

SCIENTIFIC REPORT

National survey of antimetabolite use in glaucoma surgery in the United Kingdom

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Aims: To assess the pattern of use of antimetabolites in trabeculectomy surgery by all consultant ophthalmologists in the United Kingdom.

Methods: A postal questionnaire of 12 questions regarding antimetabolite use in trabeculectomy surgery was sent to all 749 consultant ophthalmologists in the United Kingdom. The consultants were asked to estimate the number of trabeculectomies they performed per year, how often they used 5-fluorouracil (5-FU) in primary and redo surgery, their usual method of administration of 5-FU, how often they used mitomycin (MMC) in primary and redo surgery, and their usual dosage regimen of MMC. Factors that influenced the decision to use or not use antimetabolites were also assessed.

Results: The response rate of consultants returning the questionnaire was 82% (615 out of 749); 87% (533) of these consultants perform trabeculectomy surgery. Of these 533 consultants, 98 (18%) never use an antimetabolite. Most consultants (82%) use antimetabolites, but use them infrequently (only 9% using antimetabolites in more than half their cases). The preferred antimetabolite is 5-FU rather than MMC. Of the 435 consultants performing trabeculectomy surgery and using antimetabolites, 402 (93%) use 5-FU and 179 (41%) use MMC. Various factors influenced the decision to use or not use an antimetabolite, but experience of complications associated with their use was a factor for 34% of consultants.

Conclusion: The use of antimetabolites, particularly MMC, in the United Kingdom is much less than in America or Japan, where trabeculectomy with MMC is the surgical procedure preferred by glaucoma specialists.

The wound healing response is the single most important determinant of the final intraocular pressure (IOP) after glaucoma surgery.^{1,2} The increasing use of antimetabolites to modulate this response, particularly 5-fluorouracil (5-FU) and mitomycin C (MMC), represents one of the major new developments in glaucoma surgery over the past 15 years. However, antimetabolites have been associated with particular problems and side effects, such as hypotony, bleb leaks, and infections.^{3,4} The National Trabeculectomy Survey in the United Kingdom found that in 1996 glaucoma specialists (self reported) used intraoperative antimetabolites in only 14.7% of first time trabeculectomies for chronic open angle glaucoma (COAG).⁵ This is in contrast with the United States, where a survey suggested that ophthalmologists with an interest in glaucoma used intraoperative MMC in 33% to 52% of first time trabeculectomy cases.⁶

This National Survey of Antimetabolite Use is a cross sectional survey designed to assess in detail the pattern of antimetabolite use by all consultant ophthalmologists in the United Kingdom. There is a range of antifibrotic agents

available, including 5-FU applied intraoperatively on a sponge, postoperative 5-FU injections, and intraoperative MMC.^{7–9} This survey investigates which of these options is preferred practice in addition to determining if antifibrotic agents are being used in first time trabeculectomy surgery as well as redo surgery.

METHODS

A postal questionnaire (see appendix) of 12 questions regarding antimetabolite use in trabeculectomy surgery was sent to all 749 consultant ophthalmologists in the United Kingdom in December 1999. They were identified according to the Royal College of Ophthalmologists database of consultants. A pilot questionnaire had previously been performed with the aid of a mixed sample of glaucoma specialists and other ophthalmologists. This was to ensure the format covered all the questions we wanted asked, was simple to answer, and the replies could be accurately interpreted. Completed questionnaires were returned to the authors in a prepaid self addressed reply envelope. Data from the paper questionnaires were entered into a customised database and analysed using Microsoft Access 2000 and SPSS (Statistical Package for Social Sciences, 1998).

RESULTS

The response rate was high, with 82% (615 out of 749) of the consultants surveyed returning the questionnaire. Data from all 615 returned questionnaires were suitable for analysis. One quarter of consultants participating in this survey reported that they had a specialist interest in glaucoma. Eighty seven per cent (533) of consultants performed trabeculectomy surgery and information from this group was used in the subsequent analyses. When asked how many trabeculectomies they performed in the past year, 35% estimated less than 10 and 58% estimated 11 to 50. Only 7% (35) of consultants said they performed more than 50 trabeculectomies per year.

Of all consultants performing trabeculectomy, 18% (98/533) never use an antimetabolite in trabeculectomy surgery and only 9% (49/533) used an antimetabolite in more than half of their cases (fig 1). Of those consultants with a specialist interest in glaucoma 10% never use an antimetabolite in trabeculectomy surgery, while 23% used an antimetabolite in more than half of their cases.

