Systemic absorption of topically applied chloramphenicol eyedrops

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SUMMARY Five children under the age of 9 years had topical chloramphenicol drops administered 2-hourly to each eye for 5 to 7 days. Systemic absorption was not detected by 2 sensitive assays for the drug. The hazards of topical chloramphenicol and reports in the current literature are discussed.

Two cases of suspected bone marrow depression due to topical application of chloramphenicol eyedrops have been reported (Rosenthal and Blackman, 1965; Carpenter, 1975), yet there has not been a published report on the systemic absorption of this drug from the human eye. It is known, however, that topically applied chloramphenicol is absorbed into the aqueous humour in man (Beasley *et al.*, 1975) and animals (George and Hanna, 1977); systemic absorption of the antibiotic has been detected after topical administration to the eye in animals.

Methods and materials

Five children under 9 years of age, all admitted for routine squint surgery, were given chloramphenicol topically (0.5% chloramphenicol Redidrops) 2-hourly to each eye over a 5 to 7 day period until a dose of between 40 and 52 mg of chloramphenicol had been administered (Table 1). Urine samples were collected within 24 hours of the last dose. These samples were subjected to analysis by gas-liquid chromatography (Least *et al.*, 1977) which with thiamphenicol as internal standard had a lower limit of sensitivity of 1 µg/ml. Polarography was also performed on these samples with a Southern Analytical Davies Diffraction Cathode Ray Oscilloscope. This method was found to be sensitive to levels of chloramphenicol from 0.05 µg/ml upwards when aqueous standards were examined. However, because of non-specific interference from the drug-free urine the practical working limit of the assay proved to be 1 µg/ml.

Results

These assays failed to detect any chloramphenicol in urine following the dosage schedules outlined. This

Table 1 *Patients' age and total dosage of drug applied to both eyes*

Patient	Age	Total dose (mg)
I	3	48
II	8	52
III	2	47
IV	5	47
V	4	40

was the case even when the extraction procedures described above were modified to allow concentration by a factor of 10:1. It thus appears that any chloramphenicol reaching the urine after ocular administration does not attain concentrations exceeding 0.1 µg/ml.

Discussion

The primary excretory pathway for chloramphenicol is via the kidneys; 80 to 90% of an oral dose is eliminated this way within 24 hours of administration (Goodman and Gilman, 1975). If systemic absorption of chloramphenicol is suspected from the eye, one would expect chloramphenicol to appear in the urine in higher concentrations than in the plasma. This effect has been confirmed in animal studies (Conner and Gupta, 1973). It would seem either that systemic absorption directly from the eye into the circulation or via the nasolacrimal duct and through the gastrointestinal tract does not occur in children or that urinary drug levels are below the levels detectable by apparatus at present available.

To reach a total dose of 45 mg a patient would have to use 1 drop of chloramphenicol 3 times daily for 60 days, as 1 drop of 0.5% chloramphenicol is equivalent to 0.05 ml and contains 0.25 mg of chloramphenicol (Parke, Davis & Co., personal communication).

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Two types of bone marrow effects are produced by systemic chloramphenicol administration (Editorial, 1970). Two cases have been reported implicating chloramphenicol eyedrops as the cause of the severe form of bone marrow aplasia. The report by Carpenter (1975) did not provide a definite link between this drug and the aplasia. The aplasia reported by Rosenthal and Blackman (1965), however, may well have been precipitated by chloramphenicol drops, as this patient had a strong family history of fatal aplastic anaemia precipitated by oral chloramphenicol therapy and had used topical drops for an extremely long time, namely, 2 years. In this type of case the possibility of fatal or serious results must be considered, as the likelihood of systemic absorption must be higher than in the shorter periods described above.

Conclusion

Chloramphenicol is a widely used effective topical antibiotic. Even though we were unable to detect systemic absorption of this drug after topical application to both eyes in children over a 5 to 7 day period, the possibility, however remote, still exists that systemic absorption may occur if the drug is used for excessively long periods of time. Ophthalmic practitioners should be alert to this potential hazard

and its complications. Further studies to detect systemic absorption of this drug over very long periods, preferably in inflamed eyes, are indicated.

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