

WHO Essential Medicines List – Ophthalmological Preparations

1. Current data

Data from the WHO estimated that there were 161 million people in the world with visual impairment of whom 37 million are blind and 124 million have low vision (WHO, 2004 - see references). More than 82% of blind people are over 50 years of age. Approximately 90% of blind people live in developing countries; cataract is the major cause of blindness.

2. Childhood blindness

Childhood blindness is a significant problem. There is an estimated 1.4 million blind children below the age of 15 and a further 4.2 million children with visual impairment (WHO, 2004). There is no incidence data on childhood blindness from developing countries (Johnson *et al* 2003), but it is estimated that approximately 500,000 children become blind each year, the majority of whom live in developing countries.

Cataract is known to be one of the leading causes of childhood blindness with an estimated 200,000 children becoming blind with bilateral cataract every year (Foster *et al* 1997). Congenital abnormalities such as cataract and glaucoma, and external potentially blinding eye diseases, e.g. viral and fungal infections, are more difficult to identify in children than adults. A study in Uganda (Wadell 1998) showed that corneal ulceration was found to be second only to cataract as the main cause of blindness in children. Although the association with fungal keratitis is not confirmed in countries with high humidity (Johnson *et al* 2003), there is a definite increase in risk of ulceration following trauma with an organic agent (see 4.2).

Late presentation of these diseases is a major contributing factor to poor outcome after surgical or medical interventions (Eriksen *et al* 2006). The pharmaceutical rehabilitation of children is complex and long term. These, and the socio-economic conditions associated with children-in-poverty, demonstrate the need to focus health intervention policies towards this social group.

3. VISION 2020 and WHO

Seventy-five percent of blindness is estimated to be avoidable. It was to address this that WHO and the International Agency for the Prevention of Blindness established VISION 2020: The Right to Sight, a global initiative for the elimination of avoidable blindness by the year 2020. VISION 2020 was launched in February 1999. The World Health Assembly has, since then, passed two resolutions on prevention of blindness: WHA56.26 in 2003 and WHA59.25 in 2006. The latter urged Member States to make available essential medicines needed for eye care. It is for this reason that the VISION 2020 Technology Working Group, of which Sight Savers International is the Chair, decided to approach WHO with some suggested changes to the ophthalmic section of the WHO Essential Medicines List

4. Addressing the current needs in eye care through pharmaceutical products.

Prevention of blindness is now higher on the global health agenda. In implementing the recommendations of WHA 59.25 and recognising the advances in ophthalmic practice, it is important that the ophthalmological preparations section of the Essential Medicines List addresses the challenges of modern eye care. This will require changes to the current list.

4.1. Cataract surgery. The surgical methods for correcting cataract blindness in children and adults have changed over time as more sophisticated surgical equipment and techniques have been developed. Advances such as foldable, single piece intraocular lenses, and small incision paediatric and adult cataract surgery, and the related pre-and post-operative treatments, are not reflected in the current pharmaceuticals listed. Studies and results from the field (Yorston 1998, Lam *et al* 2001, Mwende *et al* 2005) have indicated that the visual acuity outcomes from children who have received intraocular (IOL) surgery are encouraging, but immediate and long-term pharmaceutical care is, along with other factors, essential to ensure optimal visual potential. The following points are important:

4.1.1. To insert an IOL into the eye of a child or adult (Extra Capsule Cataract Extraction and IOL), it is necessary to utilise more instruments and fluids during the surgical procedure. In doing so there is an associated increased risk of infection that was not necessarily as apparent with previous surgical techniques (Intra Capsule Cataract Extraction) (Barry *et al* 2006). The use of a broad-spectrum antibiotic, e.g. Ciprofloxacin, that is effective against gram-negative and gram-positive bacteria, minimises the potential risk of endophthalmitis occurring from multiple instrumentation and wet or damp hand-pieces. The use of small incision surgery assists in reducing the risk of infection but it alone cannot assure that endophthalmitis will not occur.

4.1.2. The insertion of any prosthesis into the body is associated with a risk of rejection. To address this the use of steroid and antibiotic combination drugs e.g. Betamethasone and Neomycin and/or Gentamycin 0.3% and Dexamethasone 0.1% immediately after surgery will assist in counter-acting any likelihood of rejection.

4.1.3. The intraocular lens is initially inserted into the anterior chamber of the eye. Methylcellulose (HPMC) is used as an agent to protect the endothelium while the IOL is rotated and placed into the posterior chamber of the eye. Without its use, especially in the diametrically smaller eyes of children, there could be a much higher incidence of permanent endothelial damage.

4.1.4. In the event that the posterior capsule is ruptured it is possible to insert an anterior chamber lens. In order to do this the eye is miodes. Pilocarpine 0.5% is the drug of choice.

