

INJUDICIOUS USE OF OTOTOXIC DRUGS

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SUMMARY

The study covers twenty cases of Ototoxicity caused by injudicious use of ototoxic drug "Gentamicin" over a period of two years i.e. from August, 1993 to August, 1995 in the ENT department of Hayat Shaheed Teaching Hospital, Peshawar. These cases received aminoglycoside, Gentamicin for minor illness and the dose and duration of the drug was found to be irrational. The drug was administered mostly by unqualified private practitioners to patients mostly of lower socioeconomic class. The degree of ototoxicity was from moderate to severe.

INTRODUCTION

Ototoxicity may be defined as "the tendency of certain therapeutic and chemical agents to cause functional impairment and cellular degeneration of the tissues of the inner ear and especially of the end organs and neurons of the cochlear and vestibular divisions of the 8th cranial nerve".¹

Avicenna² appears to have been the first to mention the effects of mercury inhalation on the ear. Cinchona bark, Quinine, Salicylates, and with the passage of time more ototoxic drugs were reported and it was in the early fifties into early sixties when aminoglycosides Streptomycin, Kanamycin, Neomycin and most important, Tobramycin and Gentamicin were introduced against tuberculosis. These drugs caused irreversible, at times profound ototoxicity especially when used in high doses and for longer periods.

The access of Aminoglycosides to the inner ear is by blood stream, when given systemically, by cerebro spinal fluids² when given intrathecally, and via middle ear when used ototopically.³

Most of the aminoglycosides have both cochleotoxicity and vestibulotoxicity, therefore causing deafness, tinnitus and vertigo either in combination or as isolated symptoms. Analysis have shown that these drugs are concentrated in the labyrinthine fluid damaging stria vascularis⁴ thus delaying elimination. Also their concentration in the blood may remain high for longer period due to damage to the glomerular tufts in the kidneys. It is beyond doubt that aminoglycosides are nephrotoxic as well. This points to the fact that stria vascularis and glomerular tufts have structural resemblance and are both targeted by these drugs.⁵

MATERIAL AND METHODS

Twenty cases have been selected for this study and a particular criteria was set to establish that the resultant hearing loss was only due to use of Gentamicin.

- i. Age: between 15-40 years to rule out congenital causes, specific fevers of childhood and presbycusis factor.
- ii. Occupation: not exposed to noise like factory workers, soldiers, heavy machine operators etc.
- iii. Past history: no history of ear infections, use of ototoxic drugs (like antimalarials).

diuretics, the pill, prolong use of salicylates) surgical procedures, nears head injury and tuberculosis.

- iv. Family History: no history of hear loss among the sibling (if any) and parental side.

Investigations:

Laboratory: Urinalysis, blood urea and creatinine, fasting blood sugar.

Audiological: Tuning fork tests and pure tone audiometry to establish the nature and degree of hearing loss.

Tympanometry - to rule out any middle ear defect.

RESULTS

Symptoms:

All the cases (100%) had their complaint combined with tinnitus. Five cases (25%) had a combination of hearing loss, tinnitus and vertigo.

Fifteen cases (75%) were treated by non-qualified private practitioners-four cases (20%) by qualified general medical practitioners and only one (5%) was treated by medical specialist.

Sex:

Out of twenty cases, twelve (60%) were female and eight (40%) males.

Age:

Three cases (15%) were between the age of 15-20 years.

Indications:

Thirteen cases (65%) were treated for the complaints of fever, sore throats and cough without establishing the nature of the illness or the organism.

Five cases (25%) received Gentamicin with a mere complain of fever.

Two cases (10%) for prolonged cough without investigating them.

Dosage:

Eleven cases (55%) received 80 mg per day as a single dose for a period of 5-7 days.

Four cases (20%) received 80 mg Gentamicin injections in divided doses for a period of 5-10 days.

Three cases (15%) received Gentamicin injections repeatedly and occasionally whenever they had fever. The dose could not be established from history of prescriptions.

