

Comparison of quality of life and improvement in B.P and blood glucose values of patients using branded generic and generic medicines for hypertensive and diabetes treatment

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Abstract

In India most of the drugs are generics only. But these drugs are supplied with the respective company's brand names and are thus termed as branded generics. There is no practical difference between branded generics and generics. But a difference exists at the marketing level where the generics are obtained by the retailer at a lower "price to the retailer" and there could be a difference in the way healthcare professionals perceive branded generics and generics. This work consists of a comparison of therapeutic efficacy of branded generics and generics of drugs used by B.P patients and patients having B.P and diabetes by comparing their health related quality of life (HRQOL) levels and their B.P levels and blood glucose levels, before and after treatment. The hypothesis behind the work is that if there is a significant difference between the therapeutic efficacy of branded generics and generics then there should be a significant difference between the HRQOL levels and improvements in B.P levels and blood glucose levels of the patients who are using them over a long period. This work is a study of HRQOL levels as determined by SF-36 questionnaire and B.P levels and blood glucose levels as ascertained from the case sheets of patients. Statistical analysis revealed that there is no significant difference between the branded generics and generics with respect to HRQOL values or reduction in the percentage of patients from high B.P levels to low B.P levels and from high blood glucose levels to low blood glucose levels. It was concluded that there is no difference between the therapeutic efficacy of branded generic drugs and generic drugs. It is suggested that the Drugs and Cosmetics Act 1940 be amended to differentiate between generic and branded generic products and to make it compulsory for the companies to keep a lower maximum retail price (MRP) on the labels of the generic products.

Key words: HRQOL, SF-36, hypertension (B.P.), hypertension and diabetes, Branded generics (BG), Generics (G), Maximum retail price (MRP)

INTRODUCTION

Public health is a very important issue in India which is a developing country. The Global Competitiveness Report 2008-2009¹, given by the World Economic Forum ranked India 50th among 134 countries in Global Competitive Index and 100 among 134 countries in health and primary education. Thus healthcare field is one of the areas where India is performing in a poor manner and this field needs research done in a scientific manner. Generic drugs play a very important role in health care. While there are a number of articles on generic drugs (G) vs. branded generic (BG) drugs, the scientific research on BGs and Gs is mostly confined to pharmacokinetic comparison. Cost of pharmaceuticals contributes significantly to

health care expenditure and it can be definitely brought down by the increased use of generics. Almost all Indian drugs are branded generics and all of them must be inexpensive in comparison to their brands. Though it is a fact that Indian drugs are very inexpensive when seen from an international perspective the fact remains that they can be still more inexpensive. Countries such as USA, UK, Canada, Sweden, Australia and Netherlands are taking steps to ensure that their peoples have access to generics that are bioequivalent to the brands but are priced low². In India the Drugs Price Control Order 1995 does not distinguish between generics and branded generics and hence the MRPs (Maximum Retail Price) on both varieties are usually same. So there is no benefit to the patient when he purchases a generic drug. Research was carried out in our laboratories on the bioequivalence of four marketed branded generic products of sparfloxacin³ and on the bioequivalence of a generic

product and three branded generic products of amoxicillin⁴. It was found that four different BGs of sparfloracin were bioequivalent and that the four products of amoxycillin were bio-in-equivalent. But results showed that it was one of the BGs that was inequivalent. The other three amoxicillin products, including the generic amoxycillin were bioequivalent. If a study can be undertaken to ascertain the equality or inequality between generics and branded generics it will be useful to the policy makers in India, to the prescribers and to the patients in India. In the correct sense of the word "generic" all the products being compared are generic. So this may also be named as an investigation into the appropriateness of interchangeability of generics. The objective of the present work is to investigate and to find out whether, between generics and branded generics there is any difference in clinical effect as ascertained by improvement in B.P values, reduction in blood glucose values and by health related quality of life (HQOL) values which are determined by a questionnaire (SF-36).

MATERIALS AND METHODS

This research project was started with the null hypothesis that the difference observed, if any, between generic drugs and branded generic drugs is only due to chance and is not significant and was taken up as a one tailed study. For the purpose of comparison drugs for hypertension only and drugs for hypertension and diabetes were selected. The work was pursued in the following manner.

Ethics committee approval was obtained to interview patients taking generic drugs and branded generic drugs for B.P and diabetes or only for B.P. Patients were differentiated as branded generics users and generics users. The chosen instrument for study of HRQOL is SF-36 whose copy right is owned by Quality Metric. License was obtained from Quality Metric after payment of relevant fee for SF-36, its Telugu version, and its scoring manual

Hypothesis:

There is no significant difference between the HRQOL values or improvement in B.P values or reduction in blood glucose values of patients using branded generic drugs and patients using generic drugs.

Patient population selection:

The study was planned in two hospitals. One is the Health center in Andhra University (AUHC), Visakhapatnam, where the doctors use (prescribe) branded generic medicines only for all patients. The second hospital is the King George Hospital (KGH),

Visakhapatnam, where generic medicines are used. Generic medicines are not available for many medicines, because almost all companies give company names to their medicines. Only some anti-diabetic, anti-hypertensive and non steroidal anti-inflammatory medicines are available as generics and generics are available only in government hospitals. Patients using those generic medicines were selected as the second population. This research work was approved by the Institutional Ethics Committee for Human research of Andhra University as well as by the Chief Superintendent of King George Hospital.

The researcher waited in the pharmacy area in the hospitals and selected for study, those patients who are above 14 years, who were taking medicines for hypertension or for hypertension and diabetes since more than one year and who were willing to participate in the study. To those patients who gave a written informed consent, the researcher administered the SF-36, in English or in the regional language, Telugu. She obtained the answers to different questions in an average time period of 30 mins. In both the hospitals, the doctors, pharmacists and patients were very cooperative and eagerly gave answers to the questions put to them. The QOL assessment was done for each patient only once. The idea was not to pursue comparison over a period of time but it was to make a comparison between those using generics and those using branded generics in a specific period of time.

