUCTION

Clinically and economically inappropriate prescribing in many forms including inappropriate and irrational use of antibiotics constitutes a major health problem. This problem is considered serious due to the risk of adverse clinical outcome, such as the spread of resistant bacteria and adverse economic impacts due to the high cost of clinically unnecessary antibiotics. Principles of good prescribing are based on sound knowledge and understanding of the pathophysiology of disease to be treated, and the knowledge of risks and benefits of the medicine.[1, 2] Irrational prescribing is a habit, which is difficult to change. Various factors which contribute to irrational prescribing include; lack of unbiased source of information, uncertainty about diagnosis, limited experience, aggressive drugs promotion by pharmaceutical industry and time patients demand etc. There was high prevalence of polypharmacy including antibiotic and prescriptions by brand names thus increasing the cost of prescription. Although single intervention did not show much improvement in core as well as complimentary drug use indicators but regular discussion with the prescribers would probably check the deeply rooted wrong prescription and disbeliefs about drug use. Appropriate drug use by patients and adherence to instruction given by the prescriber is an integral part of successful rational drug use programme. Patient's non adherence to the prescribed treatment is a global problem. The reasons for poor compliance could be lack of instructions provided with the prescription, low literacy and poor dispensing practice. Patients should be actively involved in the therapeutic encounter and treatment, because it is the patients who decide whether to go ahead with treatment or not. The patients should get doubtless unbiased information about the drugs they take viz; dosage, purpose, frequency of administration etc. Health planners often overlook dispensing and it can lead to determine the impact on health care delivery system. All of the resources required to bring a drug to patient

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may be wasted if dispensing dose not ensure that the correct drug is given to the right patient in an effective dosage and amount with clear instruction. Rational prescribing can be achieved by practicing evidence-based medicine.[3,4] Since pharmacist is often the final link between prescribed medication and the patient, better interaction between pharmacists and the patient can lead to better patient knowledge about drug use and compliance to therapy.

MATERIAL AND METHODS

The present study was done in the department of Dermatology at RMMC & Hospital Annamalainagar, Tamil nadu, India. This was a prospective randomized study carried out from July 2005 to April 2006 including all the patients with bacterial skin infections.

Collection of data: The prescribing pattern of antibiotics in 132 patients with bacterial skin infections were collected from both out patients and inpatients at the time of ward round on daily basis. These were analyzed according to the WHO/ DSPRUD indicators[5,12] for:

* Age distribution of patients.
* Category wise distribution of patients.
* Pattern of antibiotics usage.
* Therapeutic efficacy of the medication.
* Cost of drug therapy.
* Prevalence of prescription errors.
* Patient awareness.

RESULTS

Table I shows that out of 132 prescriptions maximum number of cases were in male between the age group of 20-39 years (21.97%) followed by 1-19 years (16.67%) and in female 1-19 years (18.94%) followed by 40-59 years (9.09%). Table II Reveals that secondary infection was found most common (56.82%) among the patients. Table III shows distribution of patients on the basis of route of administration, it was found that oral antibiotic were highly prescribed with (66.18%) than (23.04%) parenteral preparation.

Table I. Baseline demographic data of patients

Sl.no	Age in year	Male (%)	Female (%)
1	<1	2 (1.52%)	5 (3.79%)
2	1-19	22 (16.67%)	25 (18.94%)
3	20-39	29 (21.97%)	11 (8.33%)
4	40-59	15 (11.36%)	12 (9.09%)
5	>61	9 (6.82%)	2 (1.52%)

Table II. Category wise distribution of patients

Sl.no	Category	No of Patients	Percentage
1	Primary infection	51	38.64
2	Secondary infection	75	56.82
3	Recurrent infection	6	4.55

Table III. Distribution based on route of administration

Sl. no	Route of administration	No of patients	Percentage
1	Topical antibiotic	47	23.04
2	Oral antibiotic	135	66.18
3	Parenteral antibiotic	9	4.41
4	Oral combination	8	3.92
5	Topical combination	5	2.45

Table IV reveals that most commonly used topical antibiotic was mupirocin (11.52%) while highly prescribed oral antibiotic was ampicillin (26.70%) and prescribing of parenteral preparation was rare. It was found that the treatment was very effective in 72.73% patients and moderately effective in 11.36% patients (Table V). Table VI reveals that average number of drugs per prescription is 5 in secondary & recurrent infection and 4 in primary infection, and average cost per prescription was Rs.72.50, 65.14 and 56.03 in recurrent infected patients, secondary infection and in primary infected patients respectively.

Table IV. Antibiotic used pattern

Sl. no	Name of Antibiotic	No of patients	Percentage Topical
1	Mupirocin	22	11.52
2	Sisomicin	10	5.24
3	Fusidic acid	3	1.57
4	Nodifloxacin	2	1.05
5	Framycetin]	10	5.24
6	Sulfadiazine	1	0.52
Oral			
1	Ampicillin	51	26.70
2	Erythromycin	32	16.75
3	Ciprofloxacin	16	8.38
4	Gatifloxacin	1	0.52
5	Doxyfloxacin	6	3.14
6	Metronidazole	16	8.38
7	Azithromycin	1	0.52
Parenteral			
1	Amikacin	3	1.57
2	Ampicillin	2	1.05
3	Erythromycin	2	1.05
Oral combination			
1	Ampicillin and cloxacillin	3	1.57
2	Amoxicillin and cloxacillin	5	2.62
Topical combination			
1	Fluticasone propionate and mupirocin	5	2.62

Table V. Therapeutic efficacy and outcome			
Sl. no	Category	Outcome	Percentage
1	Very effective	96	72.73
2	Moderately effective	15	11.36
3	Mild/Not effective	4	3.05
4	Not follow up	17	12.88

Table VI. Category wise distribution of average number of drugs and cost per prescription			
Sl. no	Category	No of drugs	Cost (in Rs.)
1	Primary infection	4	56.03
2	Secondary infection	5	65.14
3	Recurrent infection	5	72.50

Among the prescription errors occurred during practice (Table VII), it was observed that medication related error were more (43.28%) than in duration related error (29.85%). Table VIII reveals that before counseling out of 132 patients only few patients had the knowledge about time of medication & direction (60%), importance of duration of treatment (55%). During the follow up period it was found that counseling was effective in imparting the knowledge of time of medication (80%) and the importance of duration of treatment (90%).

Table VII. Prescription error occurred during practice			
Sl. no	Prescription error	No of patients	percentage
1	Dose		
	Not mentioned	2	1.49
	Wrong	3	2.24
	Other	-	-
2	Dose frequency		
	Not mentioned	24	17.91
	Wrong	-	-
	Other	-	-
3	Dose duration		
	Not mentioned	37	27.61
	Wrong	3	2.24
	Other	-	-
4	Drug interaction	7	5.22
5	Medication error	58 4	3.28

Table VII. Prescription error occurred during practice			
Sl. no	Patients awareness	Pre counseling (% of patient known)	Post counseling (% of patients known)
1	Time of medication & direction (if applicable)	60%	80%
2	Duration of treatment	55%	90%
3	What should you do if you forget to have drugs	30%	70%
4	Do you know what other food/ medication should be advised while taking these medication	45%	65%

DISCUSSION

Antibiotics represent one of the most commonly used drugs. Their irrational use leads to a number of consequences in term of cost, side effects and bacterial resistance. Pharmacoeconomics plays an important role in rational therapeutic decision making.

In this study, we found a higher incidence of infection in male between the age group of 20-39 years and in females of 1-19 years. Secondary infection was more (in 75 patients) in comparison to other infection. The type of infection plays an important role in the management. The average number of drugs and cost per prescription was high in recurrent infection cases which was Rs.72.50 respectively. In general, due to multiple infections, patients are at a greater risk of polypharmacy.[6] In recurrent infections rather than given broad spectrum antibiotic it is better to prescribe antibiotic based on pus culture sensitivity testing.

As per as prescribing habit of antibiotic in different routes is concerned, the frequently prescribed antibiotics in oral, topical and parenteral route are ampicillin (26.70%) mupirocin (11.52%) and amikacin (1.57%) respectively. Combination of amoxicillin & cloxacillin (2.62%) is the main combination in oral route and combination of fluticasone propionate & mupirocin (2.62%) is the only combination in topical route. This is good prescribing habit oral dosage form as parenteral dosage can definitely play an important role in improving patient's adherence to treatment.[7] By the adequate use of topical antibiotics, the over use of oral antibiotic can also be reduced.

According to the study 43.28% of medication errors were found among the total prescription error followed by dose duration related error (29.85) and dose frequency related error (17.91). Prescription errors are very common, [8, 9] especially with fresh doctors.[10] The basic problem which contributes to the irrational prescribing is that the medical students were not adequately instructed. [11] Medication errors during practice should be reduced for better therapeutic efficacy.

In our study a patient awareness centre was maintained in the pharmacy where all patients were counseled and educated. We found that out of 132 patients only few patients had knowledge about drug and importance of duration of treatment before counseling. During the follow up period it was found that counseling was effective in imparting the knowledge of drugs and importance of duration of treatment.

An agreed clinical guideline helps in the selection of essential drugs. The essential drugs may be limited in number but they should be carefully selected based on the clinical guidelines. The development of treatment guidelines and essential drugs list are of more importance in resource poor situations where the availability of drugs in the public sector is often erratic.

The World Health Organization (WHO) is advocating the promotion of rational use of drugs by of promoting the implementation of standard treatment guidelines and essential drugs.[5, 12]

The process for guideline development should be aimed at identifying intervention that will ensure the best possible health outcomes. The purpose of treatment guideline is to encourage the treatment that offers individual patients maximum likelihood of benefit and minimum harm and is acceptable in terms of cost.

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CONCLUSION

The standard treatment guidelines and essential drugs are the basic tools for assisting health professionals to choose the most appropriate medicine for the given patient with a given condition. It should be followed by the appropriate use of the selected medicine. Health care providers and those responsible for dispensing medicines should take every opportunity to inform patients about the rational use of drugs, including the use of drugs for self medication at the time they are dispensed.