Two cases (10%) received the drug for a period of one month for chronic cough. The dose was 80 mg in two divided doses.

DISCUSSION

20 cases of Orototoxicity are reported here due to injudicious use of the drug, Gentamicin. It is an established fact that aminoglycosides cause irreversible vestibulo-cochlear damage incapacitating the patients for the rest of their lives. It is a grave disability and a matter of great concern if imposed on the patient by non-qualified doctors. Unless such practices are rectified, more and more patients will have to suffer resulting in already existing falling standards of life at personal, familial, communal, and above all at national level. It is suggested that mass awareness should be cultivated among the practitioners and patients through publications, research, electronic media publicity and inservice training of medical staff. A policy should be adopted by the health authorities to check the non-qualified practitioners and make them accountable.

To at least minimize the prevalence of Otototoxicity, here reference is made to certain facts which should be kept in mind prior to the administration of ototoxic drugs in general and aminoglycosides in particular.

First of all patients should be screened through good history, examination and investigations to detect susceptible persons. The susceptible patients are those with impaired renal functions, hepatic failure,⁸ previous exposure to noise, head injuries, pregnancy and extremes of age i.e. the very young and the very old. Patients using other ototoxic⁷ drugs are at risk also because of their synergism, potentiating each others ototoxicity. These drugs apart from aminoglycosides, are salicylates, diuretics,¹ antimalarials (quinine and its derivatives), oral contraceptives,² anticonvulsants,³ cytotoxics,¹⁰ beta-adrenoreceptor blocking drugs,¹¹ anticoagulants¹² etc.

Secondly, renal functions tests should be carried out to know the renal status of the patient. The dose and duration of the drug should be calculated according to the renal status. Digital computer programmes¹³ have been evolved for patients with renal insufficiency. Nomograms have been constructed from which a suitable dosage can be obtained for any individual provided the serum creatinine levels, age, sex and body weight of the patients are known. The resultant information will help in producing serum concentration of the drug within the accepted therapeutic range. But in one study, nomograms have proved to be of little value in patients with renal failure as the maintenance dose varied greatly among the patients and were unrelated to serum creatinine levels. Also the maintenance dose is affected by the concurrent use of other antibiotics which are not aminoglycosides e.g. carbenicillin, cephradine and cephalexin. Despite these advanced methods it has been found that the previous approaches are the safest i.e. a combination of calculated dose and monitoring the peak and trough serum levels at regular intervals.¹⁴

Thirdly, the dose and duration of the therapy and severity of the illness should be considered. If the total dose is limited to

less than 2 gms and duration of therapy less than 10 days, a very low incidence of ototoxicity should be expected. Furthermore, if during therapy there is a hint of ototoxicity either subjective or objective the drug should be withdrawn altogether unless it is absolutely essential for the survival and future well being of the patient.⁶

Fourthly, prior to the commencement of the therapy, a baseline audiogram should be done to detect previous hearing loss. Then during the therapy serial audiograms should be done to detect hearing loss caused by the therapy. Tympanograms are of value in patients with previous conductive loss so as not to mistake it with the high frequency sensorineural hearing loss caused by ototoxic drugs. Transtympanic electrocochleography is a safe and reliable test to detect hearing loss but being an expensive procedure should be reserved for susceptible patients. To detect hearing loss, the above audiometric tests will suffice for most of the patients except in young children and the mentally handicapped, where Brain-stem Evoked Response Audiometry is employed. Unfortunately there is no recognised test to detect vestibulotoxicity and electromyography has never been found fruitful. So one has to rely on clinical examination and patients complain of vertigo.

As stated earlier, once established, ototoxicity due to aminoglycosides is irreversible and may progress after the withdrawal of the drug.⁹ These patients could only be extended symptomatic relief in the form of graduated exercises or vestibular sedatives for vertigo, and for hearing loss in the form of hearing aids, auditory training. It is only in the totally deaf and in advanced countries where cochlear implants are being used.^{15,16}

The above discussion points to the complexity of the whole topic which has been taken so lightly as is evident in our study.

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