Assessment of QOL of patients:

The QOL of each participant was assessed using SF-36 which is considered by many to be a global instrument. For this study, SF-36 was typed by the researcher with a scoring scheme below each question. This facilitated easy answering of the SF-36 questions by the people. SF-36 includes 8 health concepts.

1. Physical functioning (PF) – 10 items measuring the extent to which health limits physical activities such as self-care, walking, climbing stairs, bending, lifting and moderate and vigorous exercises.
2. Role functioning (physical) (RP) – four items which measure the extent to which physical health interferes with work or other daily activities, including accomplishing less than wanted, limitations in the kind of activities or difficulty in performing activities.
3. Bodily pain (BP) - two items, measure intensity of pain and the effect of pain on normal work, both inside and out side the home
4. General health (GH) - five items reflecting the

general health perceptions of each subject. Subjects evaluate current health, health outlook and resistance to illness.

5. Vitality (VT) - four items measuring level of energy, ranging from energetic and full of pep (top level) to feeling tired and worn out (bottom level).
6. Social functioning (SF) - two items measuring how physical health and emotional problems impact on the social activities of an individual. The two items in the scale assess how health or emotional problems interfere with social activities with family, friends and neighbors.
7. Role function (emotional) (RE) - three items measuring how emotional problems (eg. feeling depressed or anxious) interfere with work or other daily activities in decreased time spent on activities and not working as carefully as usual.
8. Mental health (MH) - five items measuring general mental health (nervousness and cheerfulness, calmness, happiness) including depression, anxiety behavioral -emotional control and general positive affect.
9. Reported health transition (HT) - one item evaluating current health compared to one year ago.

Study format:

The patients studied may be grouped into two categories.

1. In this group patients taking medicines for their hypertension and diabetes for a period of more than one year were taken into the study. Fifty six patients from Andhra University Health center who were using branded generics and 75 patients from King George Hospital, Visakhapatnam, who were using generics, participated in the study.
2. In this group patients taking medicines for their hypertension for a period of more than one year were taken into the study. Ninety two patients from Andhra University Health Center who were using branded generics and 102 patients from King George Hospital, Visakhapatnam, who were using generics, participated in the study. The demographics of the patients who participated in the study are given in Table I.

The questionnaires filled were given scores by the scoring manual for SF-36. The scores obtained in 8 different domains were analyzed graphically and were compared by t test. The results are given below.

RESULTS

HRQOL

Along with the license for HRQOL instrument SF-36, the license for its scoring manual was also obtained from the company Quality Metric - Health Outcomes Solutions.

This is software which converts answers given by the patients in SF-36 into scores. The QOL is assessed in 8 domains. In each domain the maximum score is 100 and minimum score is 0. In each domain poor health status results in lesser score and higher health status results in better score. If the total score is 800, it indicates that the patient believes that he is in perfect QOL. The results from the questionnaires filled by the 325 patients were entered into the software and were scored by it.

B.P and Blood Glucose

The B.P and blood glucose values of all the patients who participated in the study were noted down from their case sheets. The values of B.P and blood glucose before the patients started treatment and the corresponding values at the time of the interview were noted.

Analysis

The HRQOL values of the patients were subjected to statistical analysis by Minitab - statistical software. The B.P and blood glucose values, before and after treatment were analyzed in the following manner. The patients were classified into four groups based on their B.P before treatment. The four classes were; normal B.P. (120/80), medium hypertension (120-140/80-100), high hypertension (140-190/100-120) and very high hypertension (190-250/120-180). After treatment, depending on the level of improvement he was given a number of plusses; for example if a patient improved from medium level to normal level he was given a single plus and so on. Finally the numbers of patients who recorded different number of plusses were tabulated for generics as well as for branded generics. A chi square test was performed on these values to determine whether there is any association between being generic or branded generic and the clinical effects. In a similar manner patients were classified into five groups based on their fasting blood glucose level; normal (80-110), medium (110-140), high (140-200), very high (200-250) and very-very high (250-550).

Based on reduction in fasting blood glucose level they were awarded a certain number of plusses and patients were classified based on the number of plusses. These values were tabulated for generics and branded generics and were analyzed by a chi square test. This analysis is shown in tables III.

Table .I: Demographics of the patients.

S.No.	Drugs type	Gender		Age in years			Exercise		
		M	F	30-49	50-69	70-89	Yes	Irregular	No
Group-I	B.G.	44	12	16	37	3	36	8	12
	G	46	29	17	52	6	29	20	26
Group-II	B.G.	70	22	28	57	7	50	15	27
	G	10	92	23	67	12	38	18	46

TABLE.II: Summary of T-Tests done on HRQOL of Patients.

Disease	Drug	S.no.	Component	N	Mean	SD	P-Value	Decision
B.P. and Diabetes.	Domain Scores	1	PF BG	56	84.2	17.2	0.674	N.S.
			PF G	75	82.9	16.5		
		2	RP BG	56	76.8	31.2	0.477	N.S.
			RP G	75	81	36.3		
		3	BP BG	56	79.9	20.8	0.124	N.S.
			BP G	75	85.2	17		
		4	GH BG	56	78	17.4	0.087	N.S.
			GH G	75	83.3	17.3		
		5	VT BG	56	78.6	19.4	0.338	N.S.
			VT G	75	75.2	20.4		
		6	SF BG	56	84.4	19.1	0.148	N.S.
			SF G	75	89.3	19.6		
		7	RE BG	56	86.3	29	0.442	N.S.
			RE G	75	90.2	28.4		
		8	MH BG	56	88.4	16.9	0.406	N.S.
			MH G	75	85.9	16.1		
		9	PF BG	92	89.1	14.7		
	PF G	102	84	16.7	0.023	S		
10	RP BG	92	85.9	28.8				
	RP G	102	81.1	38	0.325	N.S.		
11	BP BG	92	81.8	19.7				
	BP G	102	84.6	17.8	0.295	N.S.		
12	GH BG	92	84.4	15.3				
	GH G	102	83.9	14.4	0.83	N.S.		
13	VT BG	92	81.9	17.5				
	VT G	102	80.8	17.3	0.656	N.S.		
14	SF BG	92	85.3	19.8				
	SF G	102	89.7	13.8	0.078	N.S.		
15	RE BG	92	93.5	21.7				
	RE G	102	88.6	31.6	0.205	N.S.		
16	MH BG	92	89.9	13.1				
	MH G	102	85.7	17	0.057	N.S.		
	Total QOL	17	Total BG	92	691.7	78.3	0.338	N.S.
				102	678	113		

