Effect of β radiation on success of glaucoma drainage surgery in South Africa: randomised controlled trial

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Editorial by Ramchandani

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Abstract

Objective To evaluate whether β radiation may offer a practical method of improving surgical success for glaucoma drainage surgery in South Africa.
Design Double blind, randomised controlled trial.
Setting Three public hospitals in South Africa.
Participants 450 black Africans with primary glaucoma.
Interventions Trabeculectomy with 1000 cGy β radiation or standard trabeculectomy without β radiation (placebo).
Main outcome measures Primary outcome measure was surgical failure within 12 months (intraocular pressure >21 mm Hg while receiving no treatment for ocular hypotension). Secondary outcomes were visual acuity, surgical reintervention for cataract, and intraoperative and postoperative complications.
Results 320 people were recruited. β radiation was given to 164; 20 (6%) were not seen again after surgery. One year after surgery the estimated risk of surgical failure was 30% (95% confidence interval 22% to 38%) in the placebo arm compared with 5% (2% to 10%) in the radiation arm. The radiation group experienced a higher incidence of operable cataract (18 participants) than the placebo group (five participants; P = 0.01). At two years the estimated risks with placebo and β radiation were, respectively, 2.8% (0.9% to 8.3%) and 16.7% (10.0% to 27.3%).
Conclusion β radiation substantially reduced the risk of surgical failure after glaucoma surgery. Some evidence was, however, found of an increased risk for cataract surgery (a known complication of trabeculectomy) in the β radiation arm during the two years after surgery.
Trial registration ISRCTN62430622.

Introduction

In many low income countries surgery is the principal means of managing glaucoma. In African patients a successful outcome of glaucoma surgery is often compromised by scarring.[1 2]

β radiation is appealing for use in glaucoma surgery. Application is rapid and simple, the probe has a working life of 20 years or more, and no additional supplies are required. We evaluated the effect of β radiation for glaucoma drainage surgery in South African patients.

Participants and methods

We carried out a double blind, randomised controlled trial of trabeculectomy with 1000 cGy β radiation or standard trabeculectomy without β radiation (placebo) in three centres in South Africa. All black Africans with established glaucoma requiring trabeculectomy were invited to participate in the trial (see bmj.com for eligibility criteria). We included one eye of each patient.

Visual acuity was measured using a reduced logarithm of the minimum angle of resolution (logMAR) tumbling E test.[3] We assessed cataract using the lens opacities classification III system.[4] We found variation between the trained observers and therefore used the need for surgical intervention as an indicator of clinically important cataract. The surgeons were experienced in ophthalmic surgery (surgery and postoperative care are on bmj.com).

Each centre had two applicators, one active (see bmj.com) and one placebo. Assigned groups were distributed to each centre in opaque, sealed envelopes. Each participant was allocated a trial number. The envelope with that number was opened during surgery to determine allocation. Patients were followed up at one day; one or two weeks; and 1, 3, 6, and 12 months after surgery.

The primary outcome measurement was surgical failure within 12 months, defined as an intraocular pressure greater than 21 mm Hg while receiving no treatment for ocular hypotension. Secondary outcomes were visual acuity, surgical reintervention for cataract, and surgical complications.

Statistical analysis

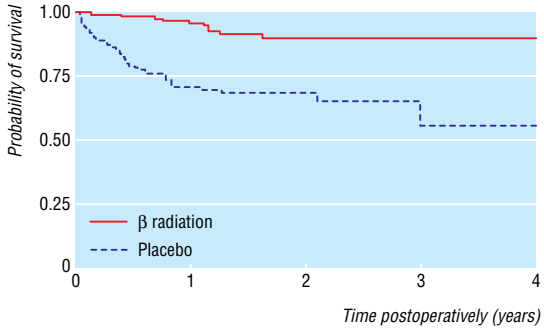
Analyses were carried out on an intention to treat basis. We plotted Kaplan-Meier survival curves of time to surgical failure and need for cataract surgery by treatment group and compared these using the log rank test. Cox regression was used to estimate the failure rate ratio between the two groups while controlling for other prognostic factors. We compared the treatment arms for changes in visual acuity using the last recorded visual acuity, which could be later than the date of surgical failure. The degree of change was classified into three categories: <0.25 logMAR, 0.25-0.39 logMAR, or ≥0.40 logMAR. We considered changes from better than count fingers to count fingers, from count fingers to perception of light, and from perception of light to no perception of light as equivalent to changes greater than 0.4 logMAR.

