Methylcellulose and lens implantation

PAUL U. FECHNER AND MARTIN U. FECHNER

From the Department of Ophthalmology, Robert Koch Hospital, 3007 Hannover-Gehrden, West Germany

SUMMARY Methylcellulose has been used since 1976 to prevent damage to the corneal endothelium during operations for implantation of intraocular lenses. Originally one drop of a 1% solution was placed on the artificial lens just before its insertion. Later the anterior chamber was completely filled with a 2% solution of methylcellulose before implantation. In this way it is possible to maintain a space between the cornea and iris even if vitreous pressure is present and to operate without risk to the corneal endothelium. This paper demonstrates the safety of the intraocular use of methylcellulose on the basis of over 400 operations. The substance is cheap, universally available, and can be easily prepared for intraocular use.

The past decade has seen the development of the endothelial specular microscope.^{1,2} This instrument led to the realisation that corneal endothelial cells are almost entirely incapable of cell division, and that healing of corneal endothelial wounds can take place only by means of enlargement and sliding of the remaining endothelial cells.³

The recognition of this fact fostered a new thinking in ophthalmic microsurgery. Utmost care with respect to the endothelium of the cornea became the law, particularly when a cataract operation was combined with the implantation of an artificial lens. Rules developed to which ophthalmic surgeons should strictly adhere⁴: as little bending of the cornea as possible⁵; as little irrigation by an irrigating solution as physiological as possible^{6,7}; absolute avoidance of contact between instruments and the endothelium, and, most important, between the artificial lens and the endothelium.^{8,9}

To lessen the danger of contact between the intraocular lens and the cornea Binkhorst *et al.* recommended the air cushion technique.¹⁰ Air tends to leave the anterior chamber quickly, however, and to prevent that happening Healon (sodium hyaluronic acid 1%) was recently introduced. The senior author has successfully used methylcellulose since 1976 to prevent the rubbing of the intraocular lens against the endothelium,^{11–14} and because his experience with this substance was extremely favourable he did not change to Healon.

This paper demonstrates the safety of the intraocular use of methylcellulose. In particular, data are

presented to show that if there is a methylcellulose-related post-surgical increase in intraocular pressure it is not clinically significant.

Material and methods

CHEMISTRY OF METHYLCELLULOSE

Methylcellulose used for intraocular surgery is a highly purified brand of hydroxypropyl methylcellulose. The hydroxypropyl and methyl groups replacing hydrogen groups increase the hydrophilicity of the compound. The cellulose polymer is widely found in nature as a structural substance—e.g., in the cells of wood and cotton. The basic molecule is D-glucose. Two monomers of glucose combine to form cellobiose, which differs from dextrose only in the way the 2 monomers are stereochemically connected: in cellobiose the bonding is beta-glycosidic, in dextrose alpha-glycosidic. The human enzyme system can hydrolyse alpha-glycosidic bonds but supposedly is incapable of breaking cellobiose bonding (and therefore methylcellulose), at least in the intestine and in larger quantities. What happens to the minute amount of methylcellulose which may remain in the body after intraocular application is uncertain, but the question seems to be without clinical significance.

PREPARATION FOR INTRAOCULAR USE

A description is given below of the preparation of a 2% solution of methylcellulose suitable for intraocular use. There are a number of essential points to be considered.

(a) The methylcellulose must be of the highest purity. Methocel E 4 M Premium of Dow

Correspondence to Dr P. U. Fechner, Schmiedest. 41, 3000 Hannover, West Germany.

Chemical Corporation is recommended for use.

(b) A physiological solvent should be used. The following solvents are suitable: Balanced salt solution (BSS) (Alcon), Ringer's solution, Ringer's lactate solution, or equivalents.

(c) Antiseptic compounds like benzalkonium, chlorbutanol, thimerosal, and others are damaging to the endothelium and must not be used. The solution therefore has to be sterilised by autoclaving. Since the internal temperature of a viscous solution rises slowly, autoclaving should last longer than the usual 20 minutes, i.e., 30–40 minutes.

(d) Some stains which in the past have been used as 'vital stains' were recently shown to be carcinogenic, e.g., trypan blue.¹⁵ Though this may be of negligible importance in our context, we now recommend 'patent blue' V (sulphan blue), which is known not to be carcinogenic.¹⁵

(e) A freshly prepared solution of methylcellulose contains crystalline complexes which form corpuscular elements. Filtration, therefore, is an essential part of the preparation of a solution destined for intraocular use.

Preparation of 100 ml of a 2% solution of methylcellulose is as follows: Dissolve 2 g in 30 ml of boiling solvent (BSS, Ringer's lactate solution, Ringer's solution). Allow to cool. Add 70 ml of cold or icy solvent. The solvent may contain 5 mg of patent blue V (sulphan blue).¹⁵ Store in a refrigerator overnight at -10 to 0°C .