Note: - BG=branded generics, G=generics

DISCUSSION

HRQOL:

Figs 1 to 2 show comparison of HRQOLs of patients using branded generics and generics in study groups I-II. The bar diagrams in the two cases show that, the scores for branded generics and generics are nearly equal. In both the groups the importance is mixed, with branded generic users showing more score in some domains and generic users showing more score in some domains.

Comparison of Generics and Branded Generics in the two study groups with respect to different domains:

Group-1:- Patients use both antihypertensives and antidiabetics.

Fig. 1 shows a domain-wise comparison of generics and branded generic users of B.P. and anti diabetic drugs. In three domains i.e. in physical functioning, in vitality and in mental health QOLs of generics users are less but the difference is not significant. Generic users show better scores than branded generic users in all the other five domains but the difference is not significant.

Group-2:- Patients use antihypertensives only.

Fig. 2 shows a domain wise comparison of QOL scores of generic and branded generic users of B.P. drugs. In six domains i.e. in all but body pain and social functioning generic users show less QOL scores than branded generics users but the difference is significant in only one case, i.e. the case of physical function.

Fig. 3 shows a comparison of total QOL values of branded generics users and generics users of different study groups. In the first group the QOLs of the branded generics users and generic users are almost equal. In the second group the QOLs of branded generics users are a little more than the QOLs of generics users but the difference is not significant.

It may be concluded from the results that generic drugs are of equal efficacy as branded generic drugs.

Figures 4 to 7 show a comparison of total QOL scores of generic users and branded generic users. Figures 4 and 6 are individual value plots of the QOL scores of the two study groups. Figures 5 and 7 are box plots of total QOL scores of the 2 study groups.

1. The individual plot in fig. 4 and box plot in fig. 5 indicate that when the total QOLs of branded generic users and generic users of B.P. and diabetic drugs are compared, the former group has less spread and the means and medians to be almost same. There are six outliers (very low scores) in the data of generic users.

2. Individual plot fig. 6 and box plot fig. 7 indicate that the spread and median are lesser but the mean is more among the total QOLs of branded generic users of B.P.

drugs in comparison to the total QOLs of generic users of B.P. drugs. There is one outlier (very low score) in the data of generic users.

Summary of t-test values are given in table-II for the two groups. The mean QOL values in different domains and their s.d.s are calculated for users of branded generics and generics. For each domain in each group, the means, the s.d.s, p-value and the conclusion, i.e. whether the difference is significant or not is given in table-1. For each study group there are 9 comparisons, 8 comparisons for domains and 1 for comparison of total (maximum total=800) QOL. In only one case out of the 18 comparisons the difference observed is significant and in all others it is not significant. The only case of significant difference is; in study group II, physical function (B.G. = 89.1, G = 84). Patients who did regular exercise showed a higher average HRQOL value than those who did not do exercise regularly. Other demographic factors had no influence on average HRQOL values.

The interpretation of these results can only be the following:

- ✎ There is no significant difference between the HRQOL values of branded generic users and generic users, in a large member of cases, it should be concluded that branded generic drugs and generic drugs result in equally good quality of life.
- ✎ The SF-36 instrument is able to measure the QOL independent of economic status. It is really reflecting the effect of the medicine and is not impinged upon by economic or social factors. In the one case where significant difference is observed, the reflection is probably on the fact that most of the generic users are patients who depended on physical labor for their livelihood, who found a difference in their physical function QOL after the onset of the disease which the medicines could not yet repair.

BP and Blood Glucose

Group I: Table III and Figure 8 show the numbers of patients who showed different levels of improvement in their B.P values and blood glucose values. A chi square test was performed on these values to find out whether there is any association between being generic or branded generic and improvement in B.P values and blood glucose values. It was found that at 0.05 level of significance the difference observed in numbers of patients with specific levels of improvement in B.P, using Gs and BGs, was not significant enough to indicate an association. But with respect to blood glucose the difference is significant and by observation we find that

the numbers of generic users showing improvement are more than the numbers of branded generics users.

Group II: Table III and figure 8 show the numbers of patients who showed different levels of improvement in their B.P values. A chi square test was performed on these values to find out whether there is any association between being generic or branded generic and improvement in B.P values. It was found that at 0.05 level of significance the difference observed in numbers of patients with specific levels of improvement in B.P, using Gs and BGs, was significant enough to indicate an association and by observation we find that the numbers of generic users showing improvement are more than the numbers of branded generics users). Patients who did regular exercise showed better clinical outcomes than those who did not do exercise regularly. Other demographic factors had no influence on clinical outcomes.

The interpretation of these results can only be the following

Considering the results of the chi square test and after the observation of the data it may be concluded that generic drugs are not inferior to branded generic drugs in causing clinical improvement.

DISCUSSION OF THE RESULTS IN COMPARISON WITH PAST REPORTED WORK

Several studies utilized SF-36 for estimating the outcome in a variety of disease situations. Some researchers used SF-36 at two time points or three time points to prove that the treatment in question had an influence on the HRQOL of patients. Ensaf Saied Abdel-Gawad⁵ carried out a one time point QOL study and concluded that overall, diabetic patients reported mild to moderate QOL, which appears to be related to demographic, medical history and management regimens. The present work used a one time point study to assess the QOL of patients with diabetes and hypertension and patients with hypertension only that are using branded generics or generics. Berna Tander⁶ et al used HRQOL to compare the functional and psychological status of rheumatoid arthritis (RA) patients, fibromyalgia (FS) patients and controls. The scores of all SF-36 subscales except mental health scores were significantly lower in FS and RA patients than in controls. While they used QOL to compare the effect of two diseases, present work used QOL to compare the effect of two drug products of the same disease. There is no previous reported work which used QOL to compare branded generics with generics. The results of this study are in agreement with the results reported from this

laboratory^{3,4} in that there is bioequivalence between BGs and Gs.

