Chloramphenicol Induced Hearing Loss

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ABSTRACT

Background: With the widespread use of the drug Chloramphenicol in treatment of typhoid fever, a number of cases of deafness are coming to light following such treatment. However the pattern and level of the resulting hearing impairment has not received much attention in the literature.
Method: A prospective study of ototoxicity over a 3- year period by means of questionnaire, clinical and otological examination and audiological tests to identify cases of significant hearing loss attributable to Chloramphenicol administration.
Result: Out of a total of 49 cases of drug ototoxicity seen during a 3-year period, 21 cases (43%) were due to Chloramphenicol and the deafness was most commonly associated with parenteral administration, though actual doses could not be ascertained from the histories. Hearing impairment was bilateral and severe to profound at onset in most cases (66%), with no improvement noticed even after cessation of drug use. Follow-up tests where possible, carried out 6 to 12 months later showed no improvement in thresholds.
Conclusion: Hearing impairment as a complication of Chloramphenicol usage is severe in most cases and associated with poor prognosis both in respect of chances of spontaneous recovery as well as the degree of concommitant hearing handicap. The need to prevent this grave iatrogenic tragedy by limiting the use of this drug is stressed.

KEY WORDS: Hearing Loss, Chloramphenicol, Typhoid Fever, Handicap

Introduction

Ototoxicity is now a well - recognised complication of the use of a large number of common drugs. Significant hearing loss has been commonly attributed to such drugs as the aminoglycoside antibiotics, salicylates, loop diuretics (ethacrynic acid, frusemide) and antimalarials (quinine, chloroquine).[1-3] A number of other antibiotics and other drugs are also known or suspected [4,5] to be ototoxic, often as result of inappropriate dosage or idiosyncracy and particularly in presence of poor renal function. However ototoxicity due to chloramphenicol has not received much attention in the literature. This broad-spectrum bacteriostatic antibiotic has for years been used effectively in treatment of enteric (typhoid) fever. [6]

The more commonly recognised side effect has been mainly haematological toxicity with bone marrow depression. Indeed its pos-sible ototoxic effect had been earlier discounted by Davies [7] in discussing adverse drug reactions. This report is part of an ongoing prospective study of the pattern and degree of hearing impairment as well as prognostic aspects of hearing impairment attributable to use of chloramphenicol.

Patients and Methods

The subjects entered into the ongoing study were all patients presenting at the Ear, Nose and Throat (ENT) Clinic of the University o Benin Teaching Hospital (UBTH) during a 3-year period (August 1997 to July 2000) with hearing loss following drug use. All cases at presentation were provided with a questionnaire in which personal biodata as well as details of the history were recorded. The information included duration of hearing loss and the interval between use of the incriminated drug and onset of deafness, the route of administration, dosage and duration of the drug, progression of the deafness as well as an indication of unilateral or bilateral loss. The presence of hearing loss, if any, before use of the drug was also noted. All patients had routine clinical examination, otoscopy and tuning fork tests. Pure-tone audiometry was carried out using an *Amplaid 300* clinical audiometer calibrated to ISO standards, in a sound - proof booth, at the frequency range of 250 - 8000 Hz, and the thresholds recorded, whilst tympanometry and acoustic reflex tests were done with Welch - *Allyn Autotymp* 262 middle -ear analyser. Follow-up repeat audiograms were carried out at 4 to 6 months intervals to determine progress or otherwise of the hearing loss; this is expected to be a continuing process. The hearing thresholds have been analysed and categorised according to the

degree of severity, using the average of the thresholds for the three speech frequencies of 500, 1000, and 2000 hertz (pure-tone average). The severity of hearing loss is rated as mild (25 - 40 dB hearing loss), moderate (40 - 70 dB), severe (70 - 90dB) and profound (> 90 dB).