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Assessment of Drug Therapy Interventions by Clinical Pharmacist in a Tertiary Care Hospital.

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ABSTRACT

The aim of the study was to assess the drug therapy interventions and the feedbacks from the clinicians on interventions. This study was a prospective, observational and interventional study. The drug therapy details of the patients were collected from inpatient case records. Clinical pharmacist reviewed the drug therapy, identified the DRPs and discussed during ward rounds with the physicians concerned and suitable suggestion was provided which had been documented. The clinical pharmacist assessed the contribution made through the above-mentioned parameters through the physician, by feedbacks. A total of 37 DRPs were identified from 31 patients case records. Male predominance was noted over females. DRPs were commonly seen in patients aged between 31-60 years of age. Majority of the DRP resulted from the inappropriate drug selection pattern 35.13%. Majority of the clinical pharmacist recommendations were on drug choice 48.64%. The acceptance rate of recommendation and change in drug therapy was found to be high 78.37%. Most of the pharmacist interventions were seen to have moderate significance in grade. In the feedbacks most of the clinicians commented that this service was helpful and this service to be continued in future. Clinical pharmacy services can produce a high number of interventions, which may benefit patients. This study showed that the Clinical pharmacist interventions in drug therapy helped clinicians in identifying and preventing drug related problems.

Key words: Clinical Pharmacist, Intervention, Drug therapy, Drug related problems.

INTRODUCTION

Drug-related problems (DRPs) can be defined as any event or circumstance involving the drug treatment, which interferes or potentially interferes with the patient, achieving an optimum outcome of medical care. Drug related problems are frequent and may result in reduced quality of life, and even morbidity and mortality[1]. Despite excellent benefits and safety profile of most medication drug related problems pose a significant risk to patients, which adversely affect quality of life, increase hospitalization and overall health care cost[2].

Drug-related problems include medication errors (involving an error in the process of prescribing, dispensing, or administering a drug, whether there are adverse consequences or not) and adverse drug reactions (any response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function). Furthermore, adverse drug events can be defined as an injury whether or not causally related to the use of a drug[3].

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Drug related problems may arise at all stages of the medication process from prescription to follow-up of treatment. Most problems are centred on administration, dispensing and the patients use of a medicinal product, but lack of follow-up and reassessment of medical treatment is also a major problem. Also problems regarding prescription could entail serious consequences. The health and economic consequences of the medication problem may appear in many ways, for instance in the form of a large extent of drug related hospitalizations. Other consequences for patient and society are unnecessary drug expenses, uncomfortable symptoms, adverse drug reactions and a poorer state of health[4].

Increased use of medication and availability of new drug therapies potentially increase the risks of patient for iatrogenic adverse drug events in hospitals. Iatrogenic adverse events are important for consideration because it cannot only prolong hospital stay but also increase patient health care expenditure. Therefore, it is important that all drug related problems resulting in serious injury or death are evaluated to assess whether improvement in the healthcare delivery system can be made to reduce the like hood of similar events occurring in the future[5,6].

Many studies are carried out in hospitals to assess and

minimize drug related problems. It is reported that medication errors occur in 3-6.9% of in-patients and the error rate for in-patients medication orders was reported to be 0.03-16.9% with each hospital experienced a medication error every 22.7 hours.[7] An Indian study reported that the incidence of drug related problems was found to be greater than quoted as an average in developed countries[8].

Drug therapy has become so difficult that no one professional is expected to optimize the drug therapy and control drug related problems alone[7]. Drug-related morbidity and mortality are often preventable, and pharmaceutical services can reduce the number of ADRs, the length of hospital stays, and the cost of care. Pharmacists must abandon factionalism and adopt patient-centred pharmaceutical care as their philosophy of practice[9]. Many studies have shown that clinical pharmacists can effectively identify and prevent clinically significant drug-related problems and that physicians acknowledge and act on the clinical pharmacists suggestions for intervention to the drug-related problems. A pro-active rather than a reactive approach on the part of the pharmacists seems prudent for obtaining most benefit. This includes participation of pharmacists in the ward rounds at the stage of ordering and prescribing where all types of drug-related problems, including also potential problems, should be discussed. Therefore participation and intervention of clinical pharmacists in health care positively influence clinical practice[1].

Intervention is defined as an action by a clinical pharmacist, which resulted in a change in the patients' therapeutic management. Though pharmacy practice has changed significantly in recent years and continues to evolve towards the provision of better pharmaceutical care, pharmacists represent an under-utilised but potential resource to optimize the usage of drugs. Studies have shown that a clinical pharmacist can reduce health service use and cost while improving the appropriateness of drug prescribing. Medication errors most often occur due to insufficient information and time during prescription[10].

Pharmacists can facilitate improved prescribing and medicines management by working closely with the medical team. This model provides a safer system, improvements in pharmaceutical care and better resource utilization. Analysis of clinical pharmacy interventions has demonstrated that pharmacists have an important role in improving patient care and advice is generally accepted by prescribers. Therefore clinical pharmacists' intervention can have a positive impact on reducing drug related errors in overall patient care[11].

Clinical pharmacists are uniquely trained in therapeutics and provide comprehensive drug management to patients and providers (includes physicians and additional members of the care team). Pharmacist intervention outcomes include health-related quality of life, patient satisfaction, medication appropriateness, adverse drug reactions and economics. This type of study is of particular importance because most studies reporting medication errors and ADEs were in hospitalized patients, and with the growth of hospital medicine there is increased focus on interventions to improve the care of hospitalized patients. The role of clinical pharmacist in the care of hospitalized patients has evolved over time, with increased emphasis on collaborative care and patient interaction. The addition of clinical pharmacist services in the care of inpatients generally results in improved care, with no evidence of harm[12].

Safe and effective medicine use is the core business of clinical pharmacists. With the focus on individual patients, comprehensive and accountable clinical pharmacy services are an essential component of contemporary healthcare practice. By working to ensure that medicine therapy is optimum, safe and cost-effective, the provision of clinical pharmacy services serves the interests of individual patients and also the wider community[13].

India is a country with significant problems with medication use, but until recently Indian pharmacist has not been educated for a patient-care role. The purpose of this study is to assess the drug therapy interventions by clinical pharmacist related to patients in a tertiary care hospital.

METHODS

This study was carried out for a period of 7 months among in-patients who were being treated under the Medicine unit of KLES's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum which is a 1500 bed hospital. This was a prospective, observational, interventional study. In-patients of either sex of any age undergoing treatment in medicine wards were included. The exclusion criterion was patients receiving treatment on outpatient basis and patients with severely ill conditions. The intervening pharmacist was a postgraduate pharmacy practice student. All the interventions made by the intervening pharmacist were preceded by consultation with the academic clinical pharmacist. The clinical pharmacist designed a standard format to collect relevant data for each intervention such as brief details of the patient, medications, problem identified, physicians response and follow up, if any. The patient's demographic data, current

medication, past medical and medication history, laboratory investigation was collected from the patient's progress records, treatment charts, laboratory reports and patient's history records. The demographic data collected includes the patient's age and gender. The current medication data includes all the drugs, their dosage, route of administration with frequency, date of drug started and stopped. The past medical and medication history data collected includes the patients previous allergies, co-morbidities and the drugs received previously. The laboratory data collected includes the relevant laboratory investigation done in the hospital.

Clinical pharmacist routinely monitored patient's drug therapy and interviewed with physicians as well as patients when necessary. The identified drug related problems were discussed during ward rounds with the physicians concerned and has been documented. The acceptance level of physician for the particular intervention was also recorded as either accepted or not accepted. Similarly, whether or not there was a change in drug therapy was noted. In addition, the total time taken by the intervening pharmacist in preparing and undertaking the intervention was recorded. The intervening pharmacist assessed the clinical significance of each intervention. The feedbacks of clinician's opinion on clinical pharmacist interventions were documented and analysed.

RESULTS

A total of 105 patients drug therapy were followed during the seven months study period. Out of which 31 patients had drug related problems. Out of 31 patients 37 drugs related problems were identified and assessed. Out of 31 patients 18 (58.06%) were male and 13 (41.93%) were female. The age group of 31- 60 years patients had more DRPs compared to age groups of 10-30 and above 60 years. The demographic details of the patients are summarized in Table 1.

The identified drug related problems are Adverse drug reactions 1 (2.70%), Interactions 4 (10.81%), Drug selection 13 (35.13%), Dosing 7 (18.91%), Drug use 6 (16.21%), Monitoring 1 (2.70%) and Patient/Provider 5 (13.51%). The drug related problems are summarized in Table 2.

Out of 37 DRPs identified, 37 recommendations were made by the clinical pharmacist and they are Drug Choice 18 (48.64%), Dosing 7 (18.91%), Optimization of administration 3 (8.10%), Need for drug monitoring 1 (2.70%) and others which is of 8 (21.62%). Various suggestions provided by the intervening pharmacist are summarized in Table 3.

Result of recommendations concerning drug related problems are suggestion accepted and therapy changed 29 (78.37%), suggestion accepted and therapy not changed 5 (13.51%) and neither suggestion accepted nor therapy changed 3 (8.10%). The result of clinical pharmacist recommendations is shown in the Table 4.

The time taken for the intervention by the clinical pharmacist were found to be 5 minutes or less 7 (18.91%), 6-15 minutes 20 (54.05%), 16-29 minutes 8 (21.62%), 30-59 minutes 2 (5.40%).

Out of 37 interventions the Clinical pharmacist contacted doctors for about 25 (67.56%) interventions, PGs 2 (5.40%), nurses 2 (5.40%) and for 8 (21.62%) interventions the personnel contacted are patients.

Out of 37 interventions, the significance grades of interventions were found to be 'moderate' 17 (45.94%), 'minor' 15 (40.54%) and 'major' 5 (13.51%). The significance grade of drug related problems is represented in Table 5.

