The fixed dilated pupil after cataract surgery – is it related to intraocular use of hypromellose?

Andrew K K Tan, Roger C Humphry

Abstract
Hypromellose can be used as a viscoelastic substance during cataract surgery. Two groups of patients, one group operated on using hypromellose, the other using sodium hyaluronate as a viscoelastic substance were followed up 2–6 months postoperatively. A total of 16.7% of the eyes operated on using hypromellose developed a non-reactive semi-dilated pupil whereas none of the eyes from the control group developed this phenomenon. It was concluded that there is a probable link between the intraocular use of hypromellose and abnormal pupils after cataract surgery.

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Hypromellose and methylcellulose have been used for the past 15 years as viscoelastic agents in cataract surgery. They have been shown in many operations to offer adequate protection against undue endothelial cell loss and to facilitate intraocular lens implantation. Many previous reports have highlighted the advantages over sodium hyaluronate in terms of cost and availability. Many clinical series have also noted no significant difference in terms of preoperative complications, postoperative inflammation, and intraocular pressure, as well as the postoperative state of the corneas in eyes operated on using hypromellose/methylcellulose and sodium hyaluronate.

However, it has been noted in our practice that some pupils of eyes operated on with hypromellose 2% used as the viscoelastic substance developed abnormalities in pupil reaction; a number of patients developed a fixed, semi-dilated pupil postoperatively (Figs 1 and 2) resulting in glare, poor quality of vision, as well as cosmetic embarrassment. We have since stopped using hypromellose as a result of these complications. This paper presents a retrospective study comparing the incidence of pupil abnormality in eyes operated on using hypromellose as viscoelastic with a consecutive batch of similar operations performed prospectively by the same surgeon (RCH) using sodium hyaluronate (Healon).

Although to our knowledge, there has been no report on the effect of intraocular use of hypromellose on pupil mobility in the ophthalmic literature to date, we were so concerned by our clinical findings that we did not consider it ethical to perform a prospective study using hypromellose.

Subjects and methods

PATIENT SELECTION
All patients who had undergone an uncomplicated extracapsular cataract extraction with intraocular lens implant between 1 January 1992 and 31 May 1992 in which hypromellose (from a UK source) was used as the viscoelastic substance were entered into the study group. A subsequent group of patients who had undergone the similar surgery between 1 June 1992 and 30 September 1992, in whom sodium hyaluronate 1% was used as the viscoelastic were recruited into the control group. All the operations were performed using similar techniques. Patients with the following characteristics were excluded from the study:

(1) those who were known to have abnormal pupil preoperatively,
(2) known cases of iritis,
(3) diabetic patients,
(4) known glaucoma patients who had had medical treatment,
(5) bilateral pseudophakia,
(6) those who had a combined trabeculectomy done in the same sitting,
(7) those who had intraoperative compli-

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{figure1.png}
\caption{Non-reactive, semi-dilated pupil in one of the eyes operated on using hypromellose 2% as viscoelastic.}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{figure2.png}
\caption{Normal pupil in the contralateral, non-operated eye of the same patient in Figure 1.}
\end{figure}
cations— for example, vitreous loss, posterior capsule rupture, or any appreciable mechanical trauma to the iris,

(8) those who had iris prolapse postoperatively.

OPERATIVE TECHNIQUE

All operations were performed by the same surgeon using the same standard technique as described below.

The superior rectus muscle was secured with a 4/0 silk bridle suture. The conjunctiva was cauterised 1-5 mm from the limbus. A partial two step scleral section 1-5 mm from the limbus was then made from 10 to 2 o'clock position with a diamond knife. Anterior capsulotomy was done either using the ‘continuous circular capsulorrhexis’ technique or the ‘tin-can’ technique, with a 25 gauge needle modified into a capsulotome connected to a drip infusion set with slow, controlled infusion of Hartman’s solution with adrenaline. The limbal-scleral section was then completed and viscoelastic substance injected into the anterior chamber. Hydrodissection of the lens nucleus was performed and the nucleus subsequently expressed. Residual soft lens matter was aspirated using an aspiration/irrigation system with Hartman’s solution. The capsular bag and anterior chamber were filled with viscoelastic substance and the intraocular lens (Surgidev PCUB-26) was inserted in the capsular bag. The section was closed with five interrupted 10/0 nylon sutures. Viscoelastic substance was aspirated and the anterior segment irrigated until visibly clear of viscoelastic (though the surgeon found that it was more difficult to be sure of complete removal of hyromellose than sodium hyaluronate). Acetylcholine chloride (Miochol) was injected intracameral only if the pupil was larger than 6 mm at the end of the surgery. All patients received a subconjunctival injection of framycetin and dexamethasone.

Results

CLINICAL

Altogether, 54 patients were recruited for the study group (hyromellose) and 48 patients for the control group (sodium hyaluronate 1%) after excluding patients with the exclusion criteria mentioned above. All patients in the study group were recalled and an examination was done by either of the authors 2 to 6 months postoperatively. Patients in the control group were followed up prospectively and examination done at 2 weeks and 2 months postoperatively. The two groups of patients were comparable, their characteristics and other clinical data are given in Table 1.