Gyorgy jermendy⁷ et al carried out an observational study to assess the status of glycemic control and associated patient – reported outcomes in ambulatory Hungarian patients with type 2 diabetes mellitus. They concluded that patients reporting hypoglycemia were also more likely to report lower health related quality of life. In the present study patients showing better improvement in their B.P or blood glucose levels also showed better quality of life. When a rank correlation coefficient was calculated between the extent of improvement and the average HRQOL values; the coefficients ranged from 0.8 to 1.0. It may be concluded that improved clinical outcome is correlated with better HRQOL.

LIMITATIONS

1. The comparison between the patients using generics and branded generics was done on the basis of interviews done at a single point. A study extended over a period of time, by interviewing the same patients at different intervals of time (for the specific categories of drug products) would have yielded much more information but because of limitation of time it could not be done.
2. In general, patients using branded generics i.e. those who were getting their treatment from Andhra University Health Center were people belonging to an economically stable class, as they were all either employees of Andhra University or their family members. The people who were using generics, i.e. those who were taking their treatment from the King George Hospital, Visakhapatnam, which is a government hospital, were mostly people in the lower middle class or people below the poverty line and people who were going for manual labour for their livelihood. This factor could be expected to have an influence on the results of the survey by SF-36 and it did show in the low QOL with respect to physical function for the generic users. But this limitation is a natural one to this work as generics are being used in this region in government hospitals only. It is precisely to understand this situation that this research project was undertaken. But when the results were analyzed it was found that the mean QOL of generic users was, excepting one case, not only not less, but many times equal and some times more than that of the branded generic users.

Table.III: Reduction levels of B.P. and blood glucose levels in group – I and II

		B.P. reduction grade	G	B.G.
Group-I Patients having both B.P. and diabetes.	B.P. levels	0	6	5
		*	35	35
		**	15	30
		***	0	5
		Blood glucose reduction grade	G	B.G.
	Blood glucose levels	0	0	1
		*	12	21
		**	30	24
		***	20	8
		****	13	2
Group – II patients having Only B.P.	B.P. levels	B.P. reduction grade	G	B.G.
		0	1	14
		*	46	46
		**	45	31
		***	10	1

Fig.1: Comparison of QOLs of patients having BP and Diabetes using Branded Generics Vs. Generics

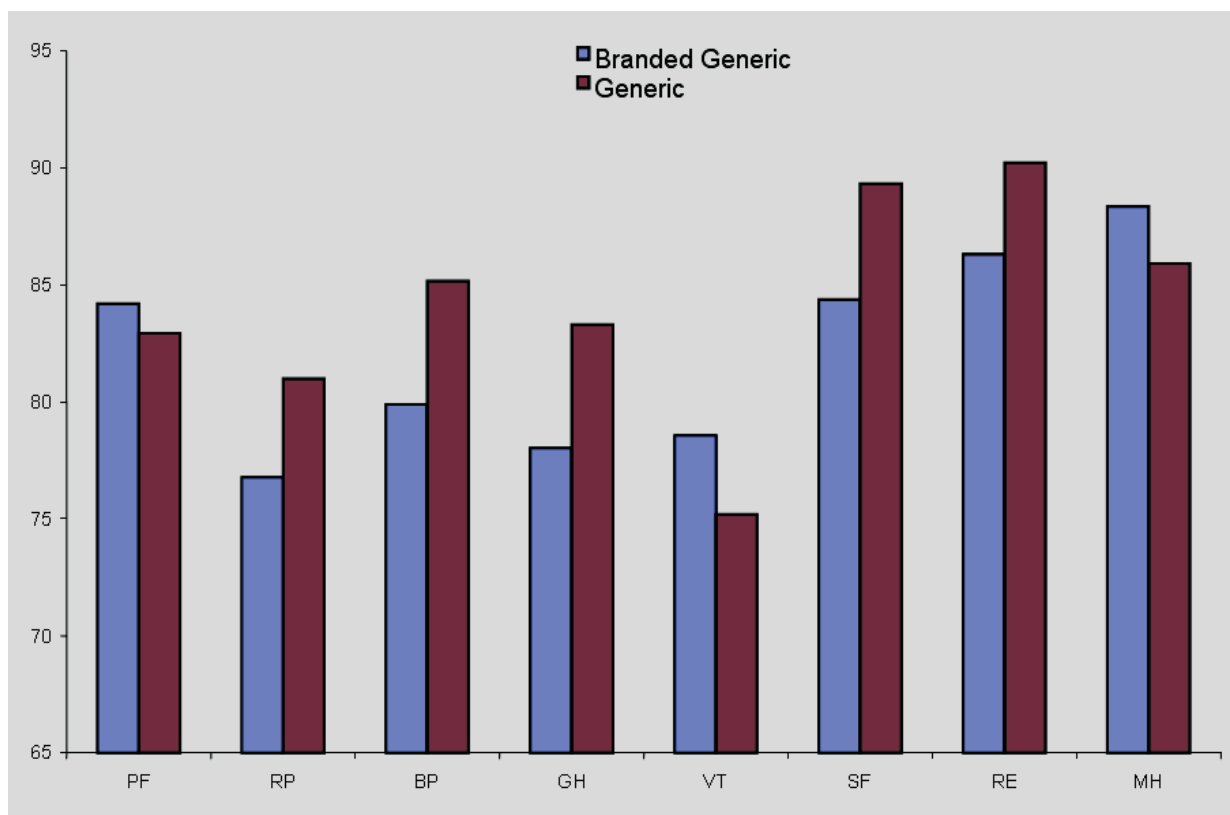


Fig.2: Comparison of QOLs of only BP patients using Branded Generics Vs. Generics (domain wise)