Out of 10 clinicians 6 (60%) of them gave the opinion that clinical pharmacist interventions were helpful and 4 (40%) of them gave the opinion that clinical pharmacist interventions were very helpful. Out of 10 clinicians 7 (70%) of them gave the opinion that the drug related intervening service provided by the clinical pharmacist was good. Out of 10 clinicians all of them 10 (100%) gave the opinion that this service to be continued in future.

DISCUSSION

Drug-related problems are relatively common in hospitalized patients and can result in patient morbidity and mortality, and increased costs[3]. The number of drugs used and the number of clinical/pharmacological risk factors significantly and independently influenced the risk for DRPs[23]. In India, clinical pharmacy service is an emerging discipline. Clinical pharmacy service is to optimize patient outcomes by working to achieve the best possible equality use of medicines. It has been shown that the clinical pharmacy activities reduce the drug related problems related to hospitalization, probability of readmission and total cost of drug therapy[2]. The aim of the study was to assess the clinical pharmacist interventions pertaining to drug therapy and the feed backs from the clinicians. Medicine department was selected for the study because patients in medicine unit are frequently prescribed a large number of drugs and having variety of diseases.

Among the 105 patients followed during the study period 31

patients were found to need pharmacist intervention in their drug therapy. A total of 37 drug related problems were identified and assessed from 31 patients. Out of 31 patients involved in drug related problems, (58.06%) were males and (41.93%) were females. This study showed a high incidence of drug related problems in males over females. This might be due to increased medication use owing to their multiple co-morbidities. This observation is in contrast with the demographic reports of the study conducted by Madhan Ramesh et al[2], cited a predominant of males over females. The incidence of drug related problems were high (54.83%) in patients aged between 31-60 years, where as age group of 10-30 years was found to be (16.12%) and the patients above 60 years of age were (29.03%) which is similar to the study conducted by Madhan Ramesh et al[2] which shows more DRPs in patients aged between 41-60 years. This can be attributed to the fact that more number of patients visited the hospital during the study period was ranged between 31-60 years of age group.

Most of the DRP observed in the study resulted from the inappropriate drug selection pattern (35.13%) which constituted more of the 'drug prescribed not needed' 6, followed by 'drug duplication' 4, 'drug needed not prescribed' 1, 'cost of therapy' 1 and 'inappropriate dosage form' 1. This observation is in contrast with the study carried out by Madhan Ramesh et al[2], in which drug use without indication accounted for highest. The high incidence of inappropriate drug selection may be attributed to lack of standard treatment protocol in the hospital, poor history taking etc. Inappropriate dosing (18.91%) was the second most common DRP observed which included more of 'duration inappropriate' 4, followed by 'dose too high' 2 and 'dose too low' 1. The study carried out by G. Parthasarti et al[8] showed that inappropriate dosing accounted for highest DRPs but in this study inappropriate dosing is the second most common DRP and this finding is consistent with the study carried out by S. Mangasuli et al[10] which showed that improper dose accounts for the second most common DRP. Drug use was accounted for (16.21%) of the total DRPs which constituted more of 'incorrect storage' 2 and 'incorrect administration' 2, followed by 'Wrong dose taken/ administered' 1 and 'drug not taken' 1. In few cases it was due to lack of patient's awareness on storage and administration. While in few other cases it was due to shift change of nursing staff. Drug related problems due to patients or provider contributed (13.51%) of the total DRPs which integrated more of 'demonstration of devices' 2 and 'non-adherence' 2, followed by 'Patient misuse (overuse/underuse)' 1. In few cases it may be ascribed to lack of patient's knowledge while in few cases it was due to economic constraints of the patients that lead to non-procurement of prescribed medicines and reluctance of patients to take the medication for unknown reasons. Drug interactions was accounted for (10.81%) of the total DRPs identified which incorporated more of 'drug-drug interaction' 3 followed by 'drug-disease interaction' 1. And both the adverse drug reactions and monitoring were accounted for (2.70%) of the total DRPs.

Recommendations, on drug choice (48.64%) was the most frequently provided recommendations which included more of 'Drug discontinuation' 16, followed by 'addition of a new drug' 1 and 'change of dosage form' 1. This finding is similar like the observation made in an Indian study[2] where the cessation of drug and addition of drug were the suggestions most frequently provided. Other recommendation made in this study was on dosing 7 (18.91%), Optimization of administration 3 (08.10%), need for drug monitoring 1(02.70%) and others 8 (21.62%) which are adherence, advices to patients, proper storage and cost effectiveness.

In this study the major reason for drug discontinuation were due to drug prescribed not needed and drug duplication. Addition of drug was suggested in case of drug needed not prescribed. This is suggested in a gastric irritation case. In most case recommendation on dosing were sought in dose too high, dose too low and in patients with renal impairment requiring dosage reduction. These finding in this study indicate that there is a scope for clinical pharmacist to suggest issues related to rational drug therapy and emphasis on the importance of involvement of pharmacist in healthcare delivery.

The acceptance rate of intervening clinical pharmacist recommendation and change in drug therapy was found to be high (78.37%). There were (13.51%) other interventions where suggestions were accepted, but therapy was not changed either because the physicians were hesitant to change the prescription immediately, without close monitoring, or because the suggestions were thought to be insignificant. In (08.10%) cases, the suggestions were neither accepted nor therapy changed. One of the reasons for this could be that the pharmacists failed to understand the sophisticated prescribing behaviour i.e., prescribing decisions governed by clinical experience of physicians. These findings in this study correlates with other published studiues[2, 10].

(18.91%) interventions took 5 min or less to complete and

(54.05%) interventions took 6 - 15 min to complete. This reflects the quick turnover of patients and the high number of problems to resolve in a limited amount of time. The philosophy of the clinical pharmacist was to see the maximum number of patients possible, prioritizing their problems to ensure that those in need receive the highest level of care. Consequently, a large number of patients are seen and problems were resolved quickly wherever possible. It should be noted that (21.62%) interventions took 16-29 min to complete and (05.40%) interventions took 30-59 min to complete reflecting the complex nature of some of the problems encountered. This finding in this study is in contrast to R. N. Price et al[17]where in Ninety per cent of interventions took 10 minutes or less to complete. This difference may be attributed to the fact that involvement of experienced clinical pharmacist would have led to the high acceptance rate and also reductions in time spend for each intervention.

The personnel mostly contacted for the interventions were doctors (67.56%) followed by PG's (05.40%). This is because the clinical pharmacist taking rounds in the medical wards along with the doctors and the PG's more over the fact that most of the time postgraduates were involved in writing the medication order. The nurses contacted for the interventions were (05.40%). This may be due to their busy work schedule or inadequate number of nurses in the medicine unit. The patients contacted for the interventions were (21.62%). This may be of lack of patient's knowledge and awareness. This data's consistent with the study carried out by R. N. Price et al[17] showed that 40 per cent of interventions the contact point was a junior doctor.

Of the 37 DRPs, (40.54%) were rated to be 'minor', (45.94%) were 'moderate' and (13.51%) were 'major' significance of interventions. This finding correlates with studies[2, 8] that reported 60% and 49% of interventions as moderate significance. The moderate significance level is the level of problems requiring adjustments, which are expected to enhance effectiveness of drug therapy producing minor reduction in patient morbidity or treatment cost.

Out of 10 clinicians most of them (60%) gave the opinion that clinical pharmacist interventions was helpful in their practice and (40%) of them gave the opinion that clinical pharmacist interventions was very helpful. Most of the PG's and interns commented that it is very helpful as this helps to improve their attitude towards patient care.

Out of 10 clinicians (70%) of them gave the opinion that the drug related intervening service provided by the clinical pharmacist was good and (30%) of them gave the opinion that the drug related intervening service provided by the clinical pharmacist was average.

Out of 10 clinicians (50%) of them gave the opinion that the time taken for the Intervention to be shown as per the requirement of the patient was ideal and (20%) of them gave the opinion that the time taken for the intervention by the clinical pharmacist was more and (30%) of them had no opinion. Most of the clinicians commented that the time taken for the intervention was ideal and its helps in patient care and treatment outcome. But in few cases the time taken was more because of lack of knowledge and the complicity of the cases.

All clinicians (100%) of them gave the opinion that this service to be continued in future as they were interested to improve the patient care and treatment outcomes by identifying and resolving the DRPs.

Out of 10 clinicians (50%) of them gave the opinion that all other services like ward round participation, patient counselling, drug information, identifying DRPs are their expectation from the clinical pharmacist, (20%) of them are expecting both the drug information and patient counselling services, another (20%) of them expecting both ward round participation and identifying DRPs and the rest (10%) of the physician expecting both ward round participation and drug information services from the clinical pharmacist.

The overall observation made from this study was that pharmacist has greater responsibility in healthcare team in minimizing and preventing drug related problems and thereby improves the patient care, treatment outcomes and enhances quality of life.

Table No.1 - Demographic details of the study patients

Characteristics		Number (n=31)
	GenderMale	18 (58.06%)
	Female 13	(41.93%)
Age Group (years)	31-60	17 (54.83%)
	Above 60 09	(29.03%)

Table No.2 Types of Drug Related Problems.

