Treatment of suppurative intraocular infections

J. J. KANSKI

Moorfields Eye Hospital, High Holborn, London, W.C.2

Suppurative intraocular infection is a devastating complication of intraocular surgery and penetrating wounds of the globe. Despite the advent of the corticosteroids and newer antibiotics, the prognosis remains very grave. Even with prompt treatment, useful vision is permanently lost in the majority of cases and frequently the globe has to be eviscerated. Fortunately during the last two decades the incidence of postoperative intraocular infections has decreased, mainly through improvements in surgical and aseptic techniques and the use of prophylactic antibiotics.

This paper describes a therapeutic regime which has been used in the treatment of twenty cases of suppurative intraocular infection. In no case did the infection lead to the loss of the globe.

Material and methods

Twenty cases of suppurative intraocular infection (Table I) arising from a variety of causes were treated as inpatients at the High Holborn Branch of Moorfields Eye Hospital from April, 1968, to November, 1969. Their ages ranged from 4 to 70 years. There were fourteen males and six females.

All twenty patients showed signs of intraocular suppuration from an exogenous source. The criteria for the diagnosis were based on clinical observations following a complete ocular examination and history, other possible causes of uveitis having been excluded. Nine cases were due to infected drainage blebs, seven were postoperative, and four followed penetrating wounds of the globe.

In the majority of cases the following regime was adopted:

(1) SUBCONJUNCTIVAL THERAPY

(a) *Immediate*

The conjunctival sac was anaesthetized with 4 per cent. cocaine and adrenaline drops. Two separate injections were given, one into the upper fornix and the other into the lower.

(i) One injection consisted of methylprednisolone acetate (Depomedrone) 40 mg. This ensures an adequate concentration of steroid in the anterior chamber for up to 5 weeks.

(ii) The other injection consisted of a "cocktail" of the following; gentamicin (Gentisin) 20 mg. (0.5 ml.), framycetin (Soframycin) 500 mg. (1 ml.), methicillin (Celbenin) 150 mg. (0.2 ml.), and mydracaine (atropine, adrenaline, and procaine) 0.3 ml. The methicillin was made up by dissolving 1 g. Celbenin used for intramuscular injection in 1.5 ml. of saline and using 0.2 ml. The total volume of the "cocktail" was 2 ml. As much as possible of this was injected beneath Tenon's capsule. It is important not to inject merely beneath loose conjunctiva.

(b) *Subsequent*

This consisted of a mixture of methicillin 150 mg., gentamicin 20 mg., and betamethasone (Betnasol) 4 mg. (1 ml.) given at 24- or 48-hourly intervals depending on the response to treatment and state of the conjunctiva.

Table I *Survey of patients*

<i>Case No.</i>	<i>Age (yrs)</i>	<i>Sex</i>	<i>Presumed aetiology</i>		<i>Anterior chamber</i>	<i>Red reflex</i>	<i>Onset of response</i>
1	66	M	Infected drainage bleb	Trephine 11 yrs ago	Hypopyon 8 mm.	±	6th day
2	70	M		Anterior flap sclerotomy 4 yrs ago	Hypopyon 3 mm. Fibrinous exudate	—	2nd day
3	68	M		Trephine 15 yrs ago	Hypopyon 2 mm.	—	5th day
4	68	M		Scheie's operation 6 mths ago	Hypopyon 1 mm.	±	3rd day
5	53	M		Drainage operation 16 yrs ago	Hypopyon 1 mm.	—	Immediate
6	67	F		Trephine 1 yr ago	Hypopyon 2 mm.	±	Immediate
7	60	F		Lens extraction resulting in "bleb" 2 yrs ago	Cells + + +	+	2nd day
8	63	M		Iridencleisis 8 yrs ago	Hypopyon 1 mm.	±	5th day
9	60	M		Anterior flap sclerotomy 10 yrs ago	Cells + + + Fibrinous exudate	—	2nd day
10	38	F	Postoperative infection	Lens extraction Hypopyon on 3rd postoperative day	Hypopyon 2 mm.	—	Immediate
11	67	M		Lens extraction Hypopyon on 2nd postoperative day	Hypopyon 1 mm.	+	Immediate
12	32	M		Lens extraction and vitrectomy Hypopyon on 2nd postoperative day	Hypopyon 3 mm.	+	Immediate
13	5	M		Irido-capsulectomy Hypopyon on 2nd postoperative day	Hypopyon 3 mm.	—	Immediate
14	53	F		Retinal detachment operation with release of sub-retinal fluid Exudate on 2nd postoperative day	Dense fibrinous exudate filling anterior chamber	+	2nd day
15	68	M		Retinal detachment operation with release of sub-retinal fluid and injection of intra-vitreous saline Exudate on 2nd postoperative day	Dense fibrinous exudate	—	2nd day
16	56	M		Re-suturing of corneal graft Hypopyon on 5th postoperative day	Hypopyon 2 mm.	—	Immediate
17	4	F	Penetrating injury	Penetrating corneal wound neglected for 2 days Iris prolapse	Dense fibrinous exudate	—	Immediate
18	55	M		Metallic intraocular foreign body removed with magnet Hypopyon on 3rd postoperative day	Hypopyon 2 mm.	+	Immediate
19	4	F		Penetrating corneal wound	Hypopyon 2 mm.	±	2nd day
20	13	M		Penetrating corneal wound	Hypopyon 2 mm.	—	5th day