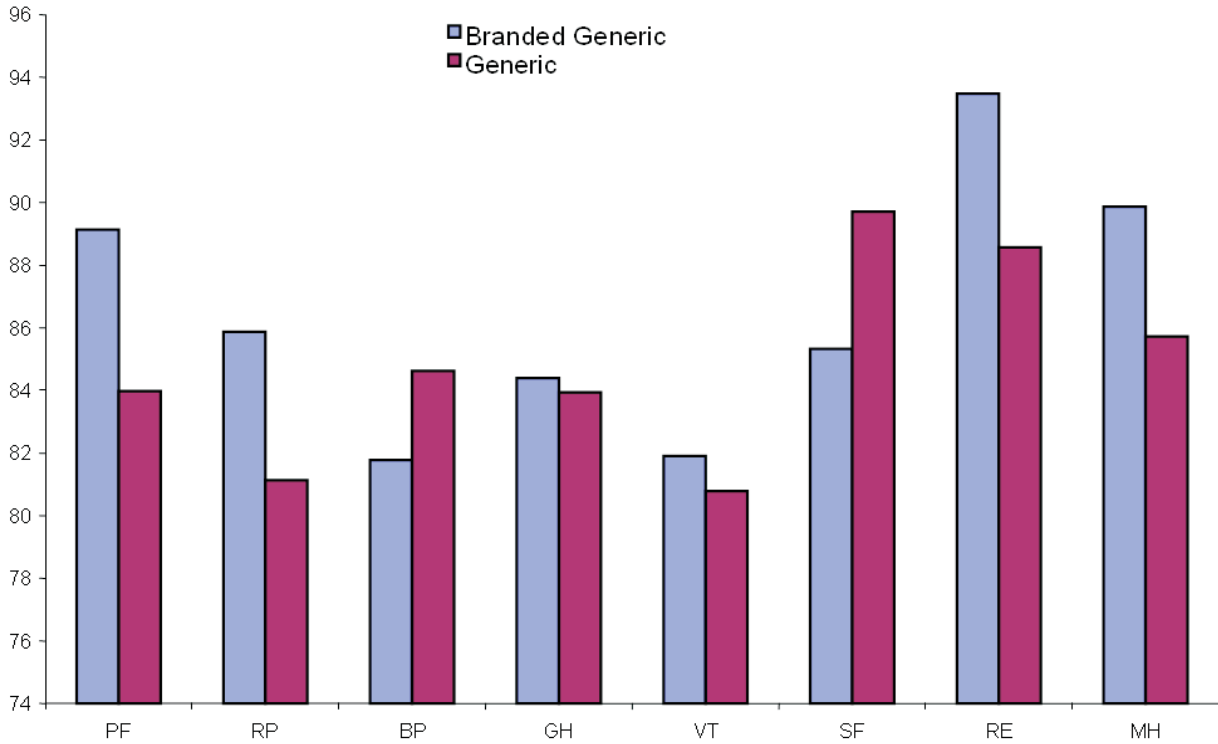


Fig.3: Comparison of total QOL of BG Vs G of different study groups (only BP and Diabetic, BP Patients)

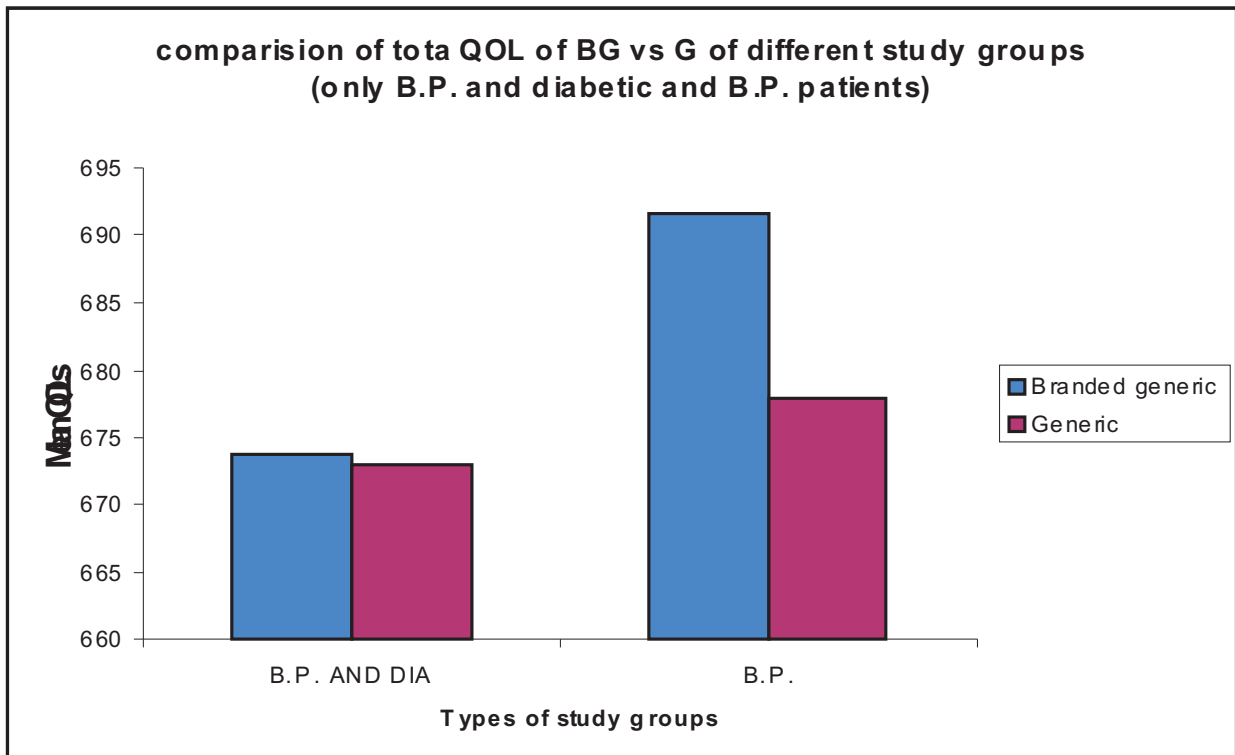


Fig.4: Individual Value Plots for QOLs of users of BP & Diabetic drugs, Branded Generics Vs. Generics