Further questioning regarding first time and redo trabeculectomy surgery revealed that 25% of all consultants never use antimetabolites in primary surgery and 5% never use antimetabolites for repeat surgery either. However, 53% use antimetabolites in more than half their redo cases (fig 2). Those consultants who expressed a specialist interest in glaucoma were not dissimilar to the national standard: 16% of these consultants never use antimetabolites in primary

Abbreviations: COAG, chronic open angle glaucoma; 5-FU, 5-fluorouracil; IOP, intraocular pressure; MMC, mitomycin C

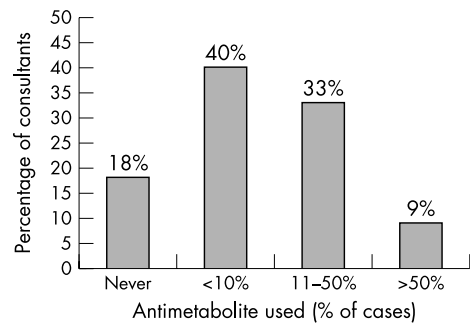


Figure 1 Frequency of antimetabolite use in trabeculectomy.

surgery, 4% never use antimetabolites for repeat surgery either, but 58% use antimetabolites in more than half of redo cases.

A total of 435 consultants participating in the survey used antimetabolites when performing trabeculectomy surgery. Data from this group were further analysed to give detailed information regarding choice of antimetabolite and method of application. Of this group, 34% (143) use 5-FU intraoperatively on a sponge only, 6% (27) use postoperative 5-FU injections only, and 53% (229) use both techniques. Interestingly, a small subgroup (7% (32)) uses MMC only and no 5-FU at all (fig 3). However, the preferred antimetabolite is 5-FU rather than MMC, with 93% (402) using 5-FU compared to 41% (179) using MMC. Of the 435 consultants performing trabeculectomy surgery with antimetabolites, 256 (59%) never use MMC. A further 129 (30%) consultants use MMC in less than 10% of cases. Only 37 (9%) use MMC in 11-50% of cases and just 10 consultants (2%) reported using mitomycin in more than half their cases (fig 4).

The concentration of MMC used ranged from 0.1-0.5 mg/ml, with 0.2 mg/ml being the most favoured dosage (fig 5). Application times ranged from less than 1 minute to more than 5 minutes, with 73% using MMC for 2-4 minutes (fig 6). Various factors influenced the decision to use or not use an antimetabolite, but experience of complications associated with their use was reported by 34% of consultants. Comparison between consultants using antimetabolites and those who never use them showed that antimetabolite users were much more likely to be influenced by recognised patient risk factors for failure such as previous topical medication (52% v 13%), failed trabeculectomy (94% vs 54%) and previous surgery (63% v 13%) (table 1).

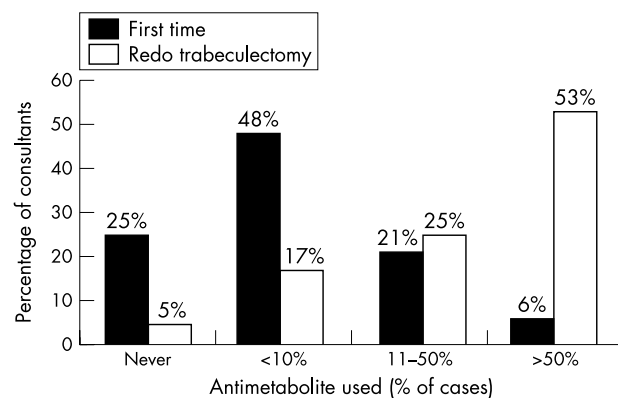


Figure 2 Frequency of antimetabolite use in first time and redo trabeculectomy.

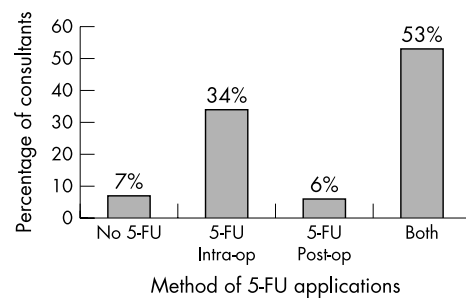


Figure 3 Technique of 5-FU administration.

