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RESEARCH ARTICLE

RENAL PROFILE IN AMIKACIN THERAPY IN NEONATAL SEPTICEMIA

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ABSTRACT

Background: Neonatal sepsis is the most common cause of neonatal deaths followed by extreme prematurity and birth asphyxia. In our hospital settings, a case of septicemia is treated with aminoglycosides (AG) combined with third generation cephalosporins. This is the standard guidelines of treatment of septicaemia.Though the duration of therapy should be 5-7days for most probable sepsis and 14 days for culture positive cases but as the cost of therapy is high, and the laboratory procedures for monitoring such duration of therapy is not possible in our hospital , short duration of 5-day therapy is practiced. Among the AGs, amikacin being extensively studied highly preferred agent because of its broadest spectrum, resistance to inactivating enzymes , least lysosomal damage, better tolerability profile and also low cost of therapy. The present piece of work aims at assessing any change in the renal profile of the babies being treated with 5-day amikacin therapy.
Materials and methods: Serum Creatinine,urea,potassium and 24 hours urinary Creatinine clearance were estimated on day 1(before initiation of therapy)and on day 3, day 5 of the septicemic neonates.These parameters were selected to assess the status of renal function of the affected neonates.
Results and conclusion: There was no significant changes in renal function with the regimen.
Key words: Aminoglycosides and nephrotoxicity, Neonatal septicemia, Amikacin and nephrotoxicity

INTRODUCTION

Neonatal septicemia is defined as presence of generalized systemic features of sepsis associated with pure growth of bacteria from one or more sites [1] . This includes Septicaemia, Pneumonia, Meningitis, UTI etc, which may present in isolation or in combination [2].A survey conducted by NNPD showed that Klebsiella is most common followed by Staph aureus and E.coli .Neonatal sepsis is the most common cause of neonatal deaths followed by extreme prematurity and birth asphyxia [3] . Overall incidence of sepsis is about 3.8% in India [3]. Mortality from neonatal sepsis is 25% to 30% [3,4]. Amikacin is an effective drug in neonatal septicemia but it has several toxic potential namely nephrotoxicity, ototoxicity and neurotoxicity [5].

In our hospital settings, a case of septicemia is treated with aminoglycosides (AG) combined with third generation cephalosporins. This is the standard guidelines of treatment of septicaemia [2,3,4]. Among the AGs, amikacin being extensively studied is by far a highly preferred agent because of its broadest spectrum, resistance to inactivating enzymes and least lysosomal damage [5,6]. Amikacin retains its sensitivity and remains effective when other AG are resistant Besides, its tolerability profile is also relatively better with intermediate ototoxicity and nephrotoxicity and also considering cost of therapy [7]. Preterm babies can be treated with recommended dosage of amikacin. In case of septicemia, renal function is impaired and it is more adversely affected when it is associated with birth asphyxia, electrolyte imbalance [5].

Though the duration of therapy should be 5-7days for most probable sepsis and 14 days for culture positive cases [6]. But as the cost of therapy is high, and the laboratory procedures for monitoring such duration of therapy is not possible in our hospital , short duration of 5-day therapy is practiced. In case of culture positive cases 14 day treatment and in probable sepsis 5 day treatment is practiced in this hospital [6,7,8]. Perhaps concern over adverse safety profile of AG therapy in general and it's nephrotoxicity in particular might have triggered the preference for such work. A baby of septicaemia have already deranged renal function, treatments with amikacin may increase the possibility of early renal profile changes. Nephrotoxicity is related to dosage, duration of therapy.

This regimen has in general reportedly yielded good results i.e mostly there is early recovery with little or no squeal. So aim of the study was detect early changes in renal profile (Safety) & to assess the efficacy of therapy that is being given.

MATERIALS & METHODS

The study has been conducted at the 'special care unit' baby nursery,Department of Paediatrics, Burdwan Medical College. 35 diagnosed neonates of septicemia (clinical and Investigation based) were selected randomly for the study. Babies with congenital malformation, Very Low Birth Weight Baby, mother received aminoglycosides during antenatal period and mother suffering from renal disease were excluded from this study. It was a hospital based cohort study. Permission was taken from institutional Ethics Committee for the study.

Babies were regarded as control before therapy. Day of starting therapy is counted as day 1. Amikacin were given for 5 days. Blood & 24 hours urinary samples were taken for day 1, day 3 and day 5.

Blood was collected from the neonates. From this collected blood serum was obtained. Serum Creatinine was measured by two point kinetic assay using Jaffe's reaction

[9]. Serum urea was measured by Berthelot method [10]. Serum Electrolyte: Na^+, K^+, has been measured by 9181 AVL electrolyte analyzer using ion selective electrode (ISE) [11].

24 hours Urine Collection was done by bag method[12,13]. Urinary creatinine clearance was considered as the marker of renal staus of the neonates under study. Urine creatinine was measured by Jaffe's reaction [9].

