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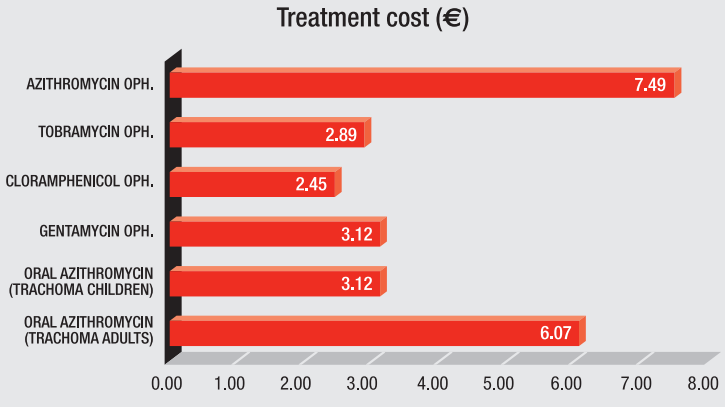
Azithromycin ophthalmic solution▲ (Azydrop®) for purulent bacterial or trachomal conjunctivitis

Similar efficacy at a higher cost



- Azithromycin in topical ophthalmic form is indicated in the treatment of susceptible strains of bacterial conjunctivitis and trachoma related conjunctivitis caused by *Chlamydia trachomatis*.
- The majority of purulent bacterial conjunctivitis cure spontaneously, and azithromycin has shown a similar efficacy and safety profile to tobramycin. There are no trials comparing other antibiotics.
- Although its posology is much more convenient, its cost is considerably higher than the other ophthalmic alternatives available.
- In the management of trachoma it has not proven superior to the administration of a single dose of oral azithromycin.

Therapeutic indications[1]

Azithromycin in topical ophthalmic solution is indicated in the treatment of infectious conjunctivitis caused by susceptible strains: purulent bacterial conjunctivitis and trachoma related conjunctivitis caused by *Chlamydia trachomatis*.

Mechanism of action and pharmacokinetics

Azithromycin is a second generation macrolid belonging to the azolid class[1]. It inhibits the synthesis of bacterial proteins by binding itself to the 50 S ribosomal subunit thus impeding peptide translocation[1,2]. It is generally active against gram positive microorganisms that cause bacterial conjunctivitis (except for meticyllin-resistant staphylococci). It is 2.4 times less active than erithromycin in its action against staphylococci and streptococci, including pneumococcus. Bacterial resistance to azithromycin is increasing[3].

Topical azithromycin should not be the first choice for treatment

After the administration of azithromycin at the recommeded dose in patients with bacterial conjunctivitis it has not been detected in the blood stream (detection limits of 0.0002 µg/ml in plasma)[1].

Posology and method of administration[1]

Administration of one eye drop in the fornix of the conjunctiva is recommended twice daily –morning and evening– for three days.

The qualification assigned to the drug was agreed by the Drug Assessment Committees of Andalusia, Basque Country, Catalonia Institute of Health, Aragon and Navarre. The current report is based on the available information and is susceptible to be updated according to the latest evidence. Let us remind the reader about the importance of notifying the Pharmacovigilance Centre when there are suspicions of adverse reactions to drugs.

There is no sufficient experience in children under two years with this agent in the treatment of purulent bacterial conjunctivitis. In children between 1-2 years no dose adjustments are required for trachoma related conjunctivitis. In children under 1 year there is no sufficient experience.

Patients should be advised to thoroughly wash their hands before and after instillation of the eye drops; avoid touching the eye and eye lids with the single dose dispenser, and to adequately dispose of the eye drop dispenser after use and not keep it for future use.

Clinical efficacy

The efficacy of ophthalmic azythromycin solution in the treatment of bacterial conjunctivitis has been evaluated in a controlled clinical trial compared to placebo[8] and also in another comparative study with ophthalmic tobramycin solution[10]. In addition there is also another comparative clinical trial comparing ophthalmic azythromycin solution in single dose with oral azithromycin in the treatment of trachoma[7].

