How Should Pregnant Glaucoma Surgeons Handle Antimetabolites?

A Survey of Current Opinions and Literature Review

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Background

Antimetabolites (mitomycin C, 5-fluorouracil) are essential to reduce scarring in glaucoma filtration surgery.

MMC and 5FU are known to be teratogenic

- Well demonstrated by animal studies[1,2,3]
- Higher rate of spontaneous miscarriage amongst nurses with frequent occupational exposure to antimetabolites[4,5]

There is limited guidance on handling antimetabolites for pregnant glaucoma surgeons and those planning a pregnancy.

We conducted a survey among ophthalmologists to evaluate current practices and attitudes regarding the handling of antimetabolites during pregnancy in the UK.

Methods

An anonymised cross-sectional online survey was distributed to ophthalmologists of all grades via the UKEGS monthly newsletter in October 2021.

There were three sections, exploring the following:

I. General awareness of risks and current guidance
II. Pressure and impact on career
III. Satisfaction with current guidance

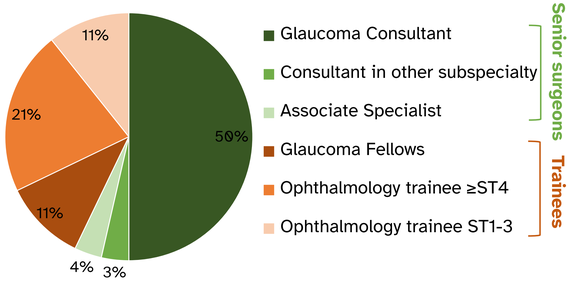
We searched PubMed, Cochrane, Ovid MEDLINE® ALL, Embase, as well as RCOphth, UKEGS and NICE websites for pre-existing guidance.

References

1. Kumar S, Lobo SW, Dubey AK, Pandey SK. Teratogenic effects of 5-fluorouracil on rat brain. Nepal Medical College journal : NMCJ 2006 Mar;8(1):7.
2. INOUYE M, KAJIWARA Y. Teratogenic interactions between methylmercury and mitomycin-c in mice. Archives of toxicology 1988;61(3):192-195.
3. Naqvo T, Saitoh Y, Yoshimura S. Possible mechanism of congenital malformations induced by exposure of mouse preimplantation embryos to mitomycin C. Teratology (Philadelphia) 2000 Apr;61(4):248-261.
4. NTP monograph on the systematic review of occupational exposure to cancer chemotherapy agents and adverse health outcomes. NTP monograph 2019 Mar(5).
5. Nassan FL, Chavarro JE, Johnson CY, Bolano JM, Rocheleau CM, Rich-Edwards JW, et al. Prepregnancy handling of antineoplastic drugs and risk of miscarriage in female nurses. Annals of epidemiology 2021 Jan;53:95-162.e2.
6. NICE Excellence. Cytotoxic drugs | Treatment summary | BNF content published by NICE. Available at: https://bnf.nice.org.uk/treatment-summary/cytotoxic-drugs.html. Accessed 27/04/ 2022.
7. González-Ventosa A, Ariz-Juan J, Sabater-Cruz N. Medidas para prevenir los riesgos asociados con la exposición a citostáticos en cirugía filtrante de glaucoma. Archivos de la Sociedad Española de Oftalmología 2020 Jul;95(7):334-344.
8. Haifler M, Lang E, Sabler I, Gutman Y, Lindner A, Zisman A. Increasing Medical Staff Safety by Using a Closed System for Intravesical Instillation of Mitomycin C. Urology (Ridgewood, N.J.) 2010;76(3):649-651.
9. Korinth G, Schmid K, Midasch O, Boettcher MI, Angerer J, Drexler H. Investigations on Permeation of Mitomycin C Through Double Layers of Natural Rubber Gloves. The Annals of occupational hygiene 2007 Oct 5;51(7):593-599.

Results

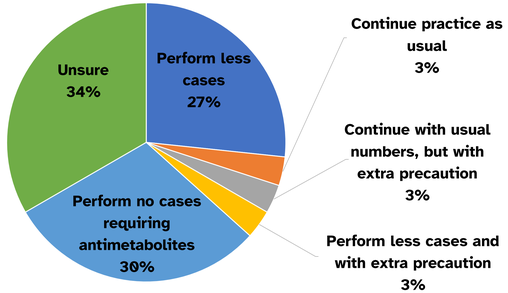
Grade of respondents (n=28)



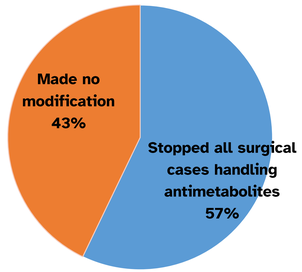
Survey Responses (✓ Trainees vs. ✓ Senior Surgeons)

Awareness of risk handling antimetabolites	Unaware- 1		5- Fully Aware
Awareness of local guidance	Unaware- 1		5- Fully Aware
Pressure to handle antimetabolites	No Pressure- 1	4.5	5- Major Pressure
Negative impact on training	No Impact- 1	3.5	5- Major Impact
Satisfaction with current guidance	Very Unsatisfied- 1		5- Very satisfied

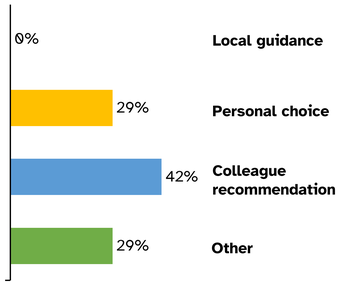
What is your current local guidance?



What did pregnant glaucoma surgeons actually do?



What was this decision based on?



Free comments:

"Like pregnancy itself this is a very personal experience"

"I would like to know how to operate when pregnant as I am considering glaucoma as a subspeciality"

"Need defined guidance from training committee at the College and local Deaneries"

"I was pregnant during my glaucoma rotation and I couldn't do much trabeculectomy which really affected my training and may have to repeat my glaucoma rotation"

"Pregnant surgeons should be assured they are free to make decisions without feeling pressure either way"

Literature Review

- No guidance on the occupational handling of MMC or 5FU in ophthalmic surgery in the context of pregnancy was found
- NICE guidance on general handling of antimetabolites exists but not in the context of pregnancy[6]
- *Gonzales et al.*[7] suggested:
  - Pre-drawn MMC/5FU
  - Discussion with occupational health to set guidelines locally

Discussion & Conclusion

Current practice is based on colleague experience and recommendations from seniors, not on robust evidence

- Glaucoma surgeons have voiced the need for clear guidance for handling antimetabolites– particularly in pregnancy and women of childbearing age
- There is a wide range of local guidance across the UK
- However, there is poor awareness of these guidance
- Worryingly, 5 out of 7 surgeons who responded to the question had felt some degree of pressure to handle antimetabolites whilst pregnant
- Trainees were more likely to experience pressure and a negative impact on training when compared to their senior colleagues

Recommendations

1. Closed administration[8]
   - e.g. subconjunctival delivery vs sponge application
2. Double-layer latex gloves as PPE standard[9]
   - Prevents permeation of MMC in-vitro
3. Change of gloves and prompt disposal post-procedure
4. Pre-drawn MMC/5FU[7]
   - Reduce open exposure and aerosol generation