Table 1: Time Interval From Drug Intake to Onset of Hearing Loss

Interval	No.
< 24 hours	1
1 - 7 days	4
1 - 4 weeks	9
1 - 6 months	4
> Months	0
Unspecified	3
Total	21

Table 2: Pure Tone Averages in 21 Patients (in dB HL)

Patient	Right ear	Left ear
1	35	47
2	73	98
3	105	105
4	116	110
5	90	105
6	55	53
7	80	18
8	25	12
9	58	23
10	15	25
11	95	100
12	103	35
13	66	110
14	72	100
15	65	68
16	106	110
17	105	100
18	90	105
19	98	110
20	96	88
21	103	96

Results

There were 21 cases of hearing loss due to chloramphenicol, accounting for 43% of the 49 cases of ototoxocity seen during the 3-year period. There were 11males and 10 females with an age range of 17 - 60 years (33.7 years).

Of the 21 cases, 17 had been treated as inpatients in various hospitals, for presumed diagnosis of typhoid fever except one female admitted for ruptured ectopic pregnancy. Four of the patients also received chloroquine and two gentamycin injections.

Route of administration and duration: In 14 cases chloram-phenicol was administered paren-terally, at least initially for varying

periods. Others had oral treatment. The total duration of drug treatment varied widely and exact information was not obtainable.

Most patients noticed deafness within 4 weeks of drug treatment (Table 1). Tinnitus in one or both ears was a common accompaniment, in 16 cases. None of the patients admitted having any hearing loss prior to use of the drug. Clinical examination did not reveal any significant findings in the ears, while tuning fork tests in all the cases showed mainly sensorineural deafness.

Table 3: Degree of Hearing Loss

Degree of Hearing Loss	No. (%)
Mild (25 - 45 dB)	4 (19%)
Moderate (45 - 70 dB)	3 (14%)
Severe (70 - 90 dB)	6 (29%)
Profound (> 90 dB)	8 (38%)
Total	21(100%)

Hearing Loss (Table 2): From the pure tone audiograms hearing loss (with pure tone averages of more than 25 db) was established to be bilateral in17 (81%)cases and unilateral in 4 (19%). Classification of the degree of hearing loss is shown in Table 3. A great majority of the cases (14, 66 %) suffered severe to profound hearing deficit.

Follow - up: Follow-up has been carried out for up to 12 months in 12 patients. No subjective improvement in hearing was reported in any instance. Repeat audiograms were only possible in 8 patients; in 7 there was no significant change, while one patient had a slight increase (worsening) in the average pure - tone thresholds.

Discussion

The ototoxic effects of the aminoglycoside antibiotics have been studied in some details, showing the histopathological changes in the hair cells of the cochlea as well as the probable mechanism of the resulting hearing (and vestibular) deficit. [8] Clinically these drugs are known to cause often progressive deafness, which is more likely with overdosage or poor renal function. The deafness from aspirin and antimalarial toxicity particularly quinine have also been well studied and is considered to result probably from vasoconstriction of the small vessels of the cochlea microvasculature; the hearing loss is potentially reversible in most cases after cessation of drug use. [2, 8] However, chloramphenicol has not been studied to the same extent to the author's knowledge. Thus the mechanism of action in causing ototoxicity is not clear, nor is the relationship

to dosage or duration of administration. The haematotoxic side effects of chloramphenicol have been recognised for long The drug may well exert the same deleterious effect on cochlear tissue as it does on the bone marrow. In particular the aplastic anaemia attributable to chloramphenicol is often irreversible, a similar situation to the severe deafness in most of our patients.

Furthermore, it is obvious that severe hearing loss, when bilateral as in most of our patients is likely to present greater difficulties and challenges in rehabilitation. It is noteworthy that most of the patients are young adults who are likely to experience great handicaps in occupational or educational activities as a result of the severe hearing
Losses. It was noted that in 4 of the patients gentamycin and chloroquine, two known potentially ototoxic agents, were also administered. However their contribution to hearing loss in the patients cannot be ascertained.

There is no known effective treatment for ototoxicity, once established, and the effectiveness of hearing aids tends to be limited with profound (>90db) hearing losses. It is therefore of paramount importance to prevent this potentially difficult to -manage defect
by exercising caution in the use of chloramphenicol as with other potentially ototoxic drugs. While appropriate dosages should be adhered to, it may also be possible to employ alternative, less harmful drugs for treating conditions such as typhoid fever.

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