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Retinal venous occlusion associated with depot medroxyprogesterone acetate

Although it is well-established that oestrogen-containing contraception has prothrombotic potential in women over 35 years of age, particularly in women who smoke, low dose progesterone-containing contraception, both oral and parenteral, has not been conclusively linked to prothrombotic events. We evaluated two patients who developed retinal vein occlusion after administration of depot medroxyprogesterone acetate (DMPA, Depo-Provera™, Pharmacia & Upjohn, Kalamazoo, Michigan, USA) for contraception.

Case reports

A 44-year-old, hypertensive, woman who smoked, presented with decreased visual acuity to the level of 6/200 in the left eye. A non-perfused hemiretinal vein occlusion was present. Ten weeks earlier, she had received a DMPA injection.

Nine months later, her right eye developed a non-perfused central retinal vein occlusion with decreased visual acuity to the level of count fingers (20/4000 visual acuity). Five weeks earlier, she had received DMPA. Family history and systemic evaluation for a hypercoaguable state was negative.

A 39-year-old, hypertensive, woman who did not smoke, noticed a change in her visual acuity to the level of 20/50 in her left amblyopic eye (20/40). Examination showed a non-perfused hemiretinal vein occlusion. She had received multiple DMPA injections over the past two years; however, her most recent injection was 10 weeks prior to presentation. Family history and limited systemic evaluation for a hypercoagulable state was negative.

Comment

Hormonal contraceptive strategies include the use of oestrogen, progesterone or a combination of both. There is a well-established association between the use of oestrogen-containing oral contraceptives and thrombotic disease; however, the association with retinal venous thrombosis is less well defined.

Medroxyprogesterone acetate is a synthetic progesterone derivative, progestin, that can be administered orally or as an intramuscular depot injection. The recommended contraceptive dose of DMPA is 150 mg by intramuscular injection every 13 weeks. The recommended oral dose of medroxyprogesterone acetate for contraception is 5–10 mg daily. Much larger daily doses of up to 1200 mg of medroxyprogesterone acetate are used in the treatment of breast, lung and prostate cancers. These larger doses have been associated with a slightly increased risk of thrombosis. Reported cases in oncology patients include pulmonary thrombosis, sagittal sinus thrombosis and intestinal thrombosis.[1–3]

The package insert for the DMPA lists retinal thrombosis as a potential complication; however, no ocular events, such as retinal arterial or venous occlusion, have been reported. The lower cumulative doses of 150 mg DMPA injected every 3 months for contraception has not been conclusively associated with systemic thromboses. Of 11 500 women treated with DMPA for a total of 208 894 patient months, there were 15 cases of thrombophlebitic or thromboembolic disease reported.[4] Three of the 15 affected patients had a prior history of thrombophlebitis or thromboembolism. None had a retinal vascular occlusion.

To our knowledge (http://www.pubmed.gov last searched 1 June 2007), the only reported ophthalmic adverse event associated with DMPA was a case of ischaemic papillopathy in a 32-year-old woman.[5] Three days after her second injection, she experienced blurred vision in both eyes and bilateral optic disc oedema was present. Neurological examination and imaging were all normal. Two days after her third injection of DMPA, she again experienced blurred vision. The diagnosis of bilateral ischaemic papillopathy was made and DMPA was discontinued. This was the only case of an ischaemic papillopathy associated with DMPA reported.

Despite DMPA having a 30-year history as a safe and effective contraception for the vast majority, the two patients presented here suggest a possible causal association with retinal vein occlusion. We documented three eyes of two women that developed a retinal vein occlusion after receiving DMPA.

Byron F Deen, R Keith Shuler Jr, Sharon Fekrat
Albert Eye Research Institute of the Duke University Eye Center, Erwin Rd, Durham, NC 27710, USA

Correspondence to: Sharon Fekrat, Duke Eye Center, DUMC Box 3802, Erwin Rd, Durham, NC 27710, USA; fekra001@mc.duke.edu

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MAILBOX

Age and cataract surgery complications

We read with interest Robbie *et al*'s article.[1] We agree with the authors that identification of risk factors for cataract surgery is important, as it has implications for patient care, surgical training, auditing and revalidation. The authors concluded that older age was not associated with an increased risk of intraoperative complications. Complication rates in patients ⩾88 years old were not significantly different to patients <88 years (4.5% vs 6.3%, p = 0.54). Complication rates in patients ⩾96 years was higher than in patients <96 years but this was not statistically significant (11.1% vs 6.3%, p = 0.45). However, the study included only 54 patients older than 90 years (number of patients older than 88 years not stated) and 9 patients older than 96 years.

In a similar study, we identified all phacoemulsification cataract procedures carried out between 2001 and 2005 at the Southampton Eye Unit. Intraoperative complications, as classified in the National Cataract Surgery Survey,[2] were recorded on a computer database for each cataract procedure. We analysed the same data as the above study,[1] including age of patient, grade of surgeon and intraoperative complications (defined as abnormality in wound closure, posterior capsule tear, zonule dehiscence, anterior chamber haemorrhage, iris trauma or persistent iris prolapse).

