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Letter to the Editor

Brief history of chloramphenicol in ophthalmology. Is it safe to use?☆



Breve historia del cloranfenicol en oftalmología. ¿Es seguro su uso?

Dear Sir,

The Increase of antibiotic resistance is a worldwide problem which has renewed interest in antibiotic drugs that were discontinued due to toxic side effects. One example is the history of chloramphenicol in the field of ophthalmology.

Chloramphenicol is an antibiotic developed in 1947¹ and initially regarded as a very promising drug due to its broad range of action. However, the safety of the ophthalmic preparations based on chloramphenicol became controversial since a case was reported in 1965² that established a possible relationship of the antibiotic with aplastic anemia.

Is the risk of developing aplastic anemia secondary to topical chloramphenicol the same as the risk of oral administration? On the one hand, publications such as that by Doona and Walse³ stated without evidence that it could be similar in both forms. On the other, lower risk when administering chloramphenicol orally was proposed due to exhibiting lower systemic absorption and not being subject to the necessary bacterial transformation to convert chloramphenicol in the toxic substance (dehydrochloramphenicol) for the DNA of the hematopoietic stem cells.⁴

In turn, McGhee and Anastas⁵ reported that data on the risk of idiosyncratic aplastic anemia produced by topical chloramphenicol remained inconclusive with a maximum death rate of 1 in 50,000–90,000. Said authors compared this rate with the risk of fatal anaphylaxis caused by penicillin therapy (through any pathway) which was quite similar, i.e., 1 in every 100,000.

The most specific study on the incidence of aplastic anemia associated to topical chloramphenicol was conducted by Laporte et al.,⁶ that estimated an incidence of less than 1 case per million treated patients. Said study collected the 10 aplastic anemia cases reported up to that date (1993) and reported the existence of concomitant diseases and the use of other

drugs during treatment with chloramphenicol in the majority of these cases.

Subsequently, the cases reported between 1993 and 2013 were reviewed^{7,8} including the databases on spontaneous reports (FDA, WHO and the national Casey Eye Registry) totaling 31 new cases of possible association between aplastic anemia and topical chloramphenicol, the reports of which were also incomplete. Once again, the authors of said studies considered the existence of an exaggerated reaction in the restriction of chloramphenicol for ophthalmological use. Similarly, they indicated that it was not possible to reach a definitive decision due to the difficulty of studying in clinic practice such a highly infrequent, unpredictable and deadly adverse reaction, leaving the possibility of conducting medullar toxicity studies during treatment as a utopian dream.

What is the current use of said antibiotic? Ophthalmic chloramphenicol is experiencing a comeback and is being widely used for treating and preventing ocular surface infections due to its broad range of activity, low resistance rates and satisfactory tolerance.

One of the latest studies⁹ supports the use of chloramphenicol due to its limited resistance rate compared to fluoroquinolones due to the low induction of bacterial resistance and antibiofilm activity as well as for its hypothetically low impact on the alteration of the ocular microbiota, which is yet to be researched.

In summary, chloramphenicol is a broad range antibiotic with demonstrated efficacy and good tolerance for daily clinic practice. In addition, it is more affordable than other new generation antibiotics available at present in the market.

To conclude, it would be recommendable to initiate a comprehensive campaign to minimize the pace of antibiotic resistance by making rational use of antibiotics, studying

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emerging microorganisms and optimizing the use of old antibiotics that are capable of maintaining their susceptibility profile.

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