4.2. Fungal keratitis. Failure to recognise and treat fungal keratitis can lead to permanent damage to the stromal layer of the cornea and impair corneal clarity. It is rarely a bilateral condition but children and adults can become monocularly blind. If the fungal infection is not adequately treated with effective anti-fungal agents, the integrity of the globe is jeopardised.

Research has shown that there is a higher incidence of fungal keratitis in developing countries for two reasons. Firstly, children and adults have a higher incidence of traumatic injuries to the eye (Johnson *et al* 2003), many of which are related to corneal abrasions with vegetable matter as they tend livestock and carry out agricultural work. Secondly, as the ambient temperature increases, countries with high humidity and moist climates, e.g. central and southern Africa and the Indian sub-continent, have climates that are conducive to fungal growth. Topical Natamycin 5% is suggested (Johnson *et al* 2003) as the first line of treatment if fungal keratitis is suspected on clinical examination and following corneal scraping. In the developing world fungal keratitis affects the poorest who cannot afford the long-term medical treatment for a corneal ulcer. The Essential Medicines List can assist in making the treatment more affordable and widely available to people living in poverty.

5. Accessing essential pharmaceutical medicines in the field

The WHO Essential Medicines List is an important tool in making the case for including specific items on national essential pharmaceutical lists. National Pharmaceutical Boards refer to the List as the benchmark for pharmaceutical products that may be exempted from import duty and hence quickly and efficiently passed through custom procedures to the distributing eye units. These factors have an effect on lowering prices and helping to make essential pharmaceuticals affordable to all patients.

6. VISION 2020 Technology Working Group

The VISION 2020 Technology Working Group is a sub-committee of VISION 2020 with the objective of acting as a focal point for IAPB regarding all matters to do with technology in support of Vision 2020 objectives. The group is responsible for maintaining and updating the *Standard List for a Vision 2020 Eye Care Service Unit 2006/7*, www.v2020.org. The objective of the Standard List is to provide guidance on essential medicines, equipment, instruments, optical supplies, and educational resources for delivering effective eye care services in developing countries. The pharmaceuticals suggested for inclusion in the WHO Essential Medicines List are taken from the VISION 2020 Standard List.

At the June 2006 meeting of the group the Ophthalmological Preparations section of the WHO Essential Medicines list (March 2005, page 20) was reviewed. It was noted that the section needed revision. These revisions, if in place, could, the Group felt, provide advice for Governments on the pharmaceutical items essential for eye units.

A list of drugs was compiled by the Group (Appendix 1), which includes ophthalmic medical advisors, as essential pharmaceuticals to complement the surgical advances in cataract surgery and related post-operative treatments required for intraocular lens surgery. Treatments for external viral, fungal, and allergic, and immuno-

suppressed related eye diseases are also needed to supplement the existing list. It is suggested that the medicines in Appendix 1, which are appropriate for adult and paediatric use, should be included in the WHO Essential Medicines List.

It has been agreed by all parties that WHO is initially requested to remove IDU from the Ophthalmological Preparations section and substitute with Acyclovir Eye Ointment 3% and Acyclovir Tablets 200mg. Cochrane Paper (2005, revision 3) indicates that Acyclovir over 7 and 14 (Appendix 3) days offers improved healing.

7. Collaboration with the Cochrane Eyes and Vision Group

Assistance was sought from the Cochrane Eyes and Vision Group for recent evidence-based data to support the recommended revisions to WHO. Unfortunately little up-to-date data is available (Appendix 2). Assistance would be required for further reviews or updating of existing reviews.

Contact person at Cochrane Eyes and Vision Group:

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8. Conclusion

Sight Savers International and the VISION 2020 Technology Working Group request WHO to consider deleting IDU from the Essential Medicines List with immediate effect, and start the process to review the case for inclusion of the medicines in Appendix 1.

References

Barry P., Seal D., Gettinby G., Lees, F., Peterson M., Crawford R., 2006. ESCRS study of prophylaxis of postoperative endophthalmitis after cataract surgery: Preliminary report of principal results from a European multicenter study, *Journal of Refractive Surgery* **32**, page 407 – 410.

Bulletin of the WHO, November 2004, 82 (11).

Eriksen J.R., Bronsard A., Mosha M., Carmichael D., Hall A., Courtright P. 2006. Predictors of Poor Follow-up in Children that had Cataract Surgery, *Ophthalmic Epidemiology* **13**, page 237 – 243.

Foster A., Gibert C., Rahl J.1997. Epidemiology of cataract in childhood: a global perspective, *Journal of Cataract Refractive Surgery* **23**, page 601-604.

Johnson G., Minassian D., Weal R. West S., 2003. The Epidemiology of Eye Diseases, 2nd Edition, OU, UK

Lam A., Seck C., Gueye N.N., Faye M, Pintart D. 2001. Cataract surgery with posterior chamber lens implantation in Senegalese children less than 15 yrs old. *French Journal of Ophthalmology* **24**, page 590-595.

