

Trabeculectomy (With Cytotoxic Adjunct) As First Line of Treatment in Chronic Glaucoma at a Rural Secondary Level Hospital in South Africa

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Abstract

Aim: To determine the incidence of trabeculectomy (with cytotoxic adjunct) as the first line of treatment in chronic glaucoma and to describe demographic data, visual acuity, Cup/Disc ratio and intraocular pressure at the time of diagnosis, and, if surgery was delayed, to describe data at the time of surgery to determine the efficacy of pharmacological management.

Design: Retrospective record review for the period 1 March 2002 to 2006.

Results: Record review included 128 eyes of 64 consecutive chronic glaucoma patients diagnosed with primary open angle glaucoma. Trabeculectomy with cytotoxic adjunct had been performed on 24 eyes of 24 patients (37.5%). The mean age of the sample of 12 females and males was 56 years representing a South African population profile of 18 Coloured, 3 African Black and 3 White persons. Pharmacological management was the first line of treatment for all patients for a period of 3 days to 2 years 7 months. All patients had decreased vision at the time of surgery but intraocular pressure was lower (30.8 to 28.1 mm Hg) in the operative eye.

Conclusions: The first line of treatment for chronic glaucoma was medical management contrary to National Guidelines recommending trabeculectomy with cytotoxic adjunct.

Keywords: Glaucoma; Trabeculectomy; Cytotoxic adjunct

Introduction

The South African National Prevention of Blindness Programme [1] is a component of the World Health Organization (WHO) Global Initiative for the elimination of avoidable blindness by the year 2020 [2]. Although primary glaucoma is not preventable it is listed amongst the WHO Vision 2020 priority eye diseases for middle income and industrialized countries because medical and surgical treatment in the early stage is effective but early diagnosis is difficult [3].

South Africa is a developing country with a population estimated at approximately 47.4 million in 2006 and estimated life expectancy at birth at 49 years for males and 53 years for females [4]. Here, glaucoma is the second leading cause of blindness and accounts for approximately 14% of the blind population [1] therefore there is a global imperative to collect data on the prevalence and types of glaucoma and the availability and use of services [2].

This study of limited scope was undertaken at the eye clinic of the rural George Provincial (secondary-level) Hospital in the Western Cape Region with a population of 250,000 as at 31 March 2006 (Moolman, 2006). We report the prevalence of trabeculectomy with cytotoxic adjunct in chronic glaucoma as the national recommended first line of treatment [1] for the public health sector. National guidelines define chronic glaucoma as "a disorder in which there is loss of visual field combined with an excavated appearance of the optic disc. The level of eye pressure is not used in defining glaucoma" [1] but the guidelines nevertheless recommend IOP for case detection at hospital level (secondary prevention) as well as optic disc examination. 'Further management' at tertiary prevention level is surgical intervention by trabeculectomy with cytotoxic adjunct (5-fluorouracil or mitomycin-C) as the first line of treatment. Repeated surgery is recommended in bleb failure resulting in poorly controlled IOP. For the purpose of this study cytotoxic adjunct refers to Mitomycin-C, an antimetabolite and broad spectrum cytostatic known to reduce collagen synthesis, which is the

basis for scar formation. In trabeculectomy mitomycin-C prevents scar formation and fibrosis of the bleb (operation site) to allow drainage of aqueous humour.

Drainage surgery is