Sl. No.	Types of DRPs	No. of DRPs	Total
1.	**Adverse drug reactions**		
	a) Allergic reaction	00	01
	b) Side effect	01	(02.70%)
2.	**Interactions**		
	a) Drug - Drug interaction	03	
	b) Drug disease interaction	01	04
	c) Drug food interaction	00	(10.81%)
3.	**Drug selection**		
	a) Drug needed not prescribed	01	
	b) Drug prescribed not needed	06	
	c) Drug Duplication	04	13
	d) Cost of therapy	01	(35.13%)
	e) Contraindication	00	
	f) Inappropriate dosage form	01	
4.	**Dosing**		
	a) Dose too low	01	07
	b) Dose too high	02	(18.91%)
	c) Duration inappropriate	04	
5.	**Drug Use**		
	a) Wrong dose taken/ administered	01	
	b) Wrong drug taken/administered	00	
	c) Drug not taken	01	06
	d) Incorrect storage	02	(16.21%)
	e) Incorrect administration	02	
6.	**Untreated Indications**		
	a) Condition not adequately treated	00	00
	b) Preventive therapy required	00	(00%)
7.	**Monitoring**		
	a) Laboratory monitoring	01	01
	b) Non-laboratory monitoring	00	(02.70%)
8.	**Patient or provider**		
	a) Demonstration of device	02	
	b) Patient didn ' t understand instruction	00	05
	c) Patient misuse (overuse/underuse)	01	(13.51%)
	d) Non-Adherence	02	

Table No.3 Clinical pharmacist recommendations

Sl.No.	Types of Recommendations	Number	Total (n=37)
1.	**Drug Choice**		
	a) Drug discontinuation	16	
	b) Addition of a new drug	01	18
	c) Change of dosage form	01	(48.64%)
2.	**Dosing**		
	a) Decrease the dose	03	
	b) Increase the dose	01	07
	c) Appropriate duration 0	03	(18.91%)
3.	**Optimization of administration**		
	a) Change of administration route	01	03
	b) Administration modalities	02	(08.10%)
4.	**Need for drug monitoring**	01	01 (02.70%)
5.	**Others ***	08	08 (21.62%)

** Adherence, Advice to patients, Proper storage and Cost effectiveness*

Table No 4 - Result of Clinical pharmacist recommendations.

Recommendations	Result (n=37)
Suggestion accepted and therapy changed	29 (78.37%)
Suggestion accepted but therapy not changed	05 (13.51%)
Neither Suggestion accepted nor therapy changed	03 (08.10%)

Table No 5 - Grade of interventions.

Grade *	Result (n=37)
Minor	15 (40.54%)
Moderate	17 (45.94%)
Major	05 (13.51%)

** **Minor**: Problems requiring small adjustments and optimization to therapy, which are not expected to significantly alter hospital stay, resource utilization or clinical outcome.*
***Moderate**: Problems requiring adjustments, which are expected to enhance effectiveness of drug therapy producing minor reductions in patient morbidity or treatment costs.*
***Major**: Problems requiring intervention, expected to prevent or address very serious drug related problems, with a minimum estimated effect on reducing hospital stay by no less than 24 hrs.*

CONCLUSION

As the patients in medicine units have a range of diseases and are frequently prescribed with large number of drugs. Clinical pharmacy services helps in monitoring of drug therapy in this area which may benefit patients. This study had presented a pattern of findings of drug related problems identified by the clinical pharmacist, which suggests that a few types of drugs and errors constitute a substantial proportion of clinical pharmacist interventions. Knowledge of the most frequent DRPs could significantly increase the efficiency of clinical pharmacist interventions. This study demonstrates that the physician ' s acceptance rate of pharmacist intervention is high. This suggests that a joint effort between physicians and pharmacist is possible that provides a safer system, improved pharmaceutical care and better resource utilization. This study showed that the Clinical pharmacist interventions in drug therapy helped clinicians in identifying and preventing drug related problems.

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Profile of Monoamine Oxidase Activity Levels in Alcohol and Tobacco Addicted Humans

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ABSTRACT

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Monoamine oxidase (MAO) activity levels have been described to be associated with the human behavioral aspects such as depressions and other neurological problems. In present study the MAO activity in the plasma of alcohol and tobacco addicted individuals were studied to check it's effect on their MAO activity. The results obtained from above study shows that, the plasma MAO activity is less in alcohol (164.78 ± 1.93 U/ml) and tobacco addicted (193.86 ± 2.97 U/ml) individuals as compared to normal individuals (453.08 ± 2.83 U/ml). This may be happens due to the effect of alcohol and tobacco on the cofactors of enzymatic reactions.

Key words: addiction, depression, monoamine oxidase,

INTRODUCTION

Amine oxidases are ubiquitous enzymes found in both microorganisms and higher organisms. Among the various types of amine oxidase, the mitochondrial flavoenzyme monoamine oxidase (MAO, EC 1.4.3.4.) is of special interest for neuropsychiatry.[1] MAO is involved in the biodegradation of aromatic monoamines, including classical neurotransmitters such as serotonin[2], noradrenalin[3], and dopamine[4]. They appear to play a central role in several psychiatric and neurological disorders. Moreover they also function as a scavengers of various other amines e.g. tyramine, octopamine, tryptamine and also able to oxidize a wide varity of primary, secondary and tertiary amines of different chemical structure.[5] MAO is a flavin-adenine dinucleotide- containing enzyme located on the mitochondrial outer membrane[6] and in human platelets.[7] It occurs in two catalitically active forms, MAO-A found primarily in catecholaminergic neurons and MAO-B localized in serotonergic neurons and in glial cells.[8] The levels of MAO activity have been strongly related with depressive and non depressive states of human being. As a part of antidepressant treatment, the prescription of MAO inhibitors antidepressant drugs is well known.

Depression refers to a wide range of mental health problems characterized by the absence of positive effect (loss of interest and enjoyment in ordinary things and experiences), low mood and a range of associated emotional, cognitive, physical and behavioral symptoms[9] It is estimate that 21% of the world population is affected by this disorder and according to the prediction of World Health Organization; it will be the second leading cause of death by the year 2020.[10] To overcome this neurological disorder variety of antidepressant MAO inhibitors such as Amitriptyline, Clomipramine, Fluoxetine, Fluvoxamine, Tranylcypromine, and Phenelzine are currently available in the pharmaceutical market.[11] These drugs decreases the activity of MAO by inhibibiting its catalytic activity.[12] Apart from the addictions, the chewing of tobacco or drinking of alcohol has been commonly observed as a transient rescue to get rid from the depressive state or day to day tensions.

Cigarette smoking is common among persons with alcohol dependence or abuse with as many as 80% of persons who are alcohol dependent also being smokers. Not only is smoking common in persons with heavy alcohol consumption, but also nicotine dependence appears more severe in smokers with a history of alcohol dependence.[13] It is reported that the habits of alcohol consumption[14, 15] and smoking[16, 17, 18, 19] are associated with changes in catecholamine metabolism and MAO activity.

In present study the levels of MAO activity in randomly selected alcohol and tobacco addicted human volunteers has been described. An attempt has been made to correlate the MAO activity in addicted and normal human beings.

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MATERIALS AND METHODS

Benzyl amine, semicarbazide, dinitro phenyl hydrazine, was obtained from s. d. Fine Chemicals Ltd. Mumbai, DPPH (2, 2-diphenyl-1-picryl hydrazine) was procured from Sigma-Aldrich Co. (St. Louis MO, USA). The tobacco, alcohol addicted and normal volunteers were selected randomly at Nanded city (MS) in the age group of 30-50. The blood samples were collected in sample bottle with the help of registered medical practitioner.

Isolation of Platelet MAO

The isolation of platelet MAO is carried out as per the described method[20] with slight modification. Briefly 5 ml of blood sample was collected in a plastic tube containing 2 ml of 0.129 M sodium citrate as anticoagulant. Platelet rich plasma (PRP) was centrifuged at 200 g for 30 min. PRP was centrifuged at 27,000 g for 10 min. and platelet pellet was resuspended in 1 ml of 0.3 M sucrose and membranes were disrupted by repeated freezing and thawing. This extract was used as a source of MAO for further studies.

Determination of MAO activity

MAO activity measurement was performed as per the published method[21, 22] with slight modifications. In brief the reaction mixture contained 0.025 M phosphate buffer pH 7, 0.0125 M semicarbazide, 10 mM benzylamine (pH adjusted to 7), and the enzyme equivalent to 3 mg protein in a total reaction volume of 2 ml. After 30 minutes incubation at 25^0 C, 1ml of acetic acid was added and boiled for 3 min in boiling water bath followed by centrifugation. The resultant supernatant (1 ml) was mixed with equal volume of 0.05% of 2, 4-DNPH and 2.5 ml of benzene was added after 10 min incubation at room temperature. After separating the benzene layer it was mixed with equal volume of 0.1N NaOH. Alkaline layer was decanted and heated at 80^0 C for 10 min. The orange-yellow colour developed was measured at 450 nm. The enzyme activity was expressed as μM benzaldehyde semicarbazine formed/hour/3 mg protein. One unit of enzyme activity was defined as the amount of enzyme which caused an increase in absorbance of 0.001 min^{-1} at 450 nm at 25^0 C and pH 7, which corresponds to the formation of 0.01μM of product. The profile of enzyme activity in alcohol addicted, tobacco chewers and normal volunteers has been summarized in Table 1, 2, 3 respectively.

RESULTS

A random sampling study of human volunteers at Nanded city (MS) was carried out to analyze the plasma MAO activity in tobacco and alcohol addicted individuals and the same was correlated with normal individuals. The result of the present investigation Table 1-3 shows the difference of MAO activity in relation to tobacco and alcohol addictions as compared to normal individuals. The average plasma MAO activity in both alcohol (164.78 ± 1.93 U/ml) and tobacco addicted (193.86 ± 2.97 U/ml) individuals was found to be less as compared to normal volunteers (458.08 ± 2.83 U/ml).

DISCUSSION

A vast body of literature is available attributing the implications of alcohol and tobacco addictions in catecholamine metabolism and MAO activities.[14-19] It has been reported that the platelet MAO activity declines during active drinking in alcoholic patients.[23,24] Moreover the low platelet MAO activity has been considered as biochemical marker for alcoholism and decrease in MAO activity during active alcohol consumption may be concealed by a transitory increase during a certain period of withdrawal.[25] It has been suggested that the low MAO platelet activity may be a result of chronic alcohol intake and may originate from a secondary effect of alcohol on certain enzymatic cofactors such as iron and riboflavin.[26,27] This may be the possible reason for decline in MAO activity in alcohol and tobacco addicted volunteers.