Bacterial conjunctivitis

When comparing with placebo, the efficacy of azithromycin was evaluated after administering a 1% solution twice daily for the first 2 days, followed by a single dose a day for 3 days. Clinical recovery was observed in 63.1% of the patients treated with azithromycin (82/130) compared to 49.7% of the patients under placebo (74/149) (difference of 13.4% CI 95%, 1.9%-25%)[8].

The trial comparing azithromycin with tobramycin was a multicenter, randomized, simple blinded non-inferiority trial carried out in 1,043 patients (adults and children) with purulent bacterial conjunctivitis. The safety profile and efficacy of 1.5% azithromycin solution (twice daily for 3 days) was compared to 0.3% tobramycin (1 drop/2 hours for 2 days followed by 1drop/4 hours 5 days). Clinical improvement was evaluated and cultures were carried out in baseline conditions on the 3rd and 9th days of treatment. Nevertheless the external validity of the study is questionable as it is a non-inferiority trial and no double blinding was applied[10].

Trachoma

In the management of trachoma 1.5% opthalmic azithromycin solution applied for 2 or 3 days was compared to a single oral dose of azithromycin at a dose of 20 mg/kg in one clinical trial evaluating the efficacy and safety profile of both treatments. This was a randomized, controlled and double blind non-inferiority trial including 670 children between one and ten years of age. In this study the efficacy, based on clinical curation, included rates of 93% with opthalmic azithromycin given for 2 days, 96.3% in those patients who receive the opthalmic solution for 3 days and 96.6% in those who took a single oral dose of azithromycin. All patients were evaluated after 60 days[7].

Safety

Adverse reactions

In a multicenter, randomized and double blinded trial comparing azithromycin with tobramycin the objectives were to evaluate the safety profile and tolerance but not efficacy[9]. The trial included 743 patients (adults and children) diagnosed with bacterial conjunctivitis. The patients were randomly assigned to 1% azithromycin (n=365; twice daily for 2 days and once a day for the next 3 days) or 0.3% tobramycin (n= 378; 4 times a day for 5 days). No differences were observed between the two treatments, though azithromycin concentration tested (1.0%) was inferior to that of the marketed form (1.5%)[9].

In the clinical trial, the most frequent adverse reaction observed (≥10%) was eye discomfort (pruritus, burning, stinging and itching) on instillation. With less frequency (1-10%) there was blurred vision, eyelid swelling, and sensation of having a foreign body in the eye[1].

Precautions

This treatment should not be employed as profilaxis for bacterial conjunctivitis in new borns.

Patients should be informed that it is not necesary to continue with the instillation of the eye drops after 3 days of treatment, despite residual symptoms of bacterial conjunctivitis that may be present.

Improvement of symptoms usually occurs within 3 days. If there are no signs of improvement then the diagnosis should be reconsidered.

Patients with bacterial conjunctivitis should not use contact lenses.

Use in special situations

Pregnancy: there is no information on the use of azithromycin solution during pregnancy and therefore precaution should be taken. **Breast feeding:** it is possible during treatment. **Children:** not recommended in children under 2 years except in trachoma related conjunctivitis which can be used in children over one year old.

Interactions

In the case of concomittant use with other eyedrops, an interval of 15 minutes should be respected between the instillation of the eyedrops. Azithromycin should be instilled in last place.

Place in therapeutics

Given that the majority of bacterial conjunctivitis are self limiting and cure spontaneously[4,11], the use of azithromycin in ophthalmic solution has proven effective in cases of purulent bacterial conjunctivitis and presents good tolerance, with no significant differences observed with regard to the rates of curation when compared to the alternatives. Although its posology is comfortable for the patient, its cost is considerably higher than other ophthalmic alternatives[11].

In the management of trachoma, azithromycin solution has not shown greater efficacy than the single dose of oral azithromycin which is the elective treatment.

Presentations

Azydrop® (Théa Laboratory) 15 mg/g eye drops in solution. Box contains 6 single dose dispensers. Prescription medicine only.

References

A full report on azithromycin eyedrops can be consulted at www.dtb.navarra.es

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