Pupils of the operated eyes were examined with regard to size (compared with the contralateral eye), reaction, and abnormality of shape. Pupil reaction was recorded as either normal, partial, or non-reactive (not at all). Any obvious abnormality of the iris such as sphincter rupture or atrophy, synechiae, and iris atrophy were noted. Any postoperative intraocular pressure rise was also noted and recorded.

OBSERVATIONS

It was observed that nine (16·7%) of the 54 patients in the study group had a fixed and semidilated pupil in the operated eye (first observed 2 days to 6 weeks postoperatively) which was neither reactive to light nor near accommodation, 15 had a partially reactive pupil, and 30 had normal pupil reaction. However, in the control group, none of the patients had a non-reactive pupil, nine had a partially reactive pupil, and 39 had normal pupil reaction. (See Table 2 and Figs 1 and 2.) The results were statistically significant (p<0·005, using χ² with Fisher exact test).

It was also noted that the iris of the patients with fixed and semidilated pupils showed the presence of generalised sphincter atrophy but no evidence of sphincter rupture. The pupils could not be constricted with pilocarpine drops 1–4%; however, some dilatation was possible with tropicamide drops 1% (dilatation of 0·5 to 1·5 mm) and further dilatation was observed when phenylephrines drops 10% were instilled 10 minutes later, showing a more extensive involvement of the pupillary sphincter compared with the dilator, which confirmed our clinical observation. Most of the pupils which were partially reactive showed some sphincter atrophy. Only one of the total of 102 patients had raised intraocular pressure postoperatively for 1 day; however, he had normal pupil reaction. There was no significant difference in severity of post-

<table>
<thead>
<tr>
<th>Pupil reaction</th>
<th>Hydrogelose</th>
<th>Sodium hyaluronate</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>30 (55·6%)</td>
<td>39 (81·3%)</td>
<td>69</td>
</tr>
<tr>
<td>Partial</td>
<td>15 (27·8%)</td>
<td>9 (18·7%)</td>
<td>24</td>
</tr>
<tr>
<td>Non-reactive</td>
<td>9 (16·7%)</td>
<td>0 (0%)</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>48</td>
<td>102</td>
</tr>
</tbody>
</table>

p Value <0·005 (χ², Fisher exact one tailed test)

Table 3: Comparison of pupil reaction against intraoperative use of acetylcholine chloride

<table>
<thead>
<tr>
<th>Pupil reaction</th>
<th>Acetylcholine use</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>6</td>
<td>63</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>Partial</td>
<td>0</td>
<td>24</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Non-reactive</td>
<td>3</td>
<td>6</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>93</td>
<td>102</td>
<td></td>
</tr>
</tbody>
</table>

p=0·01
operative uveitis between the two groups of patients.

Incidentally, of the nine patients who had acetylcholine chloride intraoperatively (who were also in the hypromellose 2% group) three developed a fixed and semidilated pupil, whereas only six out of the 93 patients who did not have acetylcholine chloride developed a fixed and semidilated pupil. The results appeared to be significant (see Table 3); however, owing to the vast difference between the numbers in each group (that is, nine had acetylcholine chloride against 93 who had none), a conclusion cannot be drawn on the effect of acetylcholine chloride on postoperative pupil reaction at this stage. Perhaps a randomised prospective trial will shed some light in this area.

Discussion

Use of hypromellose/methylcellulose as a viscoelastic agent in cataract surgery has been widely advocated for the past 10 years, and appears to offer sufficient protection against damage to corneal endothelium during intraocular lens implantation. However, there is a scarcity of reports on adverse effects of hypromellose or methylcellulose on the anterior segment structures to date. We feel there is probably an underreporting of these adverse effects possibly because of the tremendous advantage hypromellose/methylcellulose offers over the other presently available alternatives in terms of economy and easy availability.

Hypromellose is made up of two molecules of glucose that bind to form cellulose, a molecule that human bodies are supposedly unable to break down. The process by which hypromellose is cleared from the human body is at present unknown. It has been reported that a 1% solution of methylcellulose injected into the anterior chamber of rabbits produced mild iridocyclitis which was thought to be a foreign body reaction. An aqueous solution of hypromellose 1–3% was also known to cause immediate and permanent immobilisation of human spermatozoa in vitro.

Rosen et al has also found impurities and particulate matter is six samples of 2% hypromellose from European pharmacies. Whether these particles produce many adverse reactions – that is, sterile or non-sterile inflammatory responses, cellular damage, or other toxic effects has never been carefully documented in the ophthalmic literature.

It appears from the short study we have undertaken that there is a probable link between intraocular use of hypromellose 2% and abnormality of postoperative pupil reaction in patients who have undergone cataract surgery. We do not know what the actual mechanism is at present but believe that this may be the result of a yet unidentified irritating effect of hypromellose, or any other constituents contained in the final product may have on the iris sphincter or its vascular structure.

Intracameral use of acetylcholine may also have contributed to the pathogenesis of this strange phenomenon as sudden miosis induced by acetylcholine chloride causes marked distortion of cuboidal cells of the posterior pigment layer of the iris. This is four times as thick during the change from miosis to mydriasis. This may cause further insult to injury to the iris in the presence of other as yet unidentified factors.

We hope this paper will stimulate further studies on the effect of intracameral use of hypromellose on pupil mobility and its pathogenesis.

The authors have no proprietary or financial interest in the pharmaceutical agents mentioned in this study.

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