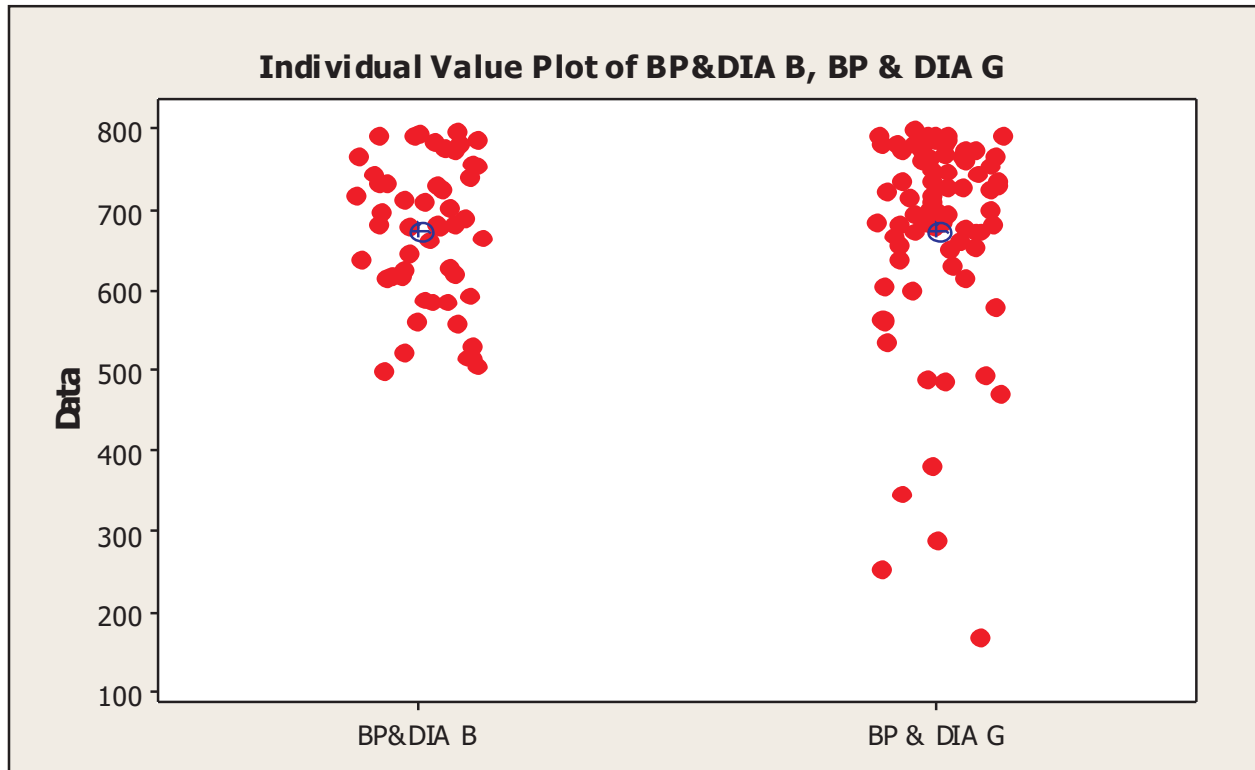


Fig.5: Box Plots for QOLs of users of BP & Diabetic drugs, Branded Generics Vs. Generics

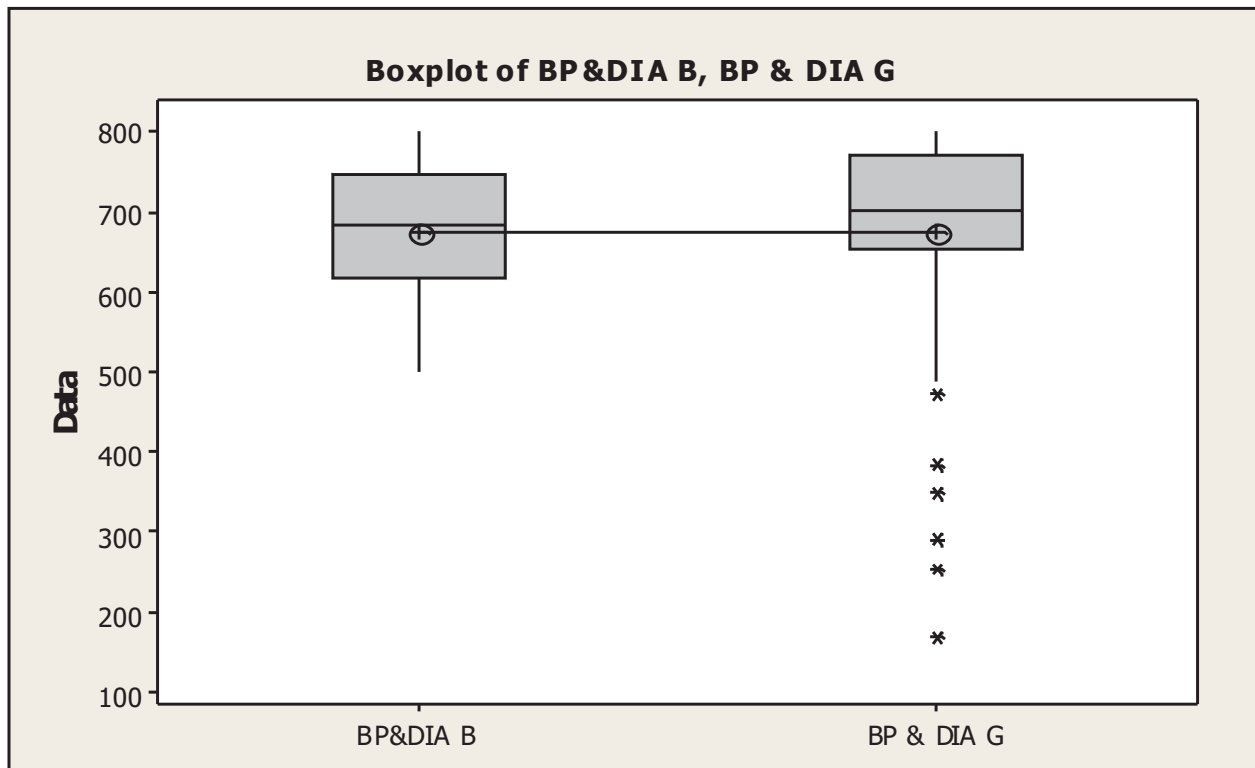


Fig.6: Individual Value Plots for QOLs of users of BP drugs, Branded Generics Vs. Generics