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Table No 1. Profile of MAO activity (U/ml) in alcohol addicted persons

Sr.No.	Sample code	MAO activity in U/ml
1	AA1	112 ± 8.08
2	AA2	200 ± 9.16
3	AA3	146 ± 9.07
4	AA4	168 ± 9.07
5	AA5	168 ± 7.50
6	AA6	149 ± 4.50
7	AA7	187 ± 6.24
8	AA8	170 ± 6.02
9	AA9	149 ± 6.11
10	AA10	165 ± 5.00
11	AA11	171 ± 3.51
12	AA12	206 ± 5.68
13	AA13	159 ± 6.00
14	AA14	180 ± 5.56
15	AA15	175 ± 4.58
16	AA16	164 ± 4.50
17	AA17	153 ± 5.29
18	AA18	141 ±3.60
19	AA19	175 ± 4.50
20	AA20	152 ± 6.00
21	Average Activity	164.78 ± 1.93

The results shown here are the mean values of n=3 ± S.D. AA = alcohol addicted persons.

Table No 2. Profile of MAO activity (U/ml) in tobacco addicted persons

Sr.No.	Sample code	MAO activity in U/ml
1	TA1	69 ± 4.04
2	TA2	162 ± 4.72
3	TA3	253 ± 3.57
4	TA4	235 ± 5.03
5	TA5	214 ± 3.60
6	TA6	223 ± 5.13
7	TA7	184 ± 4.04
8	TA8	205 ± 5.00
9	TA9	234 ± 4.00
10	TA10	211 ± 6.00
11	TA11	176 ± 5.29
12	TA12	101 ± 4.58
13	TA13	165 ± 5.13
14	TA14	233 ± 5.00
15	TA15	164 ± 4.04
16	TA16	244 ± 3.05
17	TA17	219 ± 4.04
18	TA18	202 ± 4.50
19	TA19	163 ± 5.68
20	TA20	215 ± 5.03
21	Average Activity	193.86 ± 2.97

The results summarized are the mean values of n=3 ± S.D. TA = tobacco addicted persons,

Table No 3. Profile of MAO activity (U/ml) in Normal persons

Sr.No.	Sample code	MAO activity in U/ml
1	NL1	444 ± 4.58
2	NL2	505 ± 5.00
3	NL3	555 ± 4.50
4	NL4	457 ± 5.85
5	NL5	304 ± 4.50
6	NL6	510 ± 6.50
7	NL7	496 ± 4.72
8	NL8	520 ± 4.35
9	NL9	355 ± 4.50
10	NL10	368 ± 4.16
11	NL11	426 ± 4.16 .
12	NL12	508 ± 4.50
13	NL13	487 ± 4.00
14	NL14	512 ± 3.51
15	NL15	523 ± 4.04
16	NL16	430 ± 6.02
17	NL17	368 ± 3.60
18	NL18	546 ± 5.00
19	NL19	311 ± 4.50
20	NL20	492 ± 4.50
21	Average Activity	458.08 ± 2.83

The results obtained here are the mean values of n=3 ± S.D. NL = normal persons,

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A Study on Quality of Life of Patients with Congestive Cardiac Failure

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ABSTRACT

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Quality of life (QOL) is a reflection of a person's mental and physical well-being in their everyday life. Quality of life is an "individual perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards and concerns . The study was aimed to assess and quantify the impact of patient counseling on Quality of life, medication knowledge and compliance of heart failure patients. QOL was assessed using Minnesota living with heart failure questionnaire (MLWHQ). 50 patients seen for the first time at the unit were evaluated. We analyzed the relationship between the questionnaire score and physiological variables such as age, gender, duration of disease, number of drugs and ejection fraction. Medication knowledge was assessed by giving score during interaction with patient and compliance was assessed by pill count. Finally, the patients were counseled and followed. A significant difference in QOL score (P< 0.001) and medication knowledge score (P < 0.001) was obtained compared to baseline. Most patients (78%) are complied with prescribed regimen. To sum up, patient counseling aided better understanding of their illness and role medications in its treatment and contributed to the development of a patient-led health-related Quality of life.

Key words: Quality of life, patient counseling, Heart failure, medication knowledge, compliance.

INTRODUCTION

Recently the focus of medical care has shifted towards management of chronic diseases, with the aim of optimizing quantity and quality of life. [1-3] Quality of life is a reflection of a person's mental and physical well-being in their everyday life.[4]The main clinical symptoms in Congestive Cardiac Failure (CCF) are dyspnoea, tiredness and fatigue, which affect quality of life through their limiting effect on physical functioning,[5] but may also give rise to psychological problems, adverse treatment effects and social limitations.[3,6]These factors may lead to individuals withdrawing from activities and social contact, and consequently experiencing a loss of social relationships and social support. [7]Increasing severity of CCF leads to the individual being aware of their own mortality, which contributes to depression, sleep disturbances and anxiety. [6]Personal relationships, eating, sexual activity and the ability to work are all limited while paralleled by an increasing dependence on others.[6] The prevalence of CCF in India was 18.8 million per year (1.76%) of the total population and the incidence was 1.57 million per year (0.15%).[8] According to W.H.O, QOL is defined as "an individual perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns." [9]

QOL information is important to pharmacists in three ways: [10]

1. QOL outcomes are increasingly being used to evaluate drugs in clinical trials.

2. QOL data can also be used to evaluate provider performance. Performance of health care providers is evaluated based on heath out comes achieved.

3. QOL assessment could be a useful tool for monitoring the progress of patients receiving drug therapy. Improvement in QOL may be the main goal of treatment in patients with some diseases like Rheumatoid Arthritis, CCF. In these diseases, the therapeutic goal is to avoid impairment in QOL caused by the adverse effects of the drugs, not only because of the distress this impairment causes but also because it may result in Non-Compliance.

Recognizing the usefulness of QOL information, the National Institute of health has included QOL assessments in large scale clinical trials evaluating the treatment of Cardio

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Vascular System diseases, Diabetes Mellitus, and QOL assessment in clinical practice.[10]

QOL assessment has possible application in clinical practice: [9]

1. To identify unexpected health related problems.
2. To monitor disease progression or response to therapy.
3. To enhance provider- patient communications.

Measuring QOL:

There are hundreds of health related quality of life instruments. A primary distinction among quality of life instruments is whether they are generic or specific.

1. **Generic Instruments:** [11-12]

Generic QOL instruments are designed to be applicable across all diseases or conditions, across different medical intervention and across a wide variety of populations. For instance, Nottingham Health Profile**,** Quality of Well Being Scale.

2. **Specific Instruments** [11-12]

Specific instruments are intended to provide greater detail concerning particular outcomes, in turns or functioning, uniquely associated with a condition or its treatment. For example Disease specific (Eg; Diabetes Mellitus), Population Specific (Fairly elderly).

QUALITY OF LIFE IN CCF

An important goal of medical therapy for patients with heart failure is to improve how patients feel and function during daily activities. The effect of treatments on a patient's life style or QOL is critical to the evaluation of medication for chronic heart failure management of patients with CCF aims not only to increase survival but also to improve QOL. [10]

QOL was assessed by Minnesota living with heart failure questionnaire. The living with heart failure questionnaire is a patient self assessment measure being developed to evaluate therapeutic response to interventions for heart failure. [13]

Minnesota living with heart failure questionnaire contains 21 questions focusing on the patients' perception of the effect of heart failure on their lives. These include questions regarding psychological, emotional, social and economical limitations. The patients selected a number from o to 5 as the response to each question, 0-indicates that heart failure had no effect and 5- indicates a very large effect. Therefore a high score indicates poor QOL. [13]

Counseling helps the patient to take the medication in a manner that is most likely to achieve the desired therapeutic response. Appropriate advice, and counseling by the pharmacist will make the patient understand better about their medication which have become potent and toxic with the advancement of science this will in turn increase patient compliance, which can otherwise result in inappropriate or inadequate use of drugs. [14-17]

Medication knowledge and adherence: [18]

Patients do not always understand prescription instructions and may forget considerable portions of what clinicians tell them. It is well recognized that many patients have a poor understanding of the terminology that is often used by doctors in communicating details about their illness, and many patients have little or no understanding of the details of their medication regimen. Patient compliance or adherence may be defined as the extent to which a patient takes or uses medication in accordance with the medical or health advice given.

The objective of the study is to assess and quantify the effect of patient counseling on Quality of Life of patients with congestive cardiac failure

METHODOLOGY

The Prospective Interventional Study was carried at Rajah Muthiah Medical College Hospital, Chidambaram, Tamil Nadu, between November 2009 to April 2010. Patient who shall satisfy the inclusion criteria were enrolled in the study for collection of base line data and details about their prescription. Patients were then assessed for their Quality Of Life and medication knowledge and compliance.

Quality of life:

Patients answered the 21 items using a 6-point response scale (0-5). The total summary score (Global Score) can vary from 0 to 105; a lower score reflects better QOL. Three subscale scores (dimensions) reflect physical (questions 2, 3, 4, 5, 6, 7, 12 and 13) and emotional (questions 17, 18, 19, 20 and 21) impairment and the other items are related to financial, medication side-effects, and lifestyle considerations (overall dimensions). [13, 19-22]Score is obtained by summating response to all 21 questionnaires.

Medication Knowledge

Patients answered the questions; for grading, knowledge regarding each aspect of this response was expected to each question. Each response is assigned a particular score and

then finally the scores were added to get total score of the patient. High score indicates good medication knowledge & low score indicates poor medication knowledge.

Compliance Assessment (Self assessment)

Self assessment form contains a grading scale of compliance with this form patients will grade their compliance according to their perception, Never followed prescribed regimen, Sometimes follow prescribed regimen, Compliant half of the time, Compliant most of the time, Compliant all the time.It also contains factors which effect patient compliance, Forget fullness, confusion, Apathy, health beliefs, Dissatisfaction, cost of medication, others.