(2) SYSTEMIC THERAPY

(i) Antibiotics

Cloxacillin (Orbenin) 2 g. 6-hourly orally.

(ii) Corticosteroids

Prednisolone 40 mg. daily in divided doses.

(iii) Acetazolamide (Diamox)

This was necessary in three cases in which secondary glaucoma occurred.

(3) TOPICAL THERAPY

(i) Antibiotics

Gentamicin drops hourly and ointment at night.

(ii) Corticosteroids

Predsol or dexamethasone drops hourly.

(iii) Mydriatics

Atropine 1 per cent. 6-hourly.

The sensitivity of pathogenic organisms to the various antibiotics is shown in Table II.

Table II Antibiotics

Antibiotics		Methicillin	Cloxacillin	Framycetin	Gentamicin
Sensitivity of organisms	<i>Staph. aureus</i>	++	++	++	+++
	Penicillin-resistant <i>Staph. aureus</i>	+++	+++		+++
	<i>Strept. pyogenes</i>	++	++	±	±
	<i>Pneumococcus</i>	++	++	+++	±
	<i>Proteus vulgaris</i>			++	+++
	<i>Ps. pyocyanea</i>			++	+++
Dose	Subconjunctival	150 mg.		100-500 mg.	20 mg.
	Systemic	2 g. 6-hrly intramuscular or intravenous	2 g. 6-hrly oral		
Systemic side-effects		Allergy and hypersensitivity Reversible bone marrow depression (rare) Albuminuria and haematuria	Allergy and hypersensitivity Mild gastro-intestinal upsets		

Results

The clinical response to therapy was graded as good, fair, and poor. The basic criterion for the grading was the comparison of the visual acuity before the onset of infection and the visual acuity after the completion of therapy. The response was considered good when there was no deterioration in the visual acuity, fair when the visual acuity fell by not more

than two lines on the Snellen test type or from counting fingers to hand movements, and poor when there was a more considerable loss of visual acuity.

Of the twenty patients treated, thirteen responded well with no loss in visual acuity (Table III, overleaf), two (Cases 1 and 16) showed a fair response, and in the remaining five the response was poor (Cases 2, 3, 15, 17, and 20). The results in Case 3 are shown in the Figure.

FIGURE Case 3. *Before and after treatment*

In Case 1 the visual acuity fell from 6/9 to 6/18 because of the development of lens opacities. In Case 16 a fall from counting fingers to hand movements and in Case 3 from counting fingers to perception of light was due to the development of a pupillary membrane. In Case 2 there was a dramatic fall from 6/9 to counting fingers although the eye was quiet with a clear vitreous because of the development of macular "oedema". In Case 15 the eye became blind through ischaemia resulting from an encircling procedure as well as vitreous organization. The poor result in Case 17 was due to the formation of corneal and lenticular opacities and in Case 20 to vitreous organization.

The speed of response to treatment varied considerably from case to case. Improvement was immediate in nine cases, but the other eleven showed a deterioration lasting from 2 to 6 days (Case 1) before improving. No case relapsed after an improvement.

Discussion

The treatment of suppurative intraocular infection is relatively disappointing because of the general destruction of the intraocular tissues by the inflammatory process set up by the invading organisms. Treatment must be prompt and vigorous to be of any effect, as with each hour that passes further irreversible damage is being done to the globe.

The regime described above has been used, with minor modifications, in treatment of twenty such cases. The aim of the treatment is to overcome the causative organism with antibiotics and to reduce the destructive inflammatory process to a minimum by the use of corticosteroids. Steroid therapy will not interfere with the control of the infection provided that the infecting organisms are sensitive to the antibiotics, and the dose is adequate to penetrate the intraocular tissues. The cardinal prerequisite to successful therapy is the selection of the proper drugs.

