

REVIEW OF OPHTHALMOLOGY SECTION OF WHO MODEL LIST OF ESSENTIAL MEDICINES

Anti infective agent

Medicine suggested for inclusion

Ciprofloxacin: 0.3 % eye drops

Application submitted by

Sight Savers International and The Vision 2020 Technology Group

Therapeutic Use

Prevention of postoperative infection viz., after cataract and glaucoma surgery. Also as a prophylactic agent.

Background

Antibacterial already included in ophthalmological section of WHO Model List of Essential Medicines are gentamicin eye drops 0.3 % and tetracycline eye ointment 1 %. The applicant now suggests adding ciprofloxacin 0.3 % eye drops in the list.

Application

The application provides all information about the public health relevance and the need of the suggested medicine for the majority of population. References have been quoted to justify the disease burden. However, the evidence for comparative efficacy and safety is lacking. The applicant has referred to Cochrane review but the review does not provide any information on evidence. I have been able to find some published studies. Most of them are inconclusive. They lack proper study design. Only in one randomized clinical trial, topical ciprofloxacin 0.3 % was compared with cefazolin (50 mg / ml) and fortified gentamicin (14 mg / ml) in suspected corneal ulcer. 70.6 % patients in ciprofloxacin group and 62.5 % patients in cefazolin + gentamicin group (statistically not significant) showed therapeutic response as per outcome criteria included in the study. However, visual improvement was 66.7 % in ciprofloxacin group and 46.7 % in cefazolin + gentamicin group. Authors concluded that treatment with topical ciprofloxacin in suspected bacterial corneal ulcer should be considered as an alternative to standard therapy.

Comments

Ciprofloxacin is a broad spectrum antibiotic. It has been approved in many countries for use in bacterial, conjunctivitis, keratitis and corneal ulcer. At present two antibacterials (gentamicin eye drops and tetracycline ointment) are included in the WHO Model List of Essential Medicines. Gentamicin is not a broad-spectrum antibiotic. If one goes by level III evidence i.e., BNF, STGs and textbooks, ciprofloxacin has been recommended as one of the preferred antibacterial agent in conjunctivitis keratitis and corneal ulcer. Out of two antibacterials listed in WHO Model List, tetracycline is not a preferred choice as per above evidence. I suggest that ciprofloxacin may be included in the list with "Square Box" as there are other flouroquinolans viz., Ofloxacin, lomifloxacin that are available.

Reference

Kosrirukvongs P, Buranapongs W. Topical Ciprofloxacin for bacterial corneal ulcer: J Med Assoc Thai. 2000;83(7):776 – 82.

Anti infective / Steroid Combination

Medicines Suggested for Inclusion

Betamethasone + Neomycin ointment (strength not mentioned)

Dexamethasone + Gentamicin (0.1 % + 0.3 %)

Application Submitted by

Sight savers International and Vision 2020 Technology Working Group

Therapeutic Use

Postoperative treatment after cataract and glaucoma surgery.

Background

In WHO Model List of Essential Medicines, prednisolone 0.5 % eye drops and gentamicin 0.3 % eye drops have been included. Applicants suggest including combination of corticosteroid and antibacterial agent.

Evidence for Comparative Efficacy and safety

The Public Health need for inclusion of said combination has been adequately explained. However, the application does not provide evidence on superiority of combination over individual drugs. It is mentioned in ophthalmological section of BNF that use of a combination product containing corticosteroid with anti infective agent is rarely justified. As a policy matter also, criteria for selection of essential medicines, combination product having no proven superiority in terms of efficacy and safety should not be included in the list

Recommendation

In view of above, I do not recommend combination of corticosteroid and anti-infective drug to be included in the WHO Model List of Essential Medicines.

Intraocular Lens Insertion Lubricant

Medicine suggested for Inclusion

Hydroxypropylmethylcellulose (HPMC) (strength not mentioned)

Application Submitted by

Sight Savers International and Vision 2020 Technology Working Group

Therapeutic Use

Viscoelastic substance used in cataract surgery

Background

In WHO Model List of Essential Medicines, viscoelastic substances are not included. The applicants now suggest including HPMC in the model list.

Application

The application provides the justification and public health need for inclusion of said medicine. Phacoemulsification and intraocular lens implantation (ant & post) are being carried out throughout the world both in adults and children. However, application does not provide evidence on need, efficacy and safety of HPMC for inclusion in the list.

Reviewer's Search

The need for the use of viscoelastic substance in cataract surgery has been well documented in some of articles^{1,2}. There are different types of viscoelastic substances available. Sodium Hyaluronate 1 % and HPMC 2 % are most commonly used for this purpose. The major aim for the application of viscoelastic substance in cataract surgery is prevention of corneal endothelial cell loss.

In three controlled clinical studies^{3,4,5} HPMC has been compared with Sodium Hyaluronate. Kammann J et. al. reported that both substances are of equal efficacy in cataract surgery. However, the authors have recommended the use of HPMC due to lower cost.

Ray Chaudhuri et. al compared the effects of 2 % HPMC with 1 % Sodium Hyaluronate on different parameters in small incision cataract surgery with implant. Authors concluded that 2 % HPMC is superior to 1 % Sodium Hyaluronate in protecting the corneal epithelial cells. The effect on corneal thickness was same with both substances. However, HPMC was associated with slightly higher IOP one-day post operatively. Authors recommended that HPMC is as effective as Sodium Hyaluronate and being cheaper can be used in cataract surgery.

In another study, Agarwal et. al. has compared HPMC 2 % with control (No viscoelastic agent) during trabeculectomy in patients suffering from glaucoma and concluded that intracameral injection of 2 % HPMC during trabeculectomy helps to maintain ant. Chamber depth and reduces incidence of complication.

Reviewer's Recommendation

Above evidence reveals that (a) viscoelastic agent is needed during cataract surgery, and (b) HPMC and Sodium Hyaluronate have been widely used and investigated. Both, HPMC and Sodium Hyaluronate, are equally effective and safe. However, HPMC is cheaper and should be included in the WHO Model List of Essential Medicines.

References

1. Steele AD, Andrews V. Methylcellulose for endothelial cell protection: Aust N Z J Ophthalmol. 1988 Aug; 16(3): 251 – 4.
2. Hessemer V, Dick B. Viscoelastic substances in cataract surgery. Principles and current overview: Klin Monatsbl Augenheilkd. 1996 Aug-Sep;209(2-3):55-61.
3. Kammann J, Dornbach G, Vollenberg C, Hille P. Controlled clinical study of two viscoelastic substances: Fortschr Ophthalmol. 1991;88(5):438-41.
4. Ray-Chaudhuri N, Voros G M, Sutherland S, Figueiredo FC. Comparison of the effect of sodium Hyaluronate (Ophthalin) and hydroxypropylmethylcellulose (HPMC-Ophtal) on corneal endothelium, central corneal thickness, and intraocular pressure after phacoemulsification: Eur J Ophthalmol. 2006Mar-Apr;16(2):239-46.
5. Agarwal H C, Anuradha V K, Titiyal J S, Gupta V. Effect of intraoperative intracameral 2 % hydroxypropylmethylcellulose viscoelastic during trabeculectomy. Ophthalmic Surg Lasers imaging.2005 Jul-Aug;36(4):280-5.