Patient Counseling

Patient in the study group were counseled. The session last 5-10 min. counseling was given bilingually (both in Tamil & English). Information was tailored according to the understandings of the patients. Follow up of patient was carried out during their successive monthly appointments. The patients were followed at a period of 30 d, 60 d, and 90 d intervals.

All the data available were tabulated and they were analyzed. Statistical Analysis of data was done using student't' test and ANOVA.

RESULTS

A total of 55 patients were enrolled in the study. In these 55 patients complete data of only 50 patients were available for analysis for QOL, medication knowledge and compliance. Remaining 5 patients could not be followed within study period.

Baseline Characters of Patients

Out of 50 patients included in the study 45 (90%) patients were males and 5 (10%) patients were females. (Table -1, Figure-1)

Out of 50 patients included in the study patients age ≤ 45 are 8 (16%), 46-55 are 16 (32%), and 56-65 are19 (38%) and >66 are 7 (14%). (Table -1, Figure-2)

Out of 50 patients included in the study were taking ≤2 drugs are 8 (16%), 3 drugs are 31 (62%) and ≥4 drugs are 11 (22%). (Table -1, Figure-3)

Out of 50 patients included in the study ejection fraction ≤20 was 4 (8%), 21-30 was 19 (38%), 31-40 was 15 (30%) and ≥41 was 12 (24%). (Table -1, Figure-4)

Out of 50 patients included in the study duration of disease 0.5-3 years was 23(46%), 4-7 years was 14(28%), and ≥ 8 years was 13 (26%). (Table -1, Figure-5)

Out of 50 patients included in the study 5 (10%) patients belonged to NYHA classification II, 10 (20%) patients belonged to NYHA classification III and 35 (70%), patients belonged to NYHA classification IV. (Table -1, Figure-6)

Other than congestive cardiac failure, 8(16%) patients had COPD, 31(62%) had Hypertension, 28(56%) had diabetes mellitus, 19(38%) Ischemic heart disease 8(16%) had hyperlipidaemia, 13(26%) had Myocardial Infarction, 13(26%) had other co-morbidities. (Table -2, Figure-7)

Quality Of Life: (Table -3, Figure-8)

Mean scores for QOL at end of the study of was 23.86 ± 10.03 compared to 34.3 ± 13.52 of baseline

Effect of Gender on Quality of Life: (Table -4, Figure-9)

For males' baseline QOL was 34 ± 13.55 and final score was 24.29 ± 10.35.

For females' baseline QOL is 33.8 ± 14.86 and final score was 20.4 ± 5.89.

Effect of Age on Quality of Life: (Table -5, Figure-10)

For age group ≤ 45 years the baseline QOL was 27.63 ± 9.85 and the final score was 19.5 ± 9.78.

For age group 46-55 years the baseline QOL was 34.06 ± 16.71 and the final score was 22.19 ± 10.95

For age group 56-65 years the baseline QOL was 38.16 ± 12.22 and the final score was 27.59 ± 9.78.

For age group > 66 years the baseline QOL was 32 ± 11.09 and the final score was 22.5 ± 6.65.

Effect of Number of Drugs on Quality of Life: (Table -6, Figure-11)

For patients taking ≤ 2 drugs the baseline score was 26.38 ± 12.21 and the final score was 20.25 ± 10.48.

For patients taking 3 drugs the baseline score was 34 ±12.58 and the final score was 23.23±9.18.

For patients taking ≥ 4 drugs the baseline score was 40.91 ± 14.78 and the final score was 28.27± 11.39.

Effect of Duration of Disease on Quality of Life: (Table -7, Figure-12)

For patients with duration disease of 0.5 – 3 years the baseline score was 29.5±13.69 and the final score was 21.86± 10.96.

For patients with duration disease of 4-7 years the baseline score was 38.67±10.22 and the final score was 24.87± 7.47

For patients with duration disease of ≥ 8 years the baseline score was 37.69±14.89and the final score was 26.62±11.25.

Medication Knowledge: (Table -8, Figure-13)

Mean score of medication knowledge at the end of the study was 15.82± 2.17 compare to 9.3± 3.06 at baseline.

Medication compliance:

Out of the 50 patients included in the study, 39 (78%) were compliant with prescribed regimen all the time and 11 (22%) were compliant most of the time. (Table -13, Figure-18).

The reasons cited for non compliance by the patients are 5(10%) forgetfulness, 1 (2%) confusion, 1(2%) dissatisfaction, 1(2%) could not afford the cost of the medication and 3(6%) others as their reasons for non adherence. (Table -15, Figure-20)

DISCUSSION:

Patient counseling is an integral part of Clinical Pharmacy activities, since it provides an opportunity for Pharmacist to interact with patient and establish a continuing relationship with patients.

An attempt has been made to carry out the work to the best of the ability of the department and persons involved. The results were classified under following broad categories:

1. Baseline characteristics.
2. Quality of life.
3. Medication Knowledge.
4. Medication Compliance.

Baseline characteristics:

Out of the 50 patients enrolled in the study, males exceeded females in number. Generally in this population studied male used to come regularly for check up, thus resulting in more male patients in the study.

The number of patients in the age group of 56-65 and 46-55 were nearly equal. The number of patients in age group 45years and 66 were nearly equal because this age group were the most affected by the disease condition which are focused in this study and actively utilizing the health care system.

The number of patients taking 3 drug were leading over the number of patients taking 2 and 4 groups. Most of the patients were on 3 drug therapy. Patients with duration of disease of 3 years and less dominated other groups of 4-7years and 8years or above. Newly diagnosed patients tend to remain with the healthcare system and as the time progresses dropout increases due to increased dependency on others, this resulted in more number of patients in 3year group.

Patients with Ejection fraction of 21% - 30% dominated others.

The number of patients in NYHA class-4 dominated over classes 2 and 3.

Quality Of Life

Quality of life can be influenced by various factors such as gender, age, number of drugs consumed, and duration of disease. While studying the effect of Quality of life each of the mentioned factors was taken into consideration and its influence was analyzed separately.

In a study conducted by Mendez.GF et al 2007. [22] QOL was measured by the Minnesota Living with Heart Failure Questionnaire (MLHFQ). MLHFQ score was compared between basal vs 6 months follow-up. The MLHFQ had a significant reduction with basal condition from the first evaluation. Similarly in our study the mean score in the first, second and third follow up were significant compared to baseline ($P<0.1$, $P<0.01$, $P<0.001$).

Quality of life was higher in females to males, but difference was not significant.

In the third follow up there was a significant difference between the quality of life score of different age groups. Significant difference was observed between the quality life scores of patients in the age group 45 and the group 56-65($P<0.05$).

A significant difference was observed between the quality of life scores of patients with duration of disease 0.5- 3years and patients with duration of disease 8years ($P<0.01$).

MEDICATION KNOWLEDGE:

The mean medication knowledge scores in the first, second and third follow up were significant compared to baseline

($P<0.1$, $P<0.01$, $P<0.01$).

COMPLIANCE:

In this study 78% patients rated themselves as always complaint. 22% patients rated themselves non- compliant. At the end of the study more number of patients was found to be complaint when compared to baseline. In a study conducted by Vitalina Rhozen et al. [23] they used self assessment for assessing the compliance. Most patients in their study rated themselves as always compliant. Similarly in our study also most of the patients rated themselves as always complaint.

Only a small percentage of have disclosed their non-compliance. The reasons given by the patients for their non-compliance was forgetfulness, confusion, dissatisfaction, cost of the medication and others like lack of medical stores, out of station and side effects.

Counseling the patient has to address all these issues and develop suitable strategies to overcome these obstacles. For instance, providing medication remainders, switching to less costly medication with the cooperation of the prescriber, asking the patients to refill before medications go stock out and modifying the regimen if the patient had side effects.

CONCLUSION:

In conclusion, patient counseling aided better patient understanding of their illness and the role of medications in it' s treatment, improved medication adherence, and contributed to the development of a patient-led health-related Quality of life.Moreover, a good professional rapport has been build between Pharmacist and patients. The counseling service provided by clinical pharmacist was found to be useful and beneficial to the patients of the hospital where the study was carried out. Finally, it is believed that pharmacist and other health care professionals would appreciate the role of pharmacist in counseling and educating the patients and an attempt to extend their services to include patient counseling as one of their service.

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TABLE 1 Baseline data of patients

Factors	No. of Patients
Gender	45 (90%)
Male	5 (10%)
Age	
≤ 45	8 (16%)
46-45	16 (32%)
56-65	19 (38%)
> 66	7 (14%)
No. of drugs	
≤ 2	8 (16%)
3	31 (62%)
≥ 4	11 (22%)
Ejection fraction	
≤ 20	4 (46%)
21-30	19 (38%)
31-40	15 (30%)
≥ 41	12 (24%)
Duration of disease	
0.5-3 Y	23 (46%)
4-7 Y	14 (28%)
≥ 8 Y	13 (26%)
NYHA Classification	
II	5 (16%)
III	16 (20%)
IV	35 (70%)

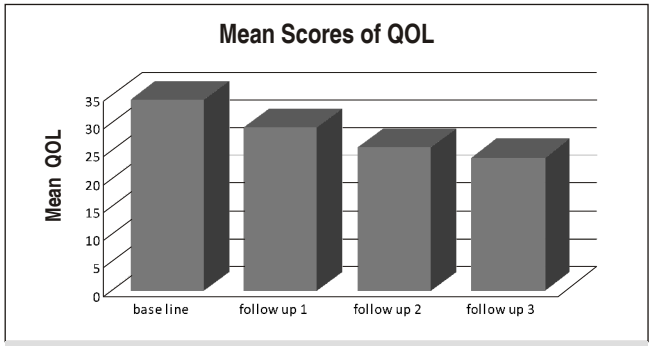
TABLE 2 Means Score of QCL

No of patients	Base line	Follow up 1	Follow up 2	Follow op 3
50	34.3 ± 13.52	29.32 ± 11.42 (a)	25.78 ± 11.06 (b)	23.86 ±10.03 (c)