Theoretically, the infecting organisms should be identified and their sensitivities to various antibiotics determined. Unfortunately, conjunctival cultures are seldom helpful and even cultures taken from the anterior chamber in cases of overwhelming infections may

Table III *Visual Acuity*

<i>Case No.</i>	<i>Before infection</i>	<i>At onset of treatment</i>	<i>After treatment</i>	<i>Result</i>
1	6/9	HM	6/18 Lens opacities	Fair
2	6/9	HM	CF Macular "oedema"	Poor
3	CF Cataract	PL	PL Cataract Pupillary membrane	Poor (see Figure)
4	6/18 Cataract	CF	6/18	Good
5	HM Cataract Corneal opacity	HM	HM	Good
6	6/9	HM	6/9	Good
7	6/6	6/9	6/6	Good
8	2/60 Gross field loss	CF	2/60	Good
9	CF Cataract	PL	CF	Good
10	6/60 Cataract	HM	6/9	Good
11	6/36 Cataract	PL	6/6	Good
12	PL Vitreous haemorrhage	PL	PL	Good
13	HM Capsular remnants	PL	HM	Good
14	6/12 Retinal detachment	HM	6/12	Good
15	HM Retinal detachment	No PL	No PL Ocular ischaemia Vitreous organization	Poor
16	CF Corneal graft	HM	HM Pupillary membrane	Fair
17	6/6	HM	PL Lens and corneal opacities	Poor
18	6/5	?	6/5	Good
19	6/6	?	6/6	Good
20	?	PL	PL Vitreous organization	Poor

CF = counting fingers
 HM = hand movements
 PL = perception of light

be negative. Even when they are positive they may not disclose the causative organism. In all but one of these patients (Case 8) conjunctival cultures were of no help and treatment was empirical.

The organism most commonly responsible for postoperative infection is *Staph. aureus*, which may be penicillin resistant. Gram-negative organisms, such as *Ps. pyocyanea* and *Proteus vulgaris*, may also occasionally be responsible. Other Gram-positive cocci, such as *Strept. pyogenes* and the *Pneumococcus*, may be responsible for infections after penetrating injuries.

The antibiotics used in the treatment of bacterial intraocular infections should be capable of covering all eventualities. If a therapeutic level of drugs is to be reached promptly and in an adequate concentration, it is necessary to combine subconjunctival with systemic and topical administration. Intracameral administration is not recommended as it gives very disappointing results. It was used only in Case 17 as a last resort.

It is important that the antibiotics administered subconjunctivally should differ from those given systemically in order to allow a greater opportunity for the pathogen to be susceptible to at least one of them.

Methicillin is the antibiotic of choice in the treatment of penicillin resistant *Staphylococci*, as it is immune to penicillinase and highly bactericidal. In this regime it was administered only subconjunctivally.

Gentamicin is a new bactericidal antibiotic which is water-soluble and well tolerated when injected subconjunctivally. It is highly active against an exceptionally wide range of bacteria, including penicillin-sensitive and resistant *Staphylococci*, group A beta-haemolytic *Streptococci*, *Proteus vulgaris*, and *Ps. pyocyanea*. It plays a very important part in the treatment of intraocular infection and was administered both subconjunctivally and topically.

Framycetin is soluble and well tolerated when given subconjunctivally. It has a wide spectrum which includes both *Staph. aureus* and *Ps. pyocyanea*. It is not, however, effective against penicillin resistant *Staphylococci* and does not play a major role in the treatment of intraocular infection.

Cloxacillin was the only antibiotic used systemically. It has the same spectrum as methicillin and has the added advantage that it may be administered orally, though it may cause nausea and vomiting when given in high doses. This happened in two of our patients and the drug had to be discontinued. It cannot be injected subconjunctivally as it causes a severe reaction. It should not be used in penicillin-sensitive patients.

In order that the inflammatory damage may be reduced to a minimum while the antibiotics are gaining control of the infection, it is essential that corticosteroids be administered simultaneously.

Prednisolone was used systemically, methylprednisolone and betamethasone subconjunctivally, and Predsol and dexamethasone topically.

Mydriatics should be administered both subconjunctivally and topically to combat the formation of posterior synechiae and to relieve pain due to pupillary and ciliary spasm.

The duration of treatment varies according to the response. It is usually unnecessary to give more than four subconjunctival injections. Systemic steroid therapy can usually be reduced after 5 days and stopped altogether after 10. Topical therapy with gentamicin and dexamethasone should be continued for several weeks until the anterior chamber is completely quiet. It is important to note that it may sometimes take several days for the patient to show a response to treatment. The eye should not be given up as lost until it has had the benefit of at least 7 days of intensive therapy.

Summary

A therapeutic regime consisting of subconjunctival, systemic, and topical administration of antibiotics and corticosteroids in the treatment of twenty cases of suppurative intraocular infection is described. The response was considered to have been good in thirteen cases, fair in two, and poor in five. The rationale of the treatment is discussed.

I am much indebted to the consultant staff of the High Holborn Branch of Moorfields Eye Hospital for permission to describe their cases, to the house surgeons for all their help, and in particular to Mr. Barrie Jay for his most helpful advice and encouragement.