DISCUSSION

This study reveals the pattern of antimetabolite use in trabeculectomy surgery in the United Kingdom. When interpreting the results of this postal survey, the issues of bias associated with sampling, recall, and non-responder rate need to be remembered. Sampling bias is limited by sending this survey to all consultants in the United Kingdom. The effect of recall bias is an important factor to consider, as we asked consultants to report on their antimetabolite use rather than measuring it directly. It is also possible that ophthalmologists with a specialist interest were more likely to respond. A high response rate in survey research increases statistical power, allows the results to be more representative of the population surveyed, and reduces (but does not eliminate) bias. This survey had a response rate of 82%. A response rate of 65% and above is usually regarded as high.¹⁰

Thirty five per cent of consultants estimated that they carry out less than 10 trabeculectomies each year, which is consistent with other evidence that the amount of glaucoma surgery being performed has declined.¹¹ Only 7% of consultants said they performed more than 50 trabeculectomies per year.

Most consultants report using antimetabolites (82%), but they use them very infrequently, with only 9% using antimetabolites in more than half their cases. Although the actual amount of use of antimetabolites was low in this survey, the finding that 82% of consultants stated they did sometimes use antimetabolites gives a different impression from the recent UK National Survey of Trabeculectomy which found antimetabolites used in 4% to 15% of cases.³ However, there may be no discrepancy between these two findings, as this survey asked for an estimate of practice over a 1 year period, while the National Survey of Trabeculectomy sampled four consecutive cases per consultant. Although most consultants will use antimetabolites, they do so very infrequently and so antimetabolite use in a sample of four consecutive cases appears low. Alternatively, there may be a true difference in the findings of these two surveys because of sampling times and case mix. The National Survey of

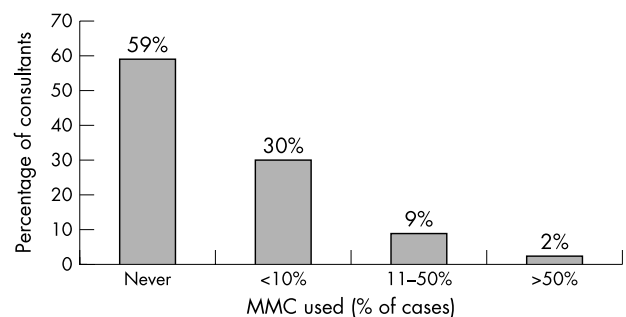


Figure 4 Frequency of MMC use in trabeculectomy.

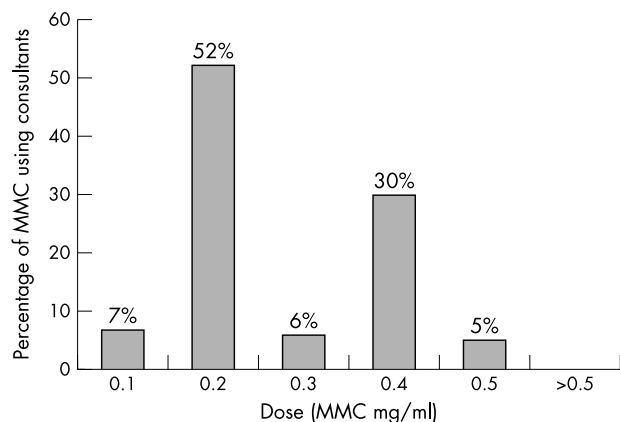


Figure 5 Concentration of MMC used.

Trabeculectomy sampled cases before June 1996, while this antimetabolite survey reflects the year up to the end of January 2000, so there may be a genuine increase in the use of antimetabolites.¹² Furthermore, the National Survey of Trabeculectomy concerned patients undergoing first time trabeculectomy for COAG and excluded cases with previous surgery or secondary glaucomas, which may account for a lower frequency of antimetabolite use in comparison with this study, which covered antimetabolite use in trabeculectomy for all types of glaucoma.

In the United Kingdom, 5-FU, particularly intraoperative sponge 5-FU, appears to be the preferred antimetabolite over MMC, with 93% of antimetabolite users utilising 5-FU in some cases and only 41% choosing MMC. The use of MMC in the United Kingdom is much less than in America or Japan, where trabeculectomy with MMC is the surgical procedure preferred by glaucoma specialists. Our results show that in the United Kingdom only 2% of consultants use MMC in more than half their cases, while in the United States the use of intraoperative MMC in first time trabeculectomy ranges from 33% to 52%.⁶ This may reflect the risk factors for conjunctival scarring felt to be present in the predominantly white UK population or it may be simply as a result of popular practice in the United Kingdom, with the emphasis on the relative safety of 5-FU compared with MMC.¹³ The commonest dose for the use of MMC was 0.2 mg/ml and the commonest time of exposure was 3 minutes. Experimental studies suggest that after 3 minutes the tissue uptake of antimetabolite begins to plateau.¹⁴

