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Systemic Absorption of Chloramphenicol Eye Drops

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ABSTRACT. Chloramphenicol blood levels were measured in 11 patients receiving chloramphenicol eye drops for a period from 9-19 days. Peripheral blood counts were also examined before and after therapy. Chloramphenicol was detected in the plasma of all the 11 patients. Levels above the lower limit of laboratory measurements were found in 7 of the 11 patients (Range 2.5-5 mg/ml). There was no change in the peripheral blood count following the use of the drug. The bone marrow aplasia reported with topical chloramphenicol drops is most likely to be due to idiosyncratic reaction rather than direct dose related reaction.

KEY WORDS: Chloramphenicol, peripheral blood counts, bone marrow aplasia, idiosyncracy.

Introduction

Topical chloramphenicol is widely used by ophthalmologists in the U.K.[1] and many other countries[2,3] due to its broad spectrum activity and low price. Since 1982, we have been using this drug in the treatment of most ocular infections, all pre- and most post-operative procedures. None of our patients developed bone marrow suppression.

Chloramphenicol blood level measurements have been recently introduced to this department, using Emit chloramphenicol assay. We conducted this study to find out:

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A. If chloramphenicol is absorbed systematically following chloramphenicol eye drops and its blood level.

B. If any change occurs in the blood cell counts following chloramphenicol eye drops therapy.

Material and Methods

Eleven patients, 5 females and 6 males, were consecutively chosen for the study. Eight of them were admitted to the University Hospital for cataract extraction, and three for Trabeculectomy. Their ages ranged from 1 to 90 years with a mean of 55.3. All patients were put on chlorampenicol 0.5% eye drops (chloroptic, allergan); 3 days pre-operatively, four times daily in both eyes and continued post-operatively for a total of 9 to 19 days. The total amount of administered chlorampenicol was calculated according to Trope's suggestion[4]. This ranged from 18-38 mg. Table 1 summarizes the data of the eleven patients studied. Blood samples were taken within 2-3 hours of the last dose of the drops, and analyzed by Emit chloramphenicol assay[5] (Syva Company, Palo Alto, Ca.) which is a homogenous enzyme immunoassay technique. The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase for binding sites on chloramphenicol antibody, therefore drug concentration in the sample can be measured in terms of enzyme activity. Active enzyme converts oxidized nicotimide adenine dinucleotide (NAD) to (NADH), resulting in an absorbance change that is measured spectrophotometrically. The test's accuracy, precision, sensitivity and specificity are comparable to high-performance liquid chromatography test[5]. It accurately quantitates chloramphenicol concentration in human serum containing 2.5 to 40 μg/ml of the drug. This implies that, chloramphenicol serum level of less than 2.5 μg/ml will be detected, but it may not give the exact concentration and this could be checked against zero control.

TABLE 1. Patient's age, sex, duration of therapy and total dosage.

Case no.	Age (years)	Sex	Duration of therapy (days)	Total dosage
1	68	M	19	38
2	1	F	11	22
3	75	M	9	18
4	60	M	12	24
5	61	M	10	20
6	90	M	14	28
7	50	M	13	26
8	70	F	12	24
9	60	F	18	36
10	15	F	9	18
11	58	M	12	24

Blood samples were taken for peripheral blood cell counts before start, and within hours after the discontinuation of chloramphenicol. Paired student's test was used for statistical analysis.

Results

Chloramphenicol was detected in the serum of all the 11 patients. Its quantity could be measured accurately only in 7 patients, the other 4 patients had levels less than 2.5 μg/ml. In all patients, the chloramphenicol serum concentration was less than 5 μg/ml (Table 2). This study has failed to show any statistically significant change in the white blood cells count ($p = 0.5$), red blood cells count ($p = 0.4$) or platelets counts ($p = 0.3$), in peripheral blood before and after the use of chloramphenicol eye drops (Table 3).

TABLE 2. Chlorampenicol blood levels after topical use.

Case no.	Chloramphenicol blood level (μg/ml)
1	2.50
2	4.5
3	2.50
4	2.50
5	4.5
6	< 2.5
7	<2.5
8	4.5
9	2.5
10	< 2.5
11	< 2.5

TABLE 3. Peripheral blood cell count before and after administration of the drug.

		1	2	3	4	5	6	7	8	9	10	11
WBC count	(B)	8.	11.1	5.1	4	6.2	8.2	5.5	11.9	8.6	7.7	3.2
12/L × 10	(A)	6.1	10.5	7	5.5	8.3	5.2	7.2	11.4	10.1	7.4	4.7
RBC count	(B)	4.64	4.57	4.64	4.6	5.41	4.06	5.38	4.69	3.66	5.82	4.4
12/L × 10	(A)	4.92	4.33	3.82	4.8	5.38	4.71	5.08	4.37	3.73	5.63	4.0
Plateletes counts	(B)	261	351	286	203	315	314	183	281	227	415	277
9/L .× 10	(A)	274	441	282	234	234	279	336	199	248	263	292

(A)= Before treatment (B) = After treatment

Discussion

Fatal aplastic anaemia has been reported in two patients following chloramphenicol treatment, one patient using both drops and ointment[6] and the other one after eye ointment only[7]. Reversible bone marrow suppression has been reported in two patients following chloramphenicol eye drops[8,9]. In all cases, systemic absorption of chloramphenicol had been suggested, but not proved. Trope *et al.*[4] failed to detect significant chloramphenicol urine levels in the 5 patients they studied. They concluded that, systemic absorption does not occur with chloramphenicol eye drops[4].

Chloramphenicol concentration has not yet been reported in human serum following topical application. It has been reported that chloramphenicol may produce toxic effects on the bone marrow by its blood level[10], or it may cause suppression of the bone marrow by hypersensitivity (idiosyncratic) reaction which is not dose related[11]. It has been found that human serum levels of chloramphenicol greater than 25 μg/ml are associated with reversible bone marrow suppression[12-14], and levels of 40 μg/ml or higher are associated with gray syndrome in infants[13,14].

Our study has shown that chloramphenicol blood level following topical administration is markedly below the toxic level.

Idiosyncracy could be the most acceptable theory for explaining bone marrow suppression following the topical use of chloramphenicol.

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امتصـــــاص قـــطرة الكلورامفنيـــكول

عدنان المرزوقي و أسامة باديب
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المستخلص . تم قياس نسبة الكلورامفنيكول في الدم في ١١ مريضًا بعد تعاطيهم قطرة الكلورامفنيكول بعد مدة تتراوح بين ٩-١٩ يومًا . كما تمت معرفة التعداد الدموي المحيطي قبل استعمال القطرة وبعدها .

أمكن اكتشاف الكلورامفنيكول في الدم في جميع المرضى الذين تم فحصهم ، وفي ٧ مرضى من الأحد عشر كان المستوى أعلى من الحد الأدنى اللازم لاكتشاف نسبة الدواء (٢,٥ - ٥ ميكروجرام) .

لم يكن هناك أي تغير في التعداد الدموي المحيطي بعد استعمال الدواء .

إن اللاتسنج النقي للكلورامفنيكول في العين ، في أغلب الظن ناتج عن التحساس الذاتي وليس نتيجة زيادة في كمية الدواء في الدم .