

A Case Report on Neonatal Bartter Syndrome and Its Effective Management-Clinical Pharmacist Perspective

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ABSTRACT

Bartter Syndrome is an inherited renal tubular disorder with hypokalaemia, hypochloremic and metabolic alkalosis. The syndrome was diagnosed by elevated serum renin levels, which is seen in our case, improved with potassium supplements and Indomethacin. In some patients Indomethacin therapy failed to resolve or prevent nephrocalcinosis. We are reporting a case of neonatal bartter syndrome responded well to Indomethacin and appropriate electrolyte therapy which gradually improved the general condition of the child. Unless there is a high degree of suspicion, patients may go undiagnosed or may be incorrectly managed for protein-energy malnutrition. Early diagnosis helps in improving the outcome by Angiotensin converting enzyme inhibitors (ACE) and NSAID's.

Key words: Bartter syndrome, Pathogenesis, Hypokalaemia, Indomethacin, Potassium supplements.

INTRODUCTION

Bartter Syndrome (BS) is a rare autosomal recessive disorder, defect of sodium and chloride absorption from the loop of henle resulting in excessive urinary electrolyte losses. Volume depletion accounts in hyperaldosteronism which leads to hypokalaemia and metabolic alkalosis.¹ It is estimated that prevalence of 1.2 cases per million.² It occurs mostly in childhood or adolescence, and initial presentation of patients over 40 yrs of age was very rare. Only isolated case reports but no case series have been reported on BS so far from India^{3,4} The neonatal variant BS typically presents life-threatening disorder that is characterized by polyhydramnios, premature delivery, growth retardation, hypercalciuria and nephrocalcinosis.⁵ Exogenous Growth hormone (GH) increases the growth rate and helps patients with GH deficiency attain normal height. Several groups of investigations have suggested that there was an obligate loss of sodium in the urine of patients with this disorder.⁶

Clinical manifestations of BS include fetal polyuria, early onset maternal polyhydramnios, intrauterine growth restriction, preterm birth, postnatal polyuria, episodes of dehydration, recurrent vomiting, and failure to thrive.⁷ Failure to thrive in infants and young children can be due to many causes and may be the only manifestation of an underlying serious systemic disease. It may be present in the neonatal period or early infancy with salt wasting.⁸ Nevertheless, the syndrome has aroused great interest in many clinical investigators because it may provide new insights in to renal electrolyte metabolism and the pathophysiology of hypertension.⁴ The primary defect in BS is an impairment in one of the transporters involved in sodium chloride reabsorption in the thick ascending limb on the loop of henle viz., Na-K-2CL co transporter (NKCC2) or apical K channel, Renal Outer Medullary Potassium channel (ROMK) or Basolateral Chloride channel.⁵ Unless there is a high degree of suspicion, patients may go undiagnosed or may be

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incorrectly managed for protein–energy malnutrition. Subsequently, a wide variety of hypokalaemia metabolic alkalotic states, with different clinical and laboratory findings as well as age-related presentations, have been reported, leading to confusing. Terms such as Bartter-Syndrome may do little to help the clinician identify the specific metabolic defect and treat the patient's illness correctly.^{8,9}

CASE REPORT

A 4 months old male child admitted in our hospital with the complaints of fever, cough and cold since 5 days and loss of social smile since 15 days. Abnormal movements of head and upper limb since 1 month, increased from the past 1 week. On admission, child had tonic posturing, involuntary movements and was lethargic with hypertonia. No other family members had similar illness and there was no history of parental consanguinity.

On examination, the child weighed 2.6 kg and was poorly nourished with length of 58 cm and head circumference of 38 cm with normal blood pressure. EEG showed diffuse slow waves with subtle asymmetry. USG abdomen showed mildly raised parenchymal echoes. Blood counts were normal. Blood gas revealed metabolic alkalosis with marked hyponatraemia, hypokalaemia and hypochloraemia with raised bicarbonate levels. Urea, creatinine, LFT, serum calcium, magnesium, and phosphorous, thyroid function tests levels were normal. Laboratory investigations showed following results- Serum potassium 1.1 mmol/L [Normal range-3.5-5 mmol/L], Serum sodium-119 mmol/L [Normal range 136-145 mmol/L], Serum chloride-50 mmol/L (96-106 mmol/L), and Serum bicarbonate 55 mmol/L [Normal range 24-28 mmol/L]. Serum renin was markedly elevated 24.68 ng/ml/hr [Normal range 0.15-2.33]. In view of clinical parameters like persistent hypokalaemia and metabolic alkalosis, failure to thrive and polyuria physician diagnosed as Bartter syndrome.

Based on the clinical picture and laboratory data, after initial fluid and potassium correction, the child was started with Syrup. Levetiracetam (0.25 ml) BD, Cap. Indomethacin 1.5 mg OD, Syrup. Potassium chloride 3.5 ml BD treated symptomatically along with appropriate dietary advice. Gradually, child showed improvement in muscle tone, hydration and electrolyte status. At the time of discharge the patient serum sodium value was 140 mmol/L, serum bicarbonate-36 mmol/L, serum chloride-98 mmol/L, serum potassium-3.2 mmol/L, serum renin level-1.23 ng/ml/hr and the patient was clinically stable and was advised for regular follow-up.

Eventually, baby thrived well, gained weight, achieved milestones normally and has improved muscle tone.

DISCUSSION

Bartter syndrome was originally described by Federic Bartter in 1962 as a combination of hyperplasia of juxtaglomerular complex, hyperaldosteronism and hypokalaemic metabolic alkalosis. Renal potassium wastage in BS may be complex since multiple factors may exacerbate the hypokalaemia. This defect is postulated to be impaired chloride reabsorption in the thick ascending limb of the Loop of Henle, which results in abnormally high sodium ion concentration in the tubular fluid available for exchange with potassium on reaching the distal tubule. Magnesium depletion, secondary hyperaldosteronism, increased renal kallikrein production, and metabolic alkalosis all contribute to the potassium loss in this syndrome.¹⁰

In our case the patient admitted with complaints of onset of fever, cough, cold, fatigue, polyuria, failure to thrive, tonic posturing, involuntary movements and was lethargic with hypertonia and clinical findings revealed hyponatraemia, hypokalaemia, hypochloraemia, metabolic alkalosis with raised serum renin levels which represents BS. Studies have showed that nearly all patients with BS have growth retardation and are given growth hormone therapy along with Indomethacin and potassium supplements. Therapeutic efforts should be directed to correct dehydration and electrolytic imbalance. Apart from potassium supplementation, administration of a well tolerated dose of Indomethacin 1-5 mg/kg/day after 6-12 weeks of life is useful. For some patients, Acetylsalicylic acid (100 mg/kg/day), ibuprofen (30 mg/kg/day) or ketoprofen (20 mg/kg/day) may be beneficial. Addition of potassium sparing diuretics may be initially effective to control hypokalaemia but their effect is transient. If the condition is not diagnosed early, it can cause progressive tubulointerstitial nephritis. Early diagnosis and treatment improves the prognosis and quality of life. Patients receiving pharmacological treatment have complications such as gastritis/gastric ulcers on long term follow up which should be monitored accordingly through surveillance of renal function and gastrointestinal endoscopy has been recommended for them.^{4,5} In our case the electrolyte levels of the patient found to be abnormal, hence the physician has suggested symptomatic treatment with Syrup. Potassium chloride (3.5 ml) BD and Indomethacin (1.5 mg) along with appropriate dietary advice, gradually showed improvement in muscle tone, hydration and electrolyte status (serum sodium level-120 mmol/L, serum bicarbonate-36 mmol/L, serum chloride-98 mmol/L,

serum potassium-3.2 mmol/L, serum renin level-1.23 ng/ml/hr) and the patient was found to be clinically stable at the time of discharge.

CONCLUSION

Although there are conflicting reports for BS, we believe that early diagnosis and clear understanding of pathophysiology plays a crucial role in selecting therapy and management. We conclude that there is a chance of recurrence of hypokalaemia and patient may develop chronic renal failure although the patient is treated initially. Hence, regular monitoring is necessary in patients diagnosed with BS.

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CONFLICT OF INTEREST

The authors have no conflict of interest.

ABBREVIATION

ACE:	Angiotensin Converting Enzyme
NSAID:	Non Steroidal Anti-Inflammatory Drug
GH:	Growth Hormone
NKCC2:	Sodium-Potassium-Chloride Transporter 2
ROMK:	Renal Outer Medullary Potassium channel
EEG:	Electroencephalogram
USG:	Ultrasonogram
LFT:	Liver Function Test