Mwende J., Bronsard A., Mosha M, Bowman R., Geneau R., Courtright P. 2005. Delay in presentation to hospital for surgery for congenital and developmental cataract in Tanzania. *British Journal of Ophthalmology* **89**, page 1478 – 1482.

Wadell K 1998 Childhood blindness and low vision in Uganda *Eye* **12**. page 184-192

Yorston D. 1998. Are intracocular lenses the solution to cataract blindness in Africa? *The British Journal of Ophthalmology* **82**, page 469-471.

**APPENDIX 1:
SUGGESTED FOR INCLUSION**

| Preparation | Use and reasons for inclusion | Target group | Comments |
|--|---|---|-----------------------------------|
| Anti- infective agents | | | |
| Ciprofloxacin Eye Drops 0.3% | Prevention of post-operative infection. Drug of choice after cataract and glaucoma surgery. In some instances may be used before surgery. | Children and adults | |
| Anti-infective/steroid combination | | | New sub-category |
| Betamethasone + Neomycin Ointment | Immediate post-operative treatment after cataract & glaucoma surgery | Children & adults | |
| Gentamycin 0.3% + Dexamethasone Eye Drops 0.1% | Long term treatment of post-op inflammation after cataract surgery | Children & adults | |
| Miotics | | | |
| Pilocarpine Nitrate Injection 0.5% | Used peri-operatively to reduce the pupil size in Anterior Chamber Intra-Ocular Lens surgery | Adults (AC IOL surgery is contra-indicated in children) | |
| Anti-fungals | | | New sub-category |
| Natamycin 1% Eye Ointment | Treatment of fungal keratitis | Children & adults | |
| Natamycin 5% Suspension | As above | Children & adults | |
| Intraocular Lens Insertion Lubricant | | | New sub-category |
| Methylcellulose HPMC for intraocular use (visco-elastic) | Used during Anterior and Posterior Intra Ocular lens cataract . | Children: vital for paediatric surgery & adults | |
| Intraocular Injection for HIV | | | |
| Ganciclovir Injection 500mg per vial | Treatment of CMV retinitis in HIV/AIDS | Adults – (need to check if suitable for children) | |
| Sodium Cromoglycate (cromglicatate) | Used for vernal and allergic conjunctivitis | Especially suitable for children who have recurrent attacks of vernal keratoconjunctivitis. | New sub-category (anti-allergic) |
| Acyclovir eye ointment 3% | See Appendix 2 | | |
| Acyclovir tablets | See Appendix 2 | | |

**APPENDIX 2:
SUMMARY OF EVIDENCE BASE FROM THE COCHRANE EYES AND VISION
GROUP**

| | |
|---|---|
| Ciprofloxacin Eye Drops | <i>Perioperative antibiotics for the prevention of acute endophthalmitis following cataract surgery.</i> Lead author: Emily West. Out shortly. |
| Betamethasone + Neomycin Ointment | Neomycin included in the above review. <i>Non steroidal versus topical steroids for cataract surgery.</i> Lead author: David Goh. Pending. NOTE: Betamethasone may be included, but combination preparations are problematic for reviews because components prevent different problems |
| Gentamycin and Dexamethasone eye drops | No specific review but trials may be detected in the above review. NOTE: as above |
| Pilocarpine injection 0.5% | No review at present |
| Natamycin ointment and suspension | <i>Medical interventions for Fungal Keratitis.</i> Lead author: Nilo Flor Cruz II. Pending |
| Acyclovir ointment and tablets | <i>Interventions for Herpes Simplex Virus Epithelial Keratitis.</i> Review issue 3 2003, currently being updated. Lead author: Kirk Wilhelmus |
| HPMC viscoelastic | <i>Viscoelastics for preventing endothelial cell loss in people undergoing cataract surgery.</i> Lead author: Archimedes Agahan. Pending |
| Intraocular Gangcyclovir | <i>Interventions for CMV retinitis.</i> No lead author currently |
| Sodium Cromoglycate | Title pending on seasonal and perennial conjunctivitis which could also address Sodium Chromoglycate. |

**APPENDIX 3:
SUGGESTIONS FOR IMMEDIATE DELETION AND SUBSTITUTION**

| Anti-infective agent | | | |
|-------------------------------------|---------------------------------------|--|---|
| Current | Use and reasons for inclusion | Target Group | Comments |
| Idoxurine 0.1% drops, 0.2% ointment | HSV | Children and adults | Acyclovir has been proved to be a more effective and reliable for long and short term usage |
| Substitution – Anti-viral | | | New sub-category |
| Acyclovir Eye Ointment 3% | Treatment of herpes simplex keratitis | Children: have a high recurrence rate of HSV & adults | To replace IDU |
| Acyclovir Tablets 200mg | As above | Children : have a high recurrence rate of HSV & adults | To replace IDU |