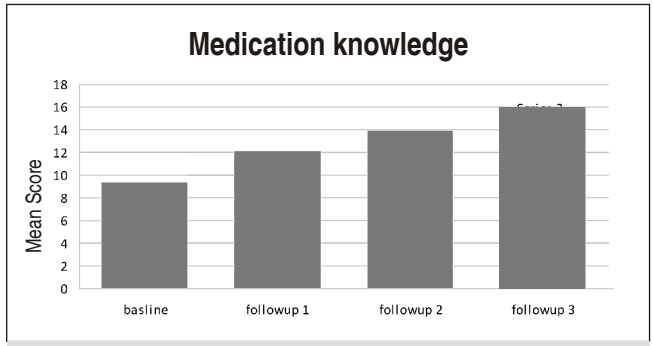
TABLE 3 Effect of age on QOL score				
Age (Years)	**Base line**	**Follow up 1**	**Follow up 2**	**Follow op 3**
≤ 45	27.63 ± 9.85	25.13 ± 10.02	21.38 ± 9.56	19.5 ± 9.78
46-55	34.06 ± 16.71	27.44 ± 17.11	25.50 ± 12.61	22.19 ± 10.95
56-65	38.16 ± 12.22	33.21 ± 10.88	30.89 ± 10.92	27.59 ± 9.78 (a)
≥66	32.00 ± 11.09	27.86 ± 08.91	25.00 ± 08.60	22.05 ± 06.65
a= P< 0.05				

TABLE 4 Mean score for medication knowledge				
No. of Patient	**Base line**	**Follow up 1**	**Follow up 2**	**Follow op 3**
50 9.3 ± 3.07	12.08 ± 3.21(a)	13.92 ± 2.87(b)	15.85 ± 2.17(c)	
a, b and c are significant at P< 0.1, P<0.01, P<0.001 compared to the base line.				

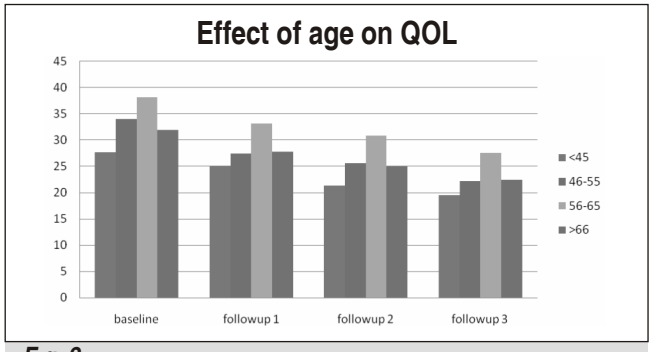
TABLE 5 Self assessment of Compliance		
Rating	Base line	Final follow up
Never compliant	—	—
Sometimes compliant	—	—
Compliant half of the time	—	—
Most of the times compliant	18 (36 %)	11 (22 %)
Compliant all the time	32 (64 %)	39 (78 %)



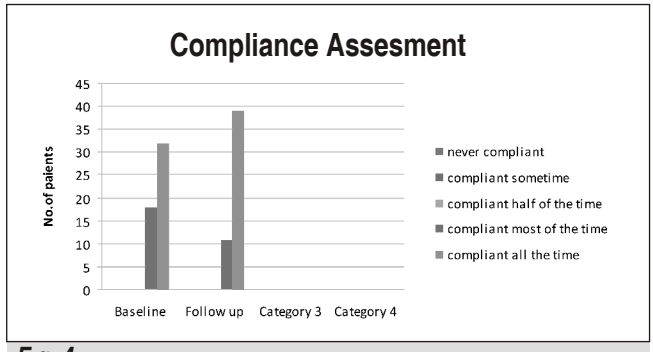
F g. 1: *a , b and c are significant at p< 0.1, p<0.01 and p< 0.001 respectively to the base line.*



F g. 3



F g. 2



F g. 4

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Dietry and lifestyle effect on Hypertension.

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ABSTRACT

Dietary and life style modification plays a crucial role in both patients who are suffering from hypertension, as well as those who are in healthy states. Weight loss by diet can reduce BP, for instance, restriction in salt intake by avoiding excessive amount of salt in food and in cooking. Other restriction are also taken into consideration during person suffering from hypertension like moderate alcohol consumption (1-2 drinks per days) while on other hand increase in potassium intake can be effective against lowering of BP by taking rich diet in fruits, vegetable and beans. Vegetarian diet also shows beneficial impacts against BP. Physical exercises play an important role in reducing BP (yoga and medication). Thus by adopting these restriction and implementations of such type of non pharmaceutical methods the BP and heart disorders can be effectively controlled.

Key-words: Lifestyle modifications, Hypertension, patient compliance.

INTRODUCTION

Hypertension is well established as a cardio vascular risk factor. A major part of population may ignore this condition and suffers a lot. The only an important factor which can prevent hypertension is to implementation of non pharmacological measures such as, diet, life style changes. Non pharmacological measures are also important due to increasing cost of anti hypertensive drugs. Hypertension is a disease of complex etiology; affecting 972 million people worldwide. It is estimated that the worldwide prevalence of hypertension would increase from 26.4% in 2000 to 29.2% in 2025.[1] Hypertension is an important risk factor for cardiovascular disease and has become a major global burden on public health. Worldwide, 7.1 million deaths (approximately 12.8% of the global total) were estimated to be due to non-optimal blood pressure.[2] The world health organization has suggested that sub optimal treatment of hypertension represents the number one risk for death in the world.[3] The Seventh report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure (JNC-7) defines hypertension as a Systolic Blood Pressure greater than 140 mmHg or a Diastolic Blood Pressure greater than 90 mm Hg.[4] Essential hypertension is commonly known as Hypertension. In most cases, elevated blood pressure is associated with an overall increase in resistance to flow of blood through arterioles, while cardiac output is usually normal. Meticulous investigation of autonomic nervous system function, baroreceptor reflexes, the renin-angiotensin-aldosterone system (RAAS) and the kidney has failed to identify a primary abnormality as the cause of increased peripheral vascular resistance in essential hypertension.[5] Secondary hypertension can be of two types, Remediable Hypertension- It is usually caused by renal disease, adrenal disease, coarctation of the aorta, or another rare condition. Drug induced hypertension-Certain drugs like oral contraceptives, NASIADS, etc, Natural products like Ma-huang, Nicotine, Ketamine etc and chemical elements like Lead and Mercury may also cause elevation in blood pressure.[5]

Role of the vascular endothelium and Regulation of blood pressure

The vascular endothelium is presently considered a vital organ, where synthesis of various vasodilating and constricting mediators occurs. Numerous hormonal, humeral vasoactive and growth and regulating peptides are produced in the vascular endothelium. These mediators include angiotensin II, bradykinin, endothelin, nitric oxide and several other growth factors. Endothelin is a potent vasoconstrictor and growth factor, dysfunction of which has been implicated in human essential hypertension.[6]

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Angiotensin II is a potent vasoconstrictor synthesized from angiotensin I with the help of an angiotensin-converting enzyme (ACE). Peripheral vascular resistance is dependent upon the sympathetic nervous system, humoral factors and local autoregulation.[6] The sympathetic nervous system produces its effects via the vasoconstrictor alpha effect or the vasodilator beta effect. The humoral actions on peripheral resistance are also mediated by other mediators such as vasoconstrictors (angiotensin and catecholamines) or vasodilators (prostaglandins and kinins). Autoregulation of blood pressure occurs by way of intravascular volume contraction and expansion, as well as by transfer of transcapillary fluid. Interactions between cardiac output and peripheral resistance are autoregulated to maintain a set blood pressure in an individual.[7] The pathogenesis of essential hypertension is multifactorial and highly complex. Multiple factors modulate the blood pressure for adequate tissue perfusion and include humoral mediators, vascular reactivity, circulating blood volume, vascular caliber, blood viscosity, cardiac output, blood vessel elasticity and neural stimulation.[7] The chronic phase of essential hypertension characteristically has normal or reduced cardiac output and elevated systemic vascular resistance.[7] Hypertension is likely to be related to multiple genes. Hypertension develops secondary to multiple environmental factors, as well as to several genes, whose inheritance appears to be complex. Very rare secondary causes are related to single genes.[7] Hypertension typically has no symptoms that is why it is known as silent killer. In majority of patients the only sign is substantially increased blood pressure. However, careful examination of retina of eye may reveal various abnormalities which are known as Keith-wagener retinal changes. If a person has high blood pressure that is severe or longstanding and left untreated, symptoms such as headache, fatigue, nausea, vomiting, shortness of breath, restlessness and blurred vision can occur as a result of damage to the brain, eyes, heart and kidneys. In rare cases, high blood pressure may cause brain swelling, which can lead to drowsiness and coma[8]. Routine Investigations of hypertensive patient should includes, chest X-Ray, ECG, echocardiography, urinalysis, fasting blood lipids and urea creatinine and blood electrolytes levels.[8]

Diagnosis of hypertension is generally on the basis of a persistently high blood pressure. Usually this requires three separate measurements atleast one week apart. Measurements in control of hypertension should be atleast 1 hour after caffeine, 30 minutes after smoking or strenuous exercise and without any stress. The person taking the measurement should be careful to inflate the cuff suitably above anticipated systolic pressure. The person should inflate the cuff to 200 mmHg and then slowly release the air while palpating the radial pulse. After one minute, the cuff should be reinflated to 30 mmHg higher than the pressure at which the radial pulse was no longer palpable. A stethoscope should be placed lightly over the brachial artery. The cuff should be at the level of the heart and the cuff should be deflated at a rate of 2 to 3 mmHg/s. Systolic pressure is the pressure reading at the onset of the sounds described by Korotkoff (Phase one). Diastolic pressure is then recorded as the pressure at which the sounds disappear (K5) or sometimes the K4 point, where the sound is abruptly muffled. Two measurements should be made at least 5 minutes apart and, if there is a discrepancy of more than 5 mmHg, a third reading should be done. The readings should then be averaged. An initial measurement should include both arms.[9]

