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Original Research Article

Assessment of Nephrotoxicity Caused by Amikacin Used as Surgical Prophylaxis

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ABSTRACT

Background: Antibiotics are administered prior to some surgical procedures to prevent surgical site infections. Aminoglycosides have potent activity against Gram negative bacilli and are often used to treat infections caused by these species, especially when resistance to beta lactam antibiotics is suspected.
Method: This is a prospective study included adult patients who underwent surgical procedures (gastrointestinal operations, biliary operations, genitourinary operations and gynecological operations) in which amikacin was used as a part of prophylactic antibiotic regimen.
Result: Result showed that amikacin-treated patients experienced a rise in the serum creatinine level that fit the designated definition of nephrotoxicity-i.e., an increase to at least 50 percent and at least 0.5 mg/dl above the baseline value.
Conclusion: In conclusion, amikacin may be nephrotoxic in humans; however, the broad applicability of this finding to other patient populations is uncertain.

Keywords: Surgical site infections, Amikacin, Serum Creatinine and Nephrotoxicity.

INTRODUCTION

Aminoglycosides have potent activity against Gram negative bacilli and are often used to treat infections caused by these species, especially when resistance to beta lactam antibiotics is suspected. However, use of aminoglycosides is limited by concerns about toxicity, primarily nephrotoxicity and ototoxicity. The drugs are usually administered intravenously in two to four doses a day in patients with normal renal function. A once daily dose is more convenient and has been proposed to be an equally effective and potentially less toxic mode of administration. [1-3]

Numerous randomized trials have compared a single daily dose with multiple doses of aminoglycosides in hospital inpatients. Although a few studies showed one or the other regimen to be of superior merit, other most found no significant difference in efficacy or toxicity between the two regimens. Individual trials, however, have been of relatively small size, and their power to detect a significant difference in outcome was low. Thus, although there is evidence from in vitro and animal studies to suggest that administering aminoglycosides once daily is advantageous, the validity of this hypothesis has not yet been established in clinical trials or in an earlier, small meta-analysis. [4]

Surgical site infections (SSIs) are the most common health care associated infection (HAI), accounting for 31% of all health-care associated infection among

hospitalized patients. [5] The SSIs are classified as Superficial Incisional SSI, Deep Incisional SSI and Organ/space SSI. Superficial SSI involves only skin and subcutaneous tissue and occurs within 30 days of operative procedures. There are two specific types of superficial surgical SSI: Primary and Secondary. Deep Incisional SSI involves deep soft tissues (e.g. fascial and muscle layer) and occurs within 30 or 90 days of operative procedures. They are also of two types: Primary and Secondary. Organ/Space SSI occur within 30 or 90 days of operative procedures and involve any part of body deeper than fascial/muscle layer. [6,7] Most SSIs result from bacterial inoculation at the time of surgery. SSIs lead to adverse patient outcomes. [8] Antibiotics are administered prior to some surgical procedures to prevent surgical site infections. Antibiotic chosen should be active against microorganisms most commonly associated with wound infections following the surgical operations and against microorganisms endogenous to operating site. [9] Prophylactic antibiotic for gastrointestinal operations, biliary operations, genitourinary operations and gynaecological operations must cover enteric gram-negative bacilli, gram positive cocci, enterococci, clostridia and anaerobes. The present study aimed to study the risk of nephrotoxicity with amikacin, when used in certain surgical procedures as prophylactic antibiotics.

MATERIALS AND METHODS

This is a prospective study included 52 adult patients who underwent surgical procedures (gastrointestinal operations, biliary operations, genitourinary operations and gynaecological operations) in which amikacin was used as a part of prophylactic antibiotic regimen. The study was carried out in co-ordination with the Department of Surgery of Gandaki Medical College during the period from September 2015 to November 2015. Ethical clearance was obtained from Institutional Ethical Committee of Gandaki Medical College.

All patients received single dose of prophylactic antibiotic (Amikacin 15 mg/kg) within 60 minutes before incision. Before surgery, baseline serum creatinine level was estimated. After surgery, serum creatinine was measured daily for first seven Postoperative days and maximal serum creatinine level during this period was recorded as after surgery value.

