ORIGINAL ARTICLE

Pattern of Ototoxicity in a Nigerian Teaching Hospital

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Abstract

Introduction: *Ototoxicity is a preventable cause of irreversible sensorineural hearing loss. This paper aims to highlight the pattern of ototoxicity seen in a tertiary health institution.*

Method: *A retrospective study of patients with ototoxicity seen over a seven year period at ENT department of Aminu Kano Teaching Hospital, Kano. Case notes were retrieved and studied.*

Results: *Fifty nine patients made up 37 males and 22 females were seen with 86% in the age group 20-60years. The commonest ototoxic drugs were aminoglycosides (37.3%), loop diuretics (27.1%), antimalarials (23.7%) and traditional concoctions (11.9%). The commonest presentation from most drugs was permanent sensorineural hearing loss (50-85%). Associated co-morbid conditions included "febrile illness" (47.5%), hypertension (30.5%), diabetes mellitus (13.6%), renal disease (5%). Follow-up was poor. Only 18 patients presented for review beyond a second hospital visit, only those with ototoxicity from antimalarials recovered hearing. There were no effective audiometric and serum drug monitoring mechanism in place before, during or after therapy with ototoxic medications.*

Conclusion: *Ototoxicity is not uncommon and attempts at prevention are feeble. Increased awareness of this condition is advised. High frequency audiometric assessment, otoacoustic emission and serum drug monitoring facilities should be provided at health institutions. Caution should be exercised when prescribing ototoxic drugs in the presence of other risk factors.*

Key words: *pattern, ototoxicity, hospital*

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Introduction

Certain drugs are known to cause damage to inner ear structures leading to ototoxicity, sometimes this damage may occur after a single dose of the medication, but more often it happens after repeated dosing.[1,2,3] The onset of ototoxicity is unpredictable, ranging from immediate onset to months or years after completion of therapy.[4]

The consequences of ototoxicity include problems with language development and learning in children and decreased socioeconomic activities and decreased overall quality of life in the adult. No therapy is currently available for reversal of the hair cell damage of ototoxic medications and so management emphasis should be on prevention. This requires an increased awareness of this condition.

This paper aims to highlight the pattern of ototoxicity seen in a hospital setting. Knowledge of this will increase awareness of this condition and reduce the incidence of ototoxicity.

Materials and Method

This is a hospital based retrospective study of 59 patients diagnosed with ototoxicity over a 7 year period (2001-2008) at the ENT department of Aminu Kano Teaching Hospital, Kano. Case notes were retrieved and studied. Information obtained included patients age, sex, incriminated drug, manifested features of ototoxicity and audiological findings. Any associated co-morbid factors were also noted. Data was analyzed by simple descriptive method.

Results

There were 37 males and 22 females (M1.7: 1F) aged between $2^{1/2}$ years to 71 years with a mean of 41 years. Eighty six percent of the patients were between the ages of 20-60years.(Table 1). The most frequent drugs causing ototoxicity were aminoglycosides- gentamycin and streptomycin 22 cases (37.3%), loop diuretics-16 cases (27.1%), antimalarials- chloroquine and quinine-14 cases (23.7%) and traditional concoction-7 cases (11.9%).

The associated co-morbid conditions included febrile illness (47.5%), hypertension (30.5%), diabetes mellitus (13.6%) and renal disease (5%).

Aminoglycoside ototoxicity manifested as severe high frequency sensorineural hearing loss (68.2% of patients), tinnitus (41%) and disturbance of balance (13.6%). Asociated co-morbid factors were febrile illness, renal failure.

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Loop diuretic ototoxicity manifested as mild to moderate high frequency sensorineural hearing loss (50%), tinnitus (43.8%) and disturbance of balance (25%). Associated co-morbid factors were hypertension, diabetes mellitus, renal failure.

Antimalarial ototoxicity manifested as tinnitus (64.3%), mild to moderate, low to mid frequency sensorineural hearing loss (57.2%) and balance disturbance (7.2%).

Ototoxicity from traditional concoction manifested as low frequency sensorineural hearing loss of varying severity ranging from mild to severe (85.7%) and tinnitus (28.6%).

Eighteen cases were available for follow-up, only those with antimalarial ototoxicity were noted to have recovered hearing.

Table I: Age and sex distribution of patients with ototoxicity

Age(yrs)	No.(%)	Males	Females
<20years	4 (6.8)	2	2
20-40yrs	26(44.1)	18	8
41-60yrs	25(42.3)	14	11
>60yrs	4(6.8)	3	1

Discussion

The magnitude of ototoxicity worldwide is not accurately known. Studies have found ototoxicity to account for about 2-20% of hearing loss in children.[1,5,6] In Tanzania, ototoxicity was noted to be the second most common cause of deafness.[1] In this study, the bulk of cases were young and middle aged adults constituting 86% of the cases. It is probable that cases of ototoxicity in children in this setting are missed or overlooked or the hearing loss blamed on some other aetiologic factor.

Aminoglycosides were the most frequent cause of ototoxicity in this study. The high prevalence of aminoglycoside ototoxicity in developing countries has been observed by other authors.[7] This high prevalence has been blamed on the drug's low cost, availability without prescription and effectiveness against gram negative bacteria and mycobacterium. This therapeutic efficacy has continued to maintain the relevance of aminoglycosides today despite the risk of ototoxicity. In the United states for instance, about 4 million courses of aminoglycosides are administered annually.[8] It is a common observation in this environment for individuals with urethritis possibly gonococcal to use high dose gentamycin without prescription.