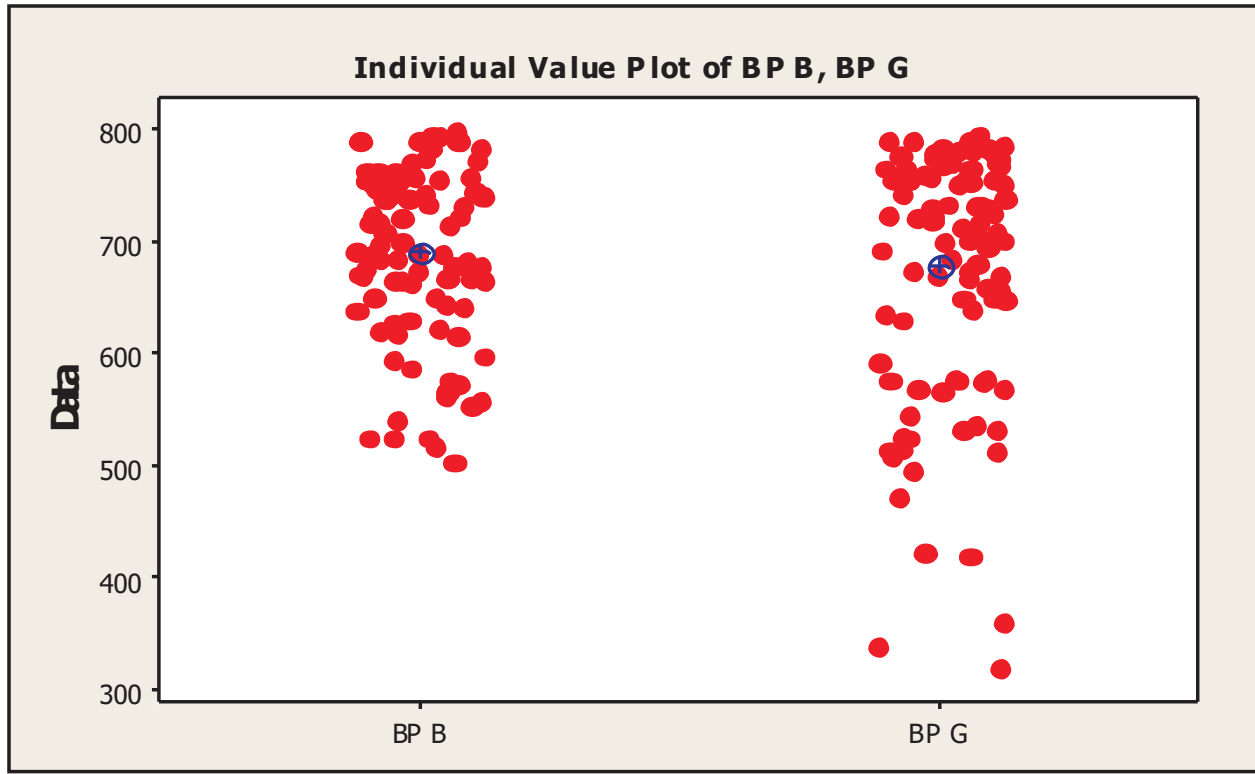


Fig.7: Box Plots for QOLs of Users of BP drugs, Branded Generics Vs. Generics

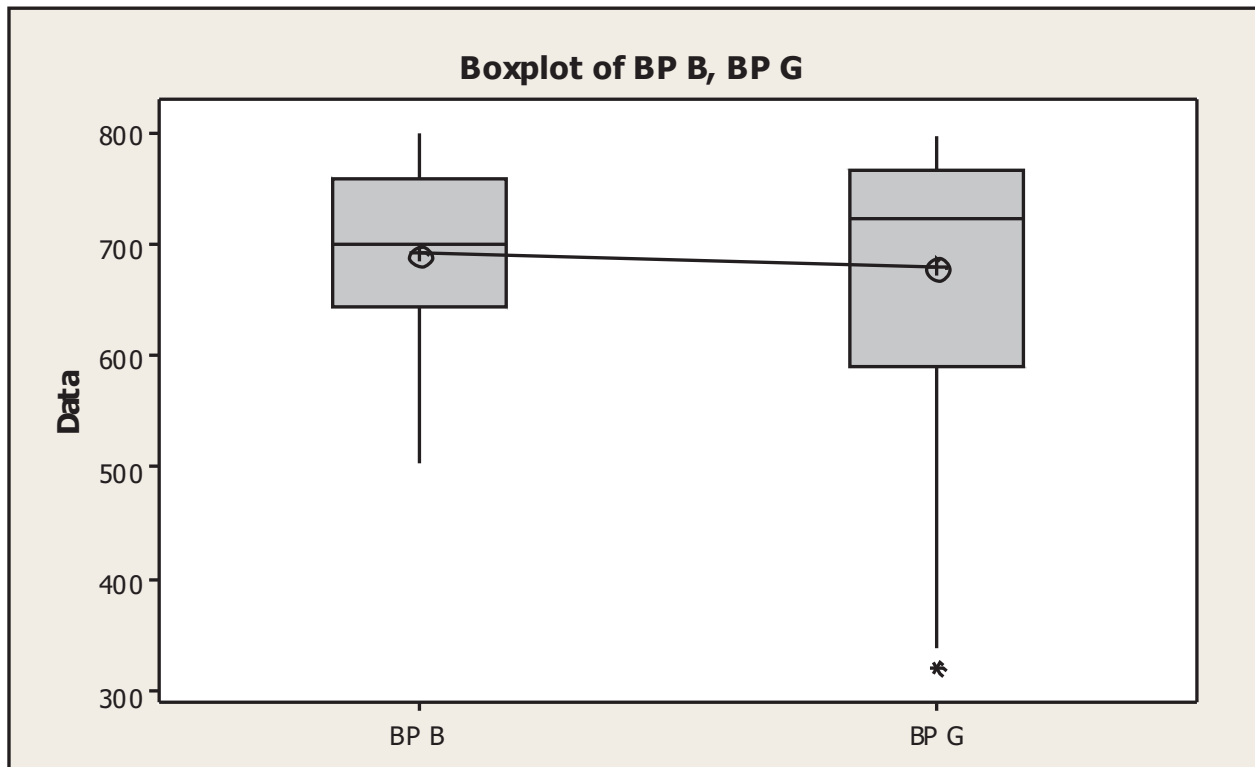
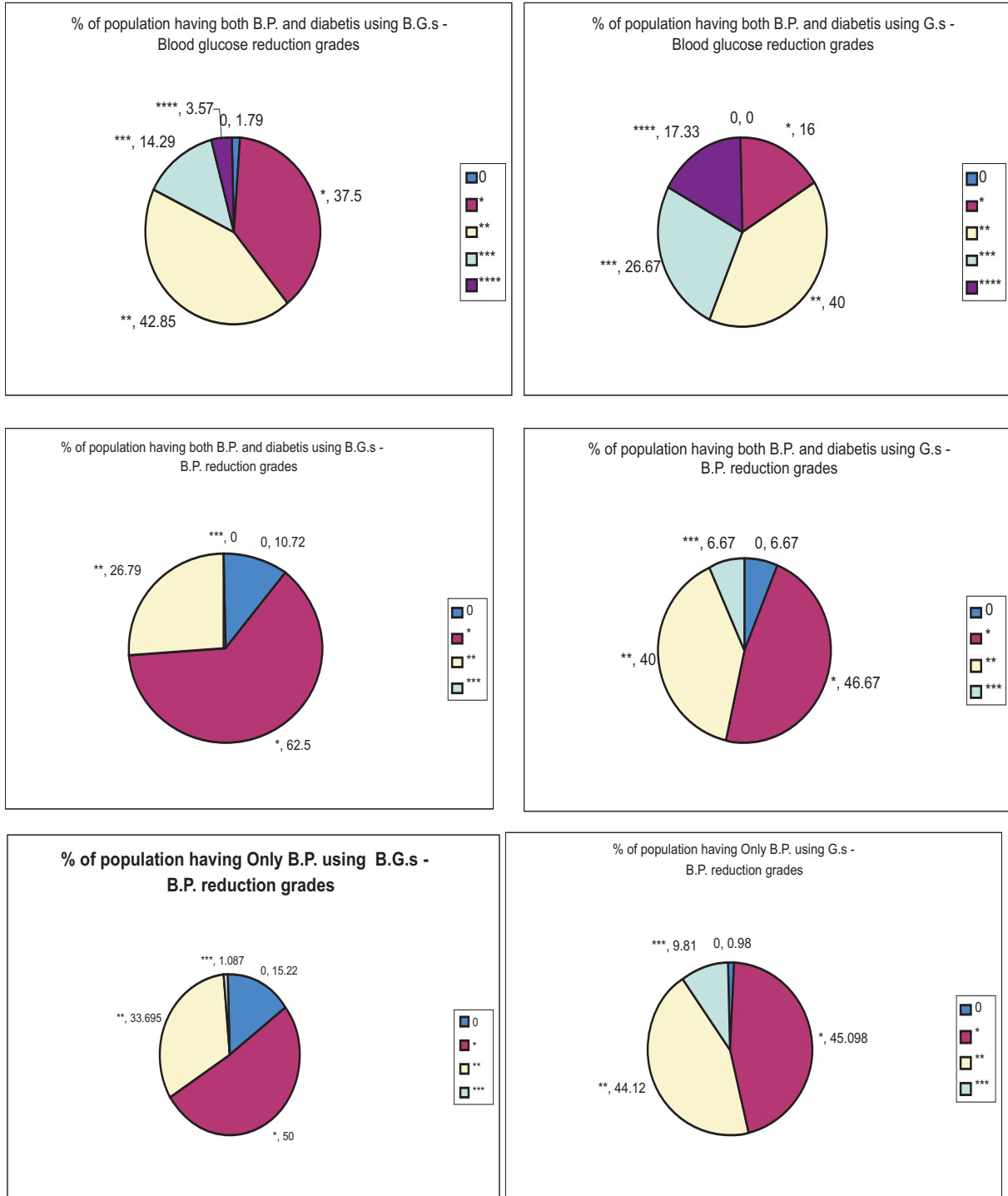


Fig.8: Reduction of BP and Blood glucose levels-% of populations in groups–I and II.



CONCLUSION

The results of this study clearly support the conclusion that there is no difference between the therapeutic efficacy of branded generic drugs and generic drugs. The Drugs and Cosmetics Act 1940 and the Drugs Price Control Order 1995 do not differentiate between BGs and Gs and do not insist on the Gs being priced lower. Hence the real situation is (Singal and Nanda)⁸ that in most cases BGs and Gs cost the same to the consumer, but to the retailer BGs cost more and Gs cost less. So the benefit that should accrue to the consumer is being snatched away by the retailer. The requirements are the Drugs and Cosmetics Act and the Drug Price Control Order should be amended to differentiate between BGs and Gs and Gs should cost less to the consumer. Then the burden on health care among patients will ease.

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