Next day the solution can be filtered. The pore size should be between $16\text{ }\mu\text{m}$ and $0.5\text{ }\mu\text{m}$. One may use suction by means of a water-stream pump through a G 3-Fritte, Jenaer Glass (pore size approximately $16\text{ }\mu\text{m}$) or more conveniently pressure (nitrogen). The solution is filtered through a Sparkler Submicron Filter Tube, cartridge CS-0.5 with a pore size of $0.5\text{ }\mu\text{m}$ (Sparkler Inc., Conroe, Texas, USA).

After the filtered solution has been divided into small bottles, these are sterilised by autoclaving at 120°C for 30–40 minutes.

OPERATIVE TECHNIQUES

All 417 operations on which this paper is based were performed by the senior author or in his presence by a junior colleague. The lenses used were mostly Medallion, but Binkhorst-four-loop, Shearing, Sinskey, or Sinskey-Kratz lenses were also implanted. Since the type of lens has no bearing on the postoperative intraocular pressure, it will not be considered further in this paper.

The technique of operation was standardised as follows. All wounds were corneoscleral under a limbus-based flap reaching from 9.30 to 2.30. All intracapsular operations were performed with the help of alpha-chymotrypsine 1:10000 for $2\frac{1}{2}$ minutes.

After implantation of the lens the wound was closed with approximately 12 8–0 silk interrupted sutures. During the operation methylcellulose was applied in 2 different ways. From 1976 to 1979 one drop of a 1% solution was applied to the artificial lens immediately previous to its insertion. Since January 1980 the anterior chamber has been filled with a 2% methylcellulose solution prior to implanting the lens. After the lens was in place, sutured to the iris, and some corneoscleral sutures had been inserted, most of the methylcellulose was removed from the eye by one of the following methods: (a) diluting it and rinsing out with a McIntyre-type coaxial infusion and aspiration cannula; (b) forcing it out by inflating the anterior chamber with air; (c) a combination of these 2 methods, either simultaneously or consecutively.

For the past few months a methylcellulose solution has been used which is stained slightly blue to help observe its disappearance. No attempt was made to remove all the methylcellulose, since the blue specks which remained at the end of the procedure had disappeared on the first postoperative day.

POSTOPERATIVE MEASURES

All patients received topical applications of dexamethasone 0.1% q.i.d. from the last preoperative day for several weeks. This might have contributed to the fact that there was a slight rise of pressure during the early postoperative period. Therefore all patients received acetazolamide in sustained release form (Diamox Sequels) 500 mg daily, from the day of the operation to the third postoperative day. Diamox Sequels was given irrespective of whether the operation was an intracapsular (with alpha-chymotrypsin) or extracapsular (without alpha-chymotrypsin) procedure. The postoperative intraocular pressures of days 1 to 3 were under the influence of acetazolamide; at day 4 there may have been a residual effect.

Applanation tonometry was performed at the first, third, and fifth postoperative days. A pressure-lowering treatment was reinstituted in about 5% of the cases on the fifth postoperative day. This did not influence the results presented below.

Results

OPERATION

The use of methylcellulose greatly facilitated the operation. If despite ocular massage the anterior chamber remained shallow, the methylcellulose always increased the depth of the chamber to allow for an easy and safe implantation (even of 3-plane lenses with the 'open-sky' route) without a Sheets glide or posterior vitrectomy. The implantation never had to be abandoned, in contrast to its abandonment

Fig. 1 Postoperative pressures after 324 planned intracapsular operations with 1% or 2% methylcellulose as an adjunct. Alpha-chymotrypsin 1/10 000 was used for 2½ minutes in all cases. Acetazolamide (Diamox) 500 mg per day was given from the day of the operation to the third postoperative day.

in about 10% of cases prior to the use of methylcellulose.

All the types of intraocular lens used by us could be implanted without touching the cornea and could, as was generally done, be sutured to the iris without harming the endothelium. Moreover, it was easier to observe the tying of the iris suture knot through the cornea if the anterior chamber was filled with methylcellulose rather than with air.

POSTOPERATIVE INTRAOCULAR PRESSURE

When the pressures after use of 1% and of 2% methylcellulose were compared it was evident that they were no higher after 2% methylcellulose. (The pressures were slightly lower in fact after both intracapsular and extracapsular procedures.) Therefore the groups of patients receiving 1% and 2% methylcellulose were combined in the figures presented below.