Results

Overall, 320 of 450 patients requiring trabeculectomy were randomised; 164 to the radiation group (see bmj.com). Twenty participants (6%) dropped out of the study after surgery. A further 68 patients were lost to follow-up before 12 months (36 in the radiation arm).

P+ *Exclusion criteria are on bmj.com*

ELPS *This is the abridged version of an article that was posted on bmj.com on 5 October 2006: http://bmj.com/cgi/doi/10.1136/bmj.38971.395301.7C*



Patients at risk

Time (years)	0	0.5	1	1.5	2	3	4
Placebo	149	97	75	44	24	7	2
β radiation	151	124	109	70	43	19	2

Survival times by treatment group after glaucoma drainage surgery in patients with an intraocular pressure ≤21 mm Hg

Similar mean numbers of follow-up visits were completed in each of the treatment groups (4.9 radiation group; 4.5 placebo group; P = 0.35). Participants who were followed up showed similar distributions for sociodemographic, ophthalmic, and surgical factors in the treatment arms (see bmj.com).

Primary outcome: surgical failure

Fifty four cases of surgical failure (median intraocular pressure >21 mm Hg) were identified. Strong evidence was found of a lower risk of surgical failure in the radiation group (figure; log rank test $\chi^2 = 26.1$; P < 0.0001). The estimated risk of failure 12 months after surgery in the placebo arm was 30% (39 cases, 95% confidence interval 22% to 38%) and in the radiation arm was 5% (six cases, 2% to 10%). In the placebo arm the risk was 21% (high) in the first six months after surgery, 30% at 12 months, and 32% at 18 months. In the radiation group the risk was 2% (low) in the first six months, 5% at 12 months, and 9% at 18 months.

Eleven cases of surgical failure in the radiation group represent 4.8 per 100 person years and 43 cases in the placebo group represent 26.0 per 100 person years. Failure rates across different subgroups were consistently lower in the radiation group. After fitting a Cox regression (proportional hazards) model, the estimated failure rate ratio in the radiation group compared with the placebo group was 0.21 (95% confidence interval. 0.11 to 0.40; likelihood ratio test $\chi^2 = 27.7$, P < 0.0001). Controlling for each of the patients' factors individually did not result in any important change to the estimated rate ratio (range 0.19-0.22).

Among patients not experiencing surgical failure and with at least six months of follow-up, the median intraocular pressure in the radiation arm at last follow-up was 11.5 mm Hg (interquartile range 8.5-14.0; n = 115) and in the placebo arm was 13.5 mm Hg (11.0-16.0; n = 82). After taking account of baseline intraocular pressure, strong evidence was found that intraocular pressures were lower in the radiation group than in the placebo group (P < 0.001, linear regression analysis). The median reduction in intraocular pressure in the radiation group was 17 mm Hg compared with 16 mm Hg in the placebo group. In relative terms, the radiation group experienced a median reduction in intraocular pressure of 61% compared with 55% for the placebo group.

Secondary outcomes

Visual acuity

The distributions of changes in visual acuity between the two groups after surgery were similar. The mean duration of follow-up was 585 days in the radiation group and 532 days in the placebo group. Overall, 58% of participants in the placebo arm compared with 56% in the radiation arm had a change <0.25 logMAR. Twenty six per cent of participants in the placebo arm and 28% in the radiation arm had deteriorations ≥0.25 logMAR.

Surgical reintervention for cataract

The radiation group experienced a higher incidence of cataract requiring extraction than did the placebo group (18 *v* 5 participants; see bmj.com; log rank test P = 0.01). One year postoperatively the risk of having developed a cataract requiring extraction in the placebo group was 0.8% (95% confidence interval 0.1% to 5.9%) and in the radiation group was 3.2% (1.2% to 8.3%). At two years the risks were 2.8% (0.9% to 8.3%) and 16.7% (10.0% to 27.3%). All participants identified as needing cataract extraction during follow-up had evidence of cataract at baseline. Their median (range) lens opacities classification scores at baseline were 2.8 (1.5-4.0) for nuclear opacity, 3.0 (1.0-4.0) for nuclear colour, 1.8 (0.1-3.6) for cortical cataract, and 1.0 (0.1-4.0) for posterior subcapsular cataract. Participants with pseudoexfoliation glaucoma were more likely to be identified as needing cataract surgery than those with primary open angle glaucoma (11 cases, rate 0.3/100 person years *v* 11 cases, rate 3.5/100 person years; P = 0.007). For both types of glaucoma there seemed to be an excess of cataract in the radiation group (primary open angle glaucoma, 8 *v* 3 cases, P = 0.10; pseudoexfoliation, 9 *v* 2 cases; P = 0.08).

