Beta radiation: an effective and potentially cheap aid to preventing sight loss from Glaucoma

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Abstract

Glaucoma is a common cause of blindness worldwide. Beta radiation using strontium 90 provides a very cost effective way of increasing the surgical success of trabeculectomy, the principle operation used to treat glaucoma globally. The use of beta radiation, though proven to be safe and effective, is significantly reduced by national and international regulations and legislation.

Introduction

The glaucomas are the world’s second most common blinding condition. Unlike cataract, (the most common cause of blindness worldwide) they are frequently asymptomatic until a late stage of the disease and the damage caused is irreversible.

In the developed world early detection often occurs during routine eye testing. Therapy involves lowering the pressure in the eye to minimise progression of the damage to the optical nerve. In the developed world treatment is normally with topical medicines, and if these fail lasers or surgery.

In the developing world the situation is very different. Routine eye testing is not common and hence the glaucomas present late, often with significant visual symptoms. This represents advanced, potentially rapidly blinding, disease. Therapeutic options at this stage are limited. Supply issues, long term compliance and cost all interplay to make medical therapy impractical. Laser therapy is not widely available leaving surgical lowering of the pressure as the most accepted practical intervention for long-term management.

Surgery normally involves the creation of a small guarded fistula. This fistula allows aqueous humour to drain from the anterior chamber of the eye to the subconjunctival space. This surgical procedure is known as a trabeculectomy. Complications of this include the closure of the fistula due to scarring, cataract formation, ptosis, and more rarely over drainage of the fistula, haemorrhage and infection. Considerable research effort has resulted in a significant reduction of the risk of scarring of the fistula by the use of antimetabolites at the time of surgery. These inhibit the fibroblastic scarring response and thus improve the chances of survival of the fistula. In the developed world the vast majority of units now employ two forms of cytotoxic anti-metabolite therapy during surgery: 5-fluorouracil or mitomycin C. In the developing world these drugs are not easily available and the skills required for administration are not frequently taught.

Beta-radiation also reduces the scarring response. The use of beta radiation to modulate wound healing is not new. In the 1940s its utility was established and it has been used for glaucoma surgery since the 1970s; especially in the pediatric population where the challenges of healing are most acute, and concerns over toxic anti-metabolites keenest. Ionizing radiation works by modulating fibroblast activity, causing cell cycle arrest. A potential advantage of beta radiation compared to anti-metabolites is that the fibroblast cells, which are essential for wound healing, are not destroyed. Instead the beta radiation induces a temporary state of dormancy which may permit a better surgical outcome.

Practical and Clinical Advantages of Beta radiation

Beta-radiation is easy to use. The solid Strontium 90 (Sr90) source is simply held against the surgical wound until the correct dose is administered. This can take between 20 seconds or so for a new source up to a couple of minutes for an old one. Beta radiation from Sr90 has high energy locally, but limited penetrating powers. This means it presents minimal risk to other tissue, such as the lens, and negligible risk to the surgeon or other staff. It has long been used in the developed world in management of ophthalmic conditions.

Its use in a developing world situation is even more attractive. The beta-radiation delivery device, once
purchased, has a long working life (20 years+), no working parts and will treat as many patients as required during it’s lifetime. In addition, the emission of beta particles ensures self sterilises a clean active surface.

No large randomised controlled trial existed to estimate the treatment effect of beta radiation. In order to estimate the treatment effect and to establish the practicality in a developing world situation we undertook a double blind, randomised controlled trial (RCT) of trabeculectomy with either 10 Gy beta-radiation or placebo in South Africa. 320 eligible individuals were randomised. There was very strong evidence (P<0.0001) that there was a clear reduction in the risk of failure of surgery in the beta-radiation group.

As noted above, a complication of trabeculectomy surgery is cataract formation. In our study, the beta-radiation group experienced a higher incidence of cataract requiring extraction (n=18) than the placebo group (n=5) (P = 0.01) at one year post-operatively. Whilst this can be easily solved by further surgery in the developed world it represents a major challenge in the developing world. The next step has been to consider combined cataract and trabeculectomy surgery. If successful, this would provide a ‘one-stop’ solution for those in the developing world presenting with glaucoma. We are more than half way through recruiting for an RCT of cataract surgery combined with trabeculectomy with either 10Gy beta-radiation or 5 Fluorouracil (5FU) – the present therapy of choice in Tanzania.

If proven effective in this circumstance this surgical procedure offers hope of a practical solution to offer the thousands of glaucoma sufferers in Africa, where open angle glaucoma is a major challenge. Sight restorative and sight preserving surgery combined and made practical as a result of the simple application of beta-radiation to the operative site at the end of surgery. The probe can treat as many patients as wished for in it’s 20 year life, hence supply and ongoing cost problems are no longer an issue. Two major obstacles however stand in the way of adoption of this appropriate technology.

Legislation

Our experience with the transport and licensed use of Strontium 90 probes has not been a positive one. Legislation impedes the use of this appropriate technology. Cytotoxic drugs produce effluent with each and every application. This requires correct disposal that is a challenge, with significant environmental implications, in areas of poor infrastructure. Regulatory laws are however remarkably lenient in the use of these substances. In contrast, beta radiation produces no toxic by products with use, but the use of all radioactive substances are very tightly controlled by legislation and regulation, both national and international. The current control environment, however, is a “one size fits all” model.

Small ophthalmic sources, such as the one we use, present no proliferation threat whatsoever. Beta radiation is stopped by a couple of sheets of paper and is very easy to shield. A wooden or plastic box is a suitable safe repository, obviously within a secure environment. The difference between our small beta sources and gamma emitting materials such a plutonium or iodine 131 is very great. We believe that some limited, pragmatic, adjustment of the regulatory environment could help develop the use of beta radiation to improve the success of trabeculectomy surgery in the developing world considerably.

Manufacture

Strontium 90 is a common by-product of nuclear fission and potentially a highly cost effective and safe form of medical treatment. However the difficulties in using beta radiation has so reduced demand for probes there are currently no commercial manufactures of them. What is needed is effective advocacy for appropriate technology provision such as this.

In conclusion, beta-radiation is clinically effective, cost-effective and a completely appropriate technology for use in the developing world in the therapy of glaucoma. Its adoption is hindered by legislative and manufacturing barriers that should be urgently addressed.

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Nil

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