Fig. 1 shows the postoperative intraocular pressure after planned intracapsular operations (i.e., with application of alpha-chymotrypsin 1/10 000 for 2½ minutes). It should be remembered that the intraocular pressures from day 1 through day 3 were influenced by the application of acetazolamide.

Fig. 2 shows the intraocular pressure after planned extracapsular operations (alpha-chymotrypsin was not used in these eyes, but the eyes did receive acetazolamide).

Fig. 3 shows the intraocular pressure in a small group of secondary implantations of medallion lenses. These operations differ from those shown in Figs. 1 and 2 in that they were less traumatic. Acetazolamide was given in these cases also.

Fig. 2 Postoperative pressures after 81 planned extracapsular operations. Methylcellulose 1% and 2% was used as an adjunct in all cases. No operation was performed with enzymatic zonulolysis. Acetazolamide (Diamox) 500 mg per day was given from the day of the operation to the third postoperative day.

The 3 figures demonstrate clearly that the increases in intraocular pressure after a cataract operation with lens implantation (or after a secondary lens implantation), during which methylcellulose has been applied, are not a complication of clinical significance.

POSTOPERATIVE INFLAMMATION

No postoperative infections occurred. Possibly because of steroid treatment postoperative intraocular inflammation was minimal. Only slight flare

Fig. 3 Postoperative pressures after 12 secondary lens implantations of medallion lenses with 1% or 2% methylcellulose used as an adjunct. Acetazolamide (Diamox) 500 mg per day was given from the day of the operation to the third postoperative day.

and a few cells were observed for a few days. No hypopyon occurred. (All lenses had been wet-sterilised by Medical Workshop.) Only a few eyes with a more pronounced exudation were observed. This could not have been the result of the methylcellulose, because the methylcellulose was always withdrawn from one bottle for several implantations, while the postoperative cases of iritis occurred only sporadically, never epidemically.

POSTOPERATIVE STATE OF THE CORNEA

Each operation was graded according to a subjective impression of quality, and later compared with the postoperative appearance of the cornea. In the cases with the highest grade (most eyes), the corneae were nearly clear at the first postoperative day, and completely clear by the third day.

The endothelium was observed postoperatively in about 100 cases by noncontact specular microscopy and with the help of a McIntyre grid and compared with the nonoperated eye. In most of the operated eyes there were about 2000 endothelial cells per square mm in both eyes. To us this indicated a lack of any toxic effect of methylcellulose on the endothelium.

Therefore as a clinical impression on the basis of approximately 2,000 postoperative slit-lamp examinations on 417 eyes it can be stated that methylcellulose did not harm the endothelium. Since the mechanical advantage of this adjunct to the operation is so evident, the overall effect on the cornea must obviously be beneficial.

Discussion

Healon was recently considered 'the most important substance to come along in cataract surgery since alpha-chymotrypsin'.¹⁶ This statement, however, must be qualified. What matters is not Healon but appropriate viscous material in the eye. Healon, despite its value, has its disadvantages: it is very expensive, not universally available, and it is difficult to dilute. For the last reason a relatively large amount of the material may remain in the eye and cause a dangerous rise of pressure postoperatively.¹⁷

We prefer methylcellulose 2% dissolved in BSS. Fleming *et al.*¹⁸ have shown that methylcellulose inside the eye is harmless. Methylcellulose has many advantages. As an adjunct to lens implantation it is perfect. It coats the lens and deepens a shallow anterior chamber. It is universally available and inexpensive. The solution is comparatively easy to prepare—at least for a moderately equipped pharmacy. This is advantageous in underdeveloped and developing countries. The solution can be resterilised, thereby further decreasing the cost

factor. It can be stained blue for easy recognition inside the anterior chamber. It is—and this is a very important point—easily diluted and can be largely removed from the anterior chamber without difficulty. If postoperative rises of intraocular pressure occur owing to its use, they are easily manageable and not clinically significant.

Because methylcellulose is a nonphysiological and possibly nonmetabolic substance consisting of large polymers, it could be argued that the residue which remains in the eye at the end of the operation might clog the trabecular meshwork and cause dangerous bouts of glaucoma, as has been reported after the use of Healon.¹⁷ Our results show that this is definitely not so. As can be seen from Figs. 1 and 2, the intraocular pressure at the first postoperative day was 33.1 mmHg after intracapsular operation, and 30.2 mmHg after extracapsular operation (with acetazolamide). Obviously the difference between the pressures must be due to the increased tension following the enzymatic zonulolysis. But even after extracapsular operation pressure rises occur which seem in the first place to be due to the trauma of the operation and lens material remaining in the anterior chamber. It is unclear whether remnants of methylcellulose in the anterior chamber in addition increase the postoperative intraocular pressure. Whether this is so—and if so, to what extent—could not be clarified. What was shown, however, was the unequivocally benign behaviour of the methylcellulose inside the eye with respect to the postoperative pressure.