It is not clear whether the co-morbid condition of "febrile illness" which many patients complained of as necessitating their use of gentamycin contributed to the prevalence of hearing loss in this study. Such "febrile illness" included but not limited to viral infection and bacterial meningitis.

There is an increased susceptibility to aminoglycoside toxicity in individuals with mutation of the 12S rRNA gene which is maternally inherited, it is therefore common to have maternal relatives with similar hearing deficit after aminoglycoside use.[9] Specific history of maternal relatives having similar hearing problems was absent from the records reviewed in this study.

Since other risk factors for aminoglycoside ototoxicity such as extremes of age or co-administration of other ototoxic drugs were not evident in this study, it is probable therefore that aminoglycoside ototoxicity in this environment may due to genetic susceptibility or may be dose related.

Sensorineural hearing loss was the commonest presentation of aminoglycoside ototoxicity in this study. This is a common finding worldwide.[10] The hearing loss is usually permanent due to irreversible destruction of the outer hair cells of the organ of corti particularly those at the basal turn of cochlea. None of the patients who turned up for follow up recovered hearing in this study. Vestibular function is said to be much more sensitive to aminoglycosides than the cochlea.[11] In the absence of a hearing loss, vestibular features may be missed as early warning sign of ototoxicity.

The dosing regime observed in this study were single large dose of aminoglycosides (which was repeated in some cases) and prolonged therapy with multiple doses of aminoglycosides. Studies have shown that if the same total daily dose is given as once daily regimen rather than multiple dosing, the drug efficacy was the same but with decreased risk of ototoxicity.[12]

Loop diuretics used in hypertensive and renal failure therapy were found to be the next most common group of ototoxic drugs in this study. High doses given intravenously are known to cause hearing loss.[13] It is not clear however, whether the prevalence of ototoxicity in this subset of patients was influenced by the primary diseases of renal failure, hypertension or diabetes mellitus. Lasisi et al reported on 2 patients with renal failure who developed profound sensorineural hearing loss after 5-7 sessions of dialysis[14]. Hypertension and Diabetes Mellitus can induce angiopathies which may compromise labyrinthine blood supply.

Loop diuretics act on the stria vascularis and produce oedema of these tissues and a temporary loss of function, resulting in a decrease of the endocochlea potential.[15] The ototoxicity caused by loop diuretics tend to be reversible with drug withdrawal. However, this study did not find any case that recovered hearing completely after withdrawal of the drug, lending support to the possibility of the associated co-morbid conditions contributing to the hearing impairment in these cases.

Kshirsagar et al from their study, concluded that when frusemide is given slowly and in lower doses, the risk of ototoxicity is low provided plasma protiens are within normal limits.[16]

Majority of patients with antimalarial induced ototoxicity presented with tinnitus and a mild to moderate hearing loss that recovered after treatment. Tinnitus preceded the hearing loss in all cases, the onset of tinnitus can therefore be taken as a warning sign of ototoxicity in those on antimalarials. Quinine appears to be more cochleotoxic than chloroquine and from laser doppler flowmetry study, it appears to cause vasoconstriction and decrease cochlea blood flow, a mechanism of action similar to that of acetyl salicylic acid.[17] The current trend of using alternative non-ototoxic antimalarials will greatly reduce the incidence of ototoxicity from antimalarials.

Traditional concoction is a commonly employed remedy for virtually any kind of illness in this environment. Several cases of ototoxicity have been recorded from its use. In this study it accounted for nearly 12% of the cases seen. It is difficult to determine what constitute any particular concoction as different traditional healers dispense different concoctions and further, most patients on traditional concoction are particularly warned not to seek orthodox attention. This makes it difficult to determine the magnitude of hearing loss from use of traditional concoction.

Ototoxicity from such medications as macrolides, salicylates, non-steroidal antinflammatory drugs, and anti-neoplastic drugs which featured in several publications were not seen in this study.[18,19] It is probable that deafness resulting from these medications in this environment may have been blamed on the primary disease.

It is also difficult to determine ototoxicity from patients using ototopical medications in this environment as the primary ear condition is mostly blamed for any resulting hearing loss. In a survey of otolaryngologists in the United states, Lundy and Graham reported that 84.1% of ORL surgeons use ototopical medications in the face of tympanic membrane perforation, and 3.4% admitted to have witnessed irreversible inner ear damage from the drugs.[20]

Auditory assessment of patients in this study utilized pure tone audiometry (PTA) at the conventional frequencies (0.25-8KHz), this is unlikely to detect the earliest signs of ototoxicity which in the case of aminoglycosides affects frequencies above 8KHz first. Early cases will therefore be missed if conventional PTA frequencies are utilized. Distortion product otoacoustic emission and high frequency auditory testing (9-20KHz) were found to be most sensitive for detecting early ototoxicity.[21,22]

Ototoxicity is a preventable disease, this study observed that such preventive methods as routine audiological assessment during drug therapy, serum drug estimation were unavailable or impracticable due to low resources. This is probably the situation in other low resource settings.

Conclusion

Ototoxicity is not uncommon and attempts at preventing it in this environment is not satisfactory. There is a need for increased awareness of the effects and consequencies of ototoxic drugs. These drugs should be used only when necessary and at minimal effective dosage.

Health authorities should ensure that facilities for audiological assessment during ototoxic drug therapy along with serum drug monitoring facilities are in place.
Risk factors such as co administrations of ototoxic drugs, exposure to noise within 6 months of ototoxic medications, renal failure and hypoproteineamic states should be carefully weighed before commencement of ototoxic medications.

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