Logistic regression analysis was carried out to examine whether patients aged ⩾88 and aged ⩾96 years were associated with an increased risk of complications. SPSS version 14 was used for statistical analysis; $p<0.05$ was considered statistically significant.

We identified 9367 consecutive phacoemulsification procedures. The mean patient age was 76.9 (SD 9.8) years. The overall complication rate was 3.1%. No significant difference was found between grades of surgeon and complication rates (trainee vs consultant: 3.2% vs 3.1%, p = 0.90).

Interestingly, the complication rate in patients ⩾88 years (837 eyes) was 4.3% compared to 3.0% in patients <88 years (OR 1.4, 95% CI 1.005 to 2.049, $p<0.05$). In patients ⩾96 years (36 eyes), the complication rate was 8.3% compared to 3.1% in patients <96 years (OR 2.8, 95% CI 0.858 to 9.228, p = 0.09).

Therefore, in contrast to the above study,[1] our results suggest that older age may be a risk factor for intraoperative complications during phacoemulsification surgery. We suggest that the rate of complications in cataract surgery in different age groups requires further study and that, in view of our results, experienced surgeons should preferentially operate on patients older than age 88 years.

Correspondence to: Thomas M Bosley, Cooper University Hospital, 3 Cooper Plaza, Camden 08103, USA; tmbosley@bosleynet

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Competing interests: None.

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Authors' response to Konstantopoulos *et al*

Editor

We thank Konstantopoulos *et al* for their interest in our paper and congratulate them for having conducted such a large study. It should be noted, however, that we did not actually conclude that older age was not associated with an increased risk of intraoperative complications,

rather we stated that our data suggest that age alone may not be a major risk factor for any complication. Clearly, absence of statistical evidence can never be equated to proof of no difference and we were careful to highlight that our numbers were small (9 patients older than 96, 111 greater than 88 years).

If we attempt to summarise data from our study, the Southampton Study and that by Berler to examine whether or not age greater than 88 is a risk factor for intraoperative complications using meta-analysis techniques, we find that there is significant inconsistency between the studies (test for heterogeneity $X^2 = 7.54$, $p = 0.02$, $I^2 = 73.5\%$). It seems likely therefore that the different findings from our work and that of Southampton are not simply a reflection of varying study sizes but arise from other differences between the studies: for example the populations being operated on, or perhaps the techniques employed.

We would therefore agree with Konstantopoulos *et al* that further research into this interesting subject is needed.

Scott J Robbie, Mohammed Muhtaseb, Kashif Qureshi, Catey Bunce, Xing Wen, and Alex Ionides

Correspondence to: Scott J Robbie, Addenbrooke's Hospital, Cambridge; robbie@addenbrookes.nhs.uk

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NOTICES

9th International Ocular Inflammation Society (IOIS) International Symposium

17–20 September 2007, Paris, France
Further details: Tel: +33 (0)1 70 08 69 82; Fax +33 (0)1 42 93 29 28; Email relamy1@wanadoo.fr; Website: www.iois-paris-2007.com.

2008 International Agency for the Prevention of Blindness (IAPB) 8th General Assembly

28 July–2 August 2008, Centro de Convenções Rebouças, Sao Paulo, Brazil
Further details: Email: agency@lvpei.org.

Second Sight

Second Sight would like to hear from experienced Indian eye surgeons returning to India after training/working in the UK. Second Sight is a London based charity dedicated to the elimination of cataract blindness in India.
Further details: Dr Lucy Mathen, lucymathen@yahoo.com.

Singapore National Eye Centre – 18th Anniversary International Meeting

14–17 March 2008, Suntec City Convention Centre, Singapore
Further details: Tel: +65 6322 8374; Fax: +65 6227 7290; Email: meet@snec.com.sg.

Inaugural Asia Cornea Society Scientific Meeting

13–14 March 2008, Shangri La's Rasa Sentosa Resort, Singapore
Further details: Fax: +65 6227 7291; Email: acs@snec.co.sg.

International Ocular Blood Flow Symposium

13 October 2007, Sutton Place Hotel, Toronto, Canada.
Further details: Tel: +416 978 2719 or +1 888 512 8173; Fax +416 946 7028; Email: ce.med@utoronto.ca.

Neuro-Ophthalmology and Strabismus – 2008 European Professors in Ophthalmology (EUPO) Residents' Course

5–6 September 2008, Geneva, Switzerland.
This course organised by Professor Avinoam B Safran will provide an overview and an update on recent advances in neuro-ophthalmology and strabismus.
Further details: http://eupo.eu.

CORRECTION

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Following the notification of several errors in the paper by Hudson *et al* (*Br J Ophthalmol* 2007;**91**:624–628) the online pdf has been corrected and replaced. Please go to the BJO website http://bjo.bmjjournals.com to view the correct pdf.

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