As regards the argument that methylcellulose cannot be metabolised, one must consider the quantity under discussion. If 20% of what was injected into the eye—say 0.5 ml—stays in the anterior chamber, this amounts to only 2 mg of the dry substance of methylcellulose, a substance considered to be inert and confirmed by our experience to be so. None of the patients showed any ill effect either systemically or locally which could be related to methylcellulose.

With respect to the cornea we did not prove that methylcellulose was more beneficial than Healon or air or no cushioning substance at all. But since most eyes which were examined by noncontact specular microscopy did show a very high endothelial cell count (practically equal to that of the nonoperated eyes) we feel justified in the assumption that methylcellulose is at least not toxic to the endothelium. That it is of benefit is a belief based on our experience that implantation in so many cases is much facilitated by its use.

In summary, our experience of over 6 years with methylcellulose leads us to believe that this substance is most valuable in intraocular surgery whenever a cushioning substance other than air is needed in the

anterior chamber. Admittedly this statement is based on clinical experience. We hope that this paper may stimulate further investigations to obtain confirmation.

We obtained the solution of methylcellulose from Raths-Apotheke, Oster-St 51, 3250 Hameln, West Germany.

References

- 1 Laing R A, Sandström M M, Leibowitz H M. In vivo photomicrography of the corneal endothelium. *Arch Ophthalmol* 1975; **93**: 143–5.
- 2 Bourne W M, Kaufman H E. Specular microscopy of human corneal endothelium in vivo. *Am J Ophthalmol* 1976; **81**: 319–23.
- 3 Hoffer K J, Philippi G. A cell membrane theory of endothelial repair and vertical cell loss after cataract surgery. *Am Intra-ocular Implant Soc J* 1978; **4**: 18–25.
- 4 Fechner P U. *Intraocular lenses*. Stuttgart: Enke, 1980: 66.
- 5 Norn M S. Vital staining of corneal endothelium in cataract extraction. *Acta Ophthalmol (Kbh)* 1971; **49**: 725–33.
- 6 Edelhauser H F, van Horn D L, Schultz R O, Hyndiuk R A. Comparative toxicity of intraocular irrigating solutions on the corneal endothelium. *Am J Ophthalmol* 1976; **81**: 473–81.
- 7 Edelhauser H F, Connering R, van Horn D L. Intraocular irrigating solutions. *Arch Ophthalmol* 1978; **96**: 516–20.
- 8 Kaufman H E, Katz J. Endothelial damage from intraocular lens insertion. *Invest Ophthalmol Visual Sci* 1976; **15**: 996–1000.
- 9 Kaufman H E, Katz J. Endothelial damage from intraocular lens insertion. *Invest Ophthalmol Visual Sci* 1977; **16**: 265.
- 10 Binkhorst C D, Loones, L H, Nygaard P. Die Bedeutung der Spiegelmikroskopie und -graphie des Hornhautendothels für die Einpflanzung künstlicher Augenlinsen. Beschreibung einer Tiefkammertechnik für Einpflanzung. *Ber Dtsch Ophthalmol Ges* 1978; **75**: 93–103.
- 11 Fechner P U. Methylcellulose in lens implantation. *Am Intra-Ocular Implant Soc J* 1977; **3**: 180–1.
- 12 Fechner P U. Erfahrungen mit der Implantation einer künstlichen Augenlinse. *Klin Monatsbl Augenheilkd* 1979; **172**: 852–62.
- 13 Fechner P U. Methylcellulose als Gleitsubstanz für die Implantation künstlicher Augenlinsen. *Klin Monatsbl Augenheilkd* 1979; **174**: 136–18.
- 14 Fechner P U. Use of methylcellulose during lens implantation. *Am Intra-Ocular Implant Soc J* 1980; **6**: 368–9.
- 15 *Martindale: the extra pharmacopoeia*. 27th ed. London: Pharmaceutical Press, 1977: 475, 615.
- 16 Drews R C. The highlights on intraocular lenses, merits of extracapsulars versus intracapsulars. In: Boyd B, ed. *Highlights of ophthalmology*. 25th ed. Panama, *Highlights of Ophthalmology*: 1981; **2**: 904.
- 17 Binkhorst C D. Inflammation and intraocular pressure after the use of Healon in intraocular lens surgery. *Am Intra-Ocular Implant Soc J* 1980; **6**: 340–1.
- 18 Fleming M A, Merrill D L, Girard L J. Studies of the irritating action of methylcellulose. *Arch Ophthalmol* 1959; **61**: 565–7.