This survey showed that 25% of consultants never use antimetabolites in first time surgery and only 6% use

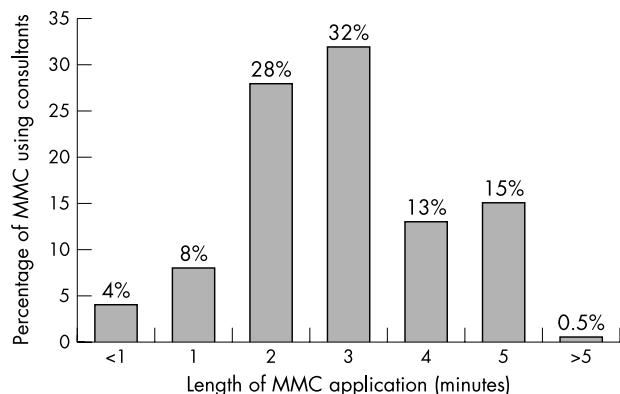


Figure 6 Time of MMC application.

Table 1 Factors influencing antimetabolite use: comparison between users and non-users

Factor	Antimetabolite users (%)	Antimetabolite non-users (%)
Complications	36	24
Race	88	48
Medications	52	13
Trab failure	94	54
Previous ops	63	13
Uveitis	64	24

antimetabolites in more than half their first time surgery cases. Randomised trials have shown that 5-FU is effective in trabeculectomy surgery in east and west Africa.^{15 16} Interestingly, in this population MMC and 5-FU may have similar efficacy in primary surgery.¹⁷

In conclusion, this survey has given an estimate of antimetabolite use in the United Kingdom with overall frequency of use being quite low compared with America or Japan.⁶ As this survey was based on estimated practice in the year up to January 2000, it would be interesting to repeat this survey in the future to assess the changing pattern of antimetabolite use, particularly with the advent of new antiscarring agents.¹⁸

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APPENDIX A: QUESTIONNAIRE

- Do you have a specialist interest in glaucoma?
 - Yes
 - No
- Do you currently perform trabeculectomy surgery?
 - Yes
 - No

If no, you do not need to answer any further questions, but please return the form.
- Can you estimate how many trabeculectomies you performed in the year ending 31st October 1999?
 - Less than 10
 - 11 to 50
 - 51 to 100
 - More than 100

4. How often do you use antimetabolites in (intraop/postop) trabeculectomy cases?
- Never
 - Less than 10% of cases
 - 11–50% of cases
 - More than 50% of cases

If never, please go to question number 12.

5. How often do you use any antimetabolite during (intraop/postop) a first time (primary) trabeculectomy?
- Never
 - Less than 10% of cases
 - 11–50% of cases
 - More than 50% of cases
6. How often do you use any antimetabolite during (intraop/postop) a redo trabeculectomy?
- Never
 - Less than 10% of cases
 - 11–50% of cases
 - More than 50% of cases
7. How often do you use intraoperative 5-FU on a sponge during a trabeculectomy (first time or redo)?
- Never
 - Less than 10% of cases
 - 11–50% of cases
 - More than 50% of cases
8. How often do you use postoperative 5-FU injections (first time or redo trabeculectomy)?
- Never
 - Less than 10% of cases
 - 11–50% of cases
 - More than 50% of cases
9. How often do you use mitomycin on a sponge during a trabeculectomy (first time or redo)?
- Never
 - Less than 10% of cases
 - 11–50% of cases
 - More than 50% of cases

If never, please go to question number 12.

10. What dose of mitomycin do you usually use? You may tick more than one box.
- 0.1 mg/ml
 - 0.2 mg/ml
 - 0.3 mg/ml
 - 0.4 mg/ml
 - 0.5 mg/ml
 - More than 0.5 mg/ml
11. For how long do you usually apply mitomycin? You may tick more than one box.

- Less than 1 minute
- 1 minute
- 2 minutes
- 3 minutes
- 4 minutes
- 5 minutes
- Longer than 5 minutes

12. Which of the following factors influence your decision to use/not use antimetabolites? You may tick more than one box.
- Patient's age
 - Patient's race
 - Patient's degree of pre-existing glaucoma damage
 - Patient has used topical medications
 - Patient has had previous failed trabeculectomy
 - Patient has had previous ocular surgery
 - Patient has history of uveitis
 - Patient has neovascular glaucoma
 - Patient has aphakic glaucoma
 - Personal experience of complications with anti-metabolites

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