Data Analysis: Data analysis was conducted using SPSS 21 version for windows and independent t test was performed. The p-value of less than 0.05 was considered significant.

RESULT AND DISCUSSION

Patients Studied

52 patients who received amikacin were evaluated for nephrotoxicity. The demographic and clinical characteristics of these patients are recorded in Table I.

Table I: Demographic and Clinical Features of Patients Treated with Amikacin.

Characteristics	Amikacin (n=52)
Gender (male)	16 (31)
Age (years)	41 ± 17
Range	6 - 83
Body weight (kg)	63 ± 17
Baseline renal profile	
Serum creatinine (mg/dl)	0.9
Creatinine clearance (ml/minute)	91.2
BUN/serum creatinine ratio	10.6
Concomitant drugs	
Cephalosporin	37 (71)
Clindamycin	4(8)
Furosemide	10(19)

*Data are median values, except where mean -c standard deviation or number (percent) is recorded.

Evaluation of Renal Function

Table II: Evaluation of Renal Function

Characteristics	Amikacin (n=52)
Nephrotoxicity	
Increase in serum creatinine ≥ 50 percent	0
Increase in serum creatinine ≥ 33.3 percent	3(6)
Increase in serum creatinine ≥ 0.5 mg/dl	10(19)
Decrease in creatinine clearance ≥ 50 percent	3(6)
Serum creatinine difference (mg/dl)	+0.1 (p=0.11)
Range	-1.0 to +0.7
Serum creatinine ratio**	1.1 (p=0.10)
Range	0.5 to 1.7
Change in creatinine clearance (percent)	-8.3 (p=0.11)

The data on renal function were analyzed in blinded fashion, as shown in Table II. 52 amikacin-treated patients experienced a rise in the serum creatinine level that fit the designated definition of

nephrotoxicity-i.e., an increase to at least 50 percent and at least 0.5 mg/dl above the baseline value. Nephrotoxicity appeared to be associated with impaired baseline renal function, greater age, presence of bacteremia, and highly correlated with amikacin treatment.

The baseline serum concentration of creatinine determinations during the period from 48 hours before to 48 hours after the initiation of amikacin therapy. However, if the last serum creatinine determination in the baseline period was 70 percent or less of the mean, that determination was considered to be the baseline value. Nephrotoxicity was evaluated in blinded fashion, and was defined as an increase in serum creatinine levels of at least 50 percent from the baseline level II such increase was equivalent to an absolute rise of at least 0.5 mg/dl.

The nephrotoxicity of amikacin has been examined in a number of clinical trials [9,10] employing various study designs and definitions of toxicity. An overall compilation [9] of prospective clinical trials of amino glycosides reported in the period 1975 to 1982 suggested that amikacin may be slightly less nephrotoxic than gentamicin. When the data were limited to those from comparative trials be-nephrotoxicity associated with amikacin was still less than that associated with gentamicin. Unfortunately, such compilations obscure the critical evaluation of study design and do not reflect the diversity of patient populations. A tabular review [10] of individual comparative trials of amikacin with other amino glycosides showed only one published report [11] of a significant difference in the incidence of nephrotoxicity- i.e., nine of 46 gentamicin-treated patients versus three of 49 amikacin-treated patients in a multi-center trial. A classic prospective, randomized, double-blind, comparative trial [11] of gentamicin and amikacin revealed no significant difference in the incidence of nephrotoxicity in the 62 patients in each of the two treatment arms.

Recent work [4,5] on analysis of risk factors for amino glycoside toxicity has revealed that the specific amino glycoside a patient receives may be less important to the development of toxicity than are differences in other characteristics of patients and their treatment courses. Thus, differences between series of patients in different treatment arms of a study may affect the comparison of the amino glycosides. Furthermore, differences among patient populations may make it difficult to compare studies or to broadly apply the results of a study.

To try to circumvent such problems, a multivariate analysis of risk factors, including the identity of the amino glycoside used, may be attempted. In order to increase the numbers and broaden the spectrum of patients for such a multivariate analysis, we plan to merge our data with a comparable database. [11]

CONCLUSION

The results of this study indicate that amikacin may be nephrotoxic in humans; however, the broad applicability of this finding to other patient populations is uncertain.

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