Surgical complications

The two most common surgical complications were clinically important uveitis and hypotony, both slightly more common in the radiation group (see bmj.com). Severe complications were seen in five participants (1.6%), two of whom received placebo.

Discussion

β radiation has a beneficial effect on intraocular pressure and is a useful adjunct to glaucoma drainage surgery in South African patients.

The major disadvantage of β radiation we identified was an increase in the risk of surgical reintervention for cataract. One reason for this observed increased risk could be that clinicians give more attention to cataract in the presence of controlled intraocular pressure. If this is so, we would expect those with controlled pressure to undergo further cataract surgery. This does not seem to be the case (data not shown).

β radiation could itself cause cataract. The calculated amount of radiation reaching the germinal

What is already known on this topic

The efficacy of glaucoma surgery in South Africa is limited by postoperative scarring

No universally accepted method exists for dealing with this problem

What this study adds

β radiation as an adjunct to glaucoma drainage surgery in South African patients significantly improves surgical success rates over at least two years

The radiation group seemed to develop an excess of cataract

epithelium of lenses in our trial was, however, less than the minimum dose reported to cause cataract (200 cGy).[5 6] In addition β radiation is often used on bare sclera to treat pterygia. Despite a larger dose of radiation to the lens, cataract is not common. Finally, radiation induced cataract is a characteristic pattern of cortical opacity, starting at the site of application.[7] This pattern was not observed in our patients.

Extremely shallow anterior chambers have been linked with cataract formation.[8 9] In our study such chambers were rare. It has also been suggested, although reports vary, that eyes with slightly low intraocular pressures may be at higher risk of cataract formation.[10 11] Lower intraocular pressures in the β radiation arm could explain some of the increase in cataract risk.

We observed a higher incidence of mild uveitis among the radiation group. After controlling for this, evidence of an association between β radiation and risk of cataract remained. Uveitis therefore does not explain all of the increased risk.

The use of steroids during the postoperative period may induce cataract formation but would require differential use between the two groups. Randomisation and a similar pattern of follow-up visits in the two groups make this less likely.

β radiation is carried out at the time of original glaucoma drainage surgery and does not require postoperative compliance or direct costs. It has a major, clinically important benefit on control of intraocular pressure and has appeal in resource poor settings.

Although blindness caused by cataract is reversible, blindness caused by glaucoma is not. Restoration of vision with subsequent cataract surgery must represent a better outcome than permanent blindness from glaucoma.

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Competing interests: None declared.

Ethical approval: This study was approved by the research ethics committees of all included centres, along with the Institute of Ophthalmology.

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Corrections and clarifications

August is medical staffing month
Iain Varley, the author of this filler article (*BMJ* 2006;333:751, 7 Oct), has asked us to point out that the medical staffing department that he criticised was not that of York Hospital, whose address he gave as the place where he was working at the time. The *BMJ* apologises for a failure of communication that meant we didn't edit the filler to make this clear.

Watchdog brands two thirds of NHS trusts as "fair" or "weak"
After we went to press, we were alerted to an error in one of the Health Commission's results given in this news article by Adrian O'Dowd (*BMJ* 2006;333:769, 14 Oct). In the fifth paragraph, we said that, of all the NHS trusts in England examined in the commission's annual "health check," primary care trusts performed least well, with 78% of them being rated as "fair or weak." In fact, the percentage should have been 70%.

Anaesthesia, Elvis, and lawnmowers
The Association of Anaesthetists' Anaesthesia Heritage Centre mentioned by M Dylan Bould in this filler article (*BMJ* 2006;333:793, 14 Oct) is at 21 Portland Place (not Portland Road), London W1B 1PY (see www.aagbi.org/ for more details).

Clinical problem solving and diagnostic decision making: selective review of the cognitive literature
A misspelling of an author's name has rather belatedly been brought to our attention. In this Education and Debate article by Arthur S Elstein and Alan Schwartz, we wrongly omitted the "t" from the second author's name (*BMJ* 2002;324:729-32).