Goals of Hypertension Treatment

The primary goal of treatment of the hypertensive patient is to achieve the maximum reduction in the long-term total risk of cardiovascular morbidity and mortality. This requires treatment of all the reversible risk factors identified, including smoking, dyslipidaemia or diabetes and the appropriate management of associated clinical conditions, as well as treatment of the raised blood pressure.[10] Hypertension is usually present for many years before its complications develop. The idea, therefore, is to treat hypertension early, before it damages important organs in the body. Accordingly, increased public awareness and screening programs to detect early, uncomplicated hypertension are the keys to successful treatment of high blood pressure. By treating high blood pressure successfully early enough, the risk of stroke, heart attack and kidney failure can be reduced.[11]

Lifestyle Modifications

Lifestyle modifications are generally beneficial in reducing a variety of CVD risk factors (including high BP) and promoting good health and should therefore be used in all hypertensive patients, either as definitive treatment or as an adjunct to drug therapy[12]. A reasonable generalized approach for all patients includes weight loss for the overweight patients, regular physical activity, alcohol cessation or moderate intake, dietary modification to reduce sodium and fat and increase calcium, potassium, magnesium, vitamins and fiber from food sources; and cessation of smoking[12]. Following Points should be considered while starting treatment for hypertension. Blood pressure that is persistently

higher than 140/ 90 mm Hg usually is treated with lifestyle modifications and medication. If the diastolic pressure remains at a borderline level (usually under 90 mm Hg, yet persistently above 85) then more aggressive treatment also may be started in certain circumstances. [13] The choice of drugs will be influenced by many factors, like previous experience of the patient with antihypertensive agents, cost of drugs, risk profile, presence or absence of target organ damage, clinical cardiovascular or renal diseases or diabetes and patient's preference.

Quality of life (QOL)

Quality of life is generally considered a multidimensional construct that includes physical, mental and social functioning, as well as perceptions of general well-being. Nowadays, QOL can be measured objectively with questionnaires (instruments) possessing sufficient sensitivity to change, reliability and validity properties.[14] It has been a fundamental research topic in health, as its results are important to assess the effectiveness of care as well as to obtain social and health funding.[15]

mRole of pharmacist in pharmaceutical care of hypertension.

Involvement by the pharmacist in the Pharmaceutical care for essential hypertension patients has been shown to have a consistently positive impact on both community pharmacy [16] and organized health care settings [17]. In these trials, involvement by pharmacist has been shown to bring about improved compliance, improved BP control, improved patient understanding of hypertension and improved satisfaction with care. The JNC-7 Guidelines strongly recommend the use of a multidisciplinary approach to the hypertensive patients, with the pharmacist as the integral part of the team of care. Hypertension remains a largely untapped area for pharmacist participation in collaborative drug therapy management to optimize control of BP in a vast patient population.

CONCLUSION

Dietary and life style modification highly influenced hypertensive condition for better prevention of hypertension. It is also important in reduction of BP in large population and reduction of various cardiac disorders. This targets can be achieved only by nurse based health care settings and proper monitoring for patient compliance.

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Cutaneous Reactions due to Antibacterials Drug (Fluoroquinolone Derivative)

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ABSTRACT

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A 27-year old woman received Ciprofloxacin + tinidazole 500mg for 5 days. In addition to that pantoprazole tablet 40mg was prescribed for lacrimation (excessive), Uterine infection, Fever, and rigors . on day 6 rash was the commonest ADR of ciprofloxacin and was graded according to standard guidelines. Stevens Johnson's syndrome was observed in the case. This article outlines the adverse reactions of ciprofloxacin observed in patients. It may be concluded that the clinical patterns and the drugs causing ADR are remarkably similar to those observed in other countries except for minor variations.

Keywords : Adverse drug reaction; Rashes; Ciprofloxacin.

INTRODUCTION

Cutaneous drug reaction, characterized by skin lesions, pruritus, hypersensitivity are the most prominently occur in ADRs. Acute lesions appear as round or oval, sharply marginated erythmatous plaques that sometimes develop central bullae . The lesions are usually found on the lips and genitalia, although any skin or mucosal surface may be involved.[1,2] The eruption usually occurs within hours of administration of the offending agent and resolves spontaneously without scarring after few weeks of onset, usually with residual post-inflammatory pigmentation.[3] Most common "cutaneous adverse drug reaction" (CADRs) producing drugs are Ciprofloxacin, Carbamazepine, dapsone, isoniazid, clindamycin, diclofenac, rifampicin and zidovudine.[4]

CASE REPORT

A 27-year old female was admitted in the hospital with pruritic skin rashes, fever, vomiting,dysphagia, loss of appetite, episodic pain, and swelling of lips . The patient had a medical history of lacrimation (excessive), uterine infection, fever, and rigors since 5 days and she was started on the standard dosing regimen of ciprofloxacin with tinidazole followed by pantoprazole tablet for 5 days. On examination drug induced mucoscitis with febrile and tachycardia. She had diffuse erythema all over the body [Figure 1,2,3]. Crusting of lips, edema of hand and feet. Skin and mucous membrane are very common sites involved in any adverse drug reaction ranging form mild skin rash to Steven-Johnson's syndrome. Lab investigations revealed elevated WBC count and ESR. The patient's condition improved with systemic steroids and supportive medications.

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DISCUSSION

The various types of cutaneous ADR, maculopapular rash was the commonest seen in patients, as reported earlier.[5,6] The most common cause of muculopapular rash was due to anticonvulsants mainly the phenytoin followed by antimicrobial and NSAIDs drugs.[7] Recently ciprofloxacin has emerged as one of the important causes fixed drug eruptions. (FDE)[8] In consonance with the earlier reports, antibacterials were the main group of drugs causing different types of drugs skin reactions in our series. Ciprofloxacin drugs caused rashes in female patient. It may be concluded that the clinical patterns and the drugs causing ADR are remarkably similar to those observed in other countries except for minor variations.

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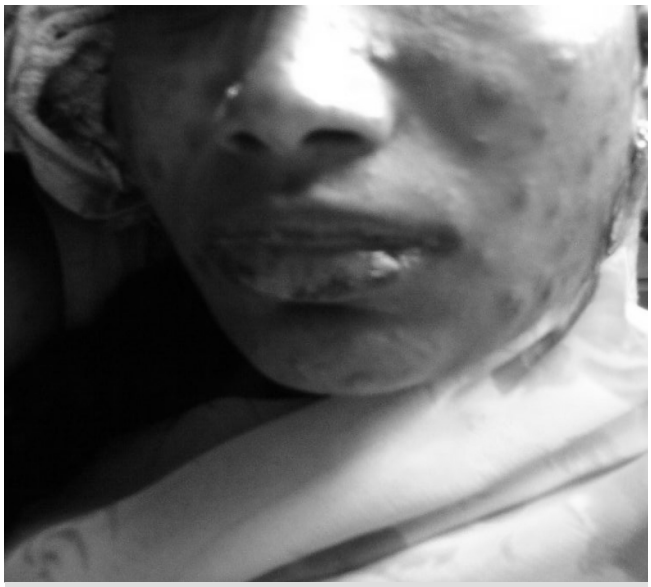

Fig.1: Swelling of lips

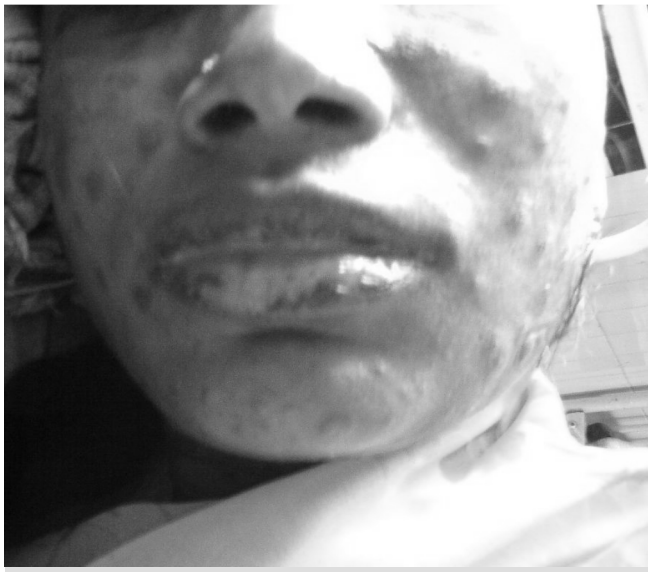

Fig .2: Fixed drug eruption on Facial

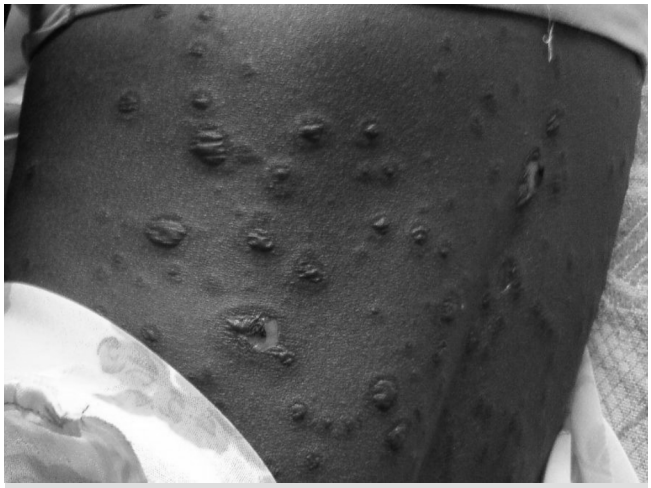

Fig. 3: Skin rashes over lumbar region

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