Creatinine clearance was measured [14] using the following formula:

$$\text{Creatinine clearance (ml/min/1.73m}^2\text{)} = \frac{\text{Urinary creatinine (mg/dl)}}{\text{Serum creatinine (mg/dl)}} \text{X} \frac{\text{Urine volume (ml/min)}}{\text{Surface area of baby}} \text{X } 1.73$$

RESULT & ANALYSIS:

Data for day 1 was considered as control . Day 1 means the day of starting therapy. Level of all the analytes of day 1 was compared with day 3 and day 5 respectively.

Table 1:Profile of the selected cases	
Sex distribution of cases	Male 20 (57%) Female 15(43%)
Birth weight	>2.5 kg 15 (42.85 %) <2.5 Kg 20 (57.15%)
Mode of Delivery	Normal 21 (60%) LUCS 12 (34.29%) Forceps 01 (2.86%) Breech 01 (2.86%)
Nature of sepsis	Probable sepsis 22 (62.85) Proven Sepsis 13 (37.15)

Table 2: Differences between the mean values of selected parameters in different days of administration of aminoglycosides

	Concentration of Na^+ in serum (mmole/L)	Concentration of K^+ in serum (mmole/L)	Creatinine clearance (ml/min)
Before administration of aminoglycosides (Variable 1)	142.03 ± 5.96	5.08 ± 0.90	50.91 ± 6.38
On 3rd day of administration of aminoglycosides (Variable 2)	142.66 ± 5.62	5.17 ± 0.85	49.26 ± 6.31
On 5th day of administration of aminoglycosides (Variable 3)	143.37 ± 6.62	5.53 ± 0.76	48.81 ± 6.40
Significance of Correlation between Variable 1 and 2	> 0.05	>0.05	>0.05
Significance of Correlation between Variable 1 and 3	>0.05	>0.05	>0.05

All data expressed in the form of Mean ± SD

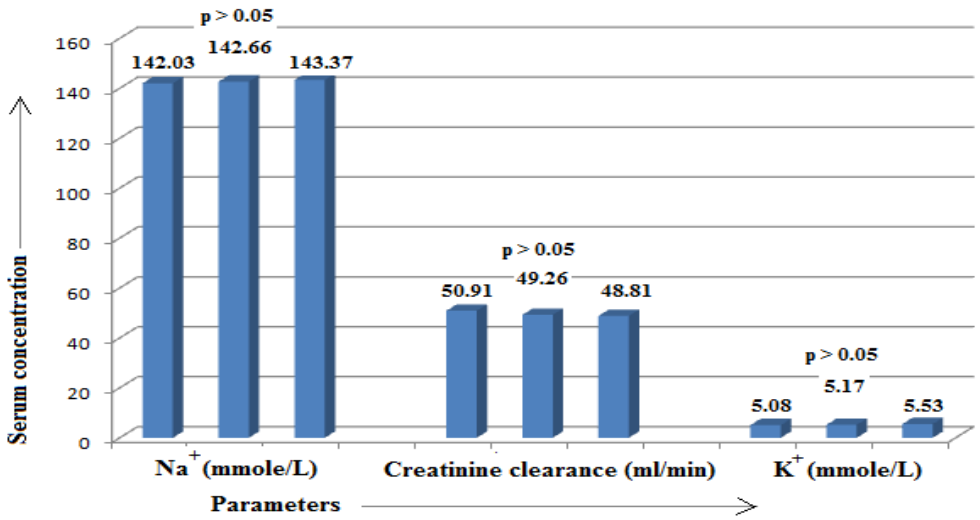

Figure 1: histogram shows the mean value of analytes in Day1 ,Day 2 & Day 3 respectively

DISCUSSION

It is evident from this study that a patient of septicemia may have some renal function derangements and AGs have got nephrotoxic potential but 5 days therapy does not affect renal function. Though further studies are needed to define safe duration of therapy. Safety for treatment periods which are longer than 14 days has not been established [15,16]. Aminoglycosides (AG) provided for less than 5 days to neonates do not produce a marked disturbance of creatinine clearance or tubular sodium handling [6,16]. A study was carried out for nephrotoxicity and evaluated 124 patients for nephrotoxicity associated with gentamicin or amikacin therapy. The incidence of definite nephrotoxicity was 10.5% during therapy, with a mean increase in creatinine of 1.0 mg/100 ml (range, 0.5-3.6 mg/100 ml). Nephrotoxicity developed late in therapy (mean, day[10] and the creatinine continued to increase after cessation of therapy for as long as nine days [17]. This Study was conducted to see the changes in renal profile with Amikacin therapy in a case of neonatal septicaemia. No significant differences were found in 5 days therapy .Findings of this study will help us to use this regimen of AG with greater level of confidence.Further studies may be undertaken to have more meaningful and reliable information on the same problem.

CONCLUSION

Though potential for nephrotoxicity depends upon dose, coexisting medical condition, kidney function and duration of therapy, our study searched whether 5 days therapy is safe or not. In our settings, urinary enzymes detection was not possible, though it was more sensitive and early indicator, also it is noninvasive. So, considering all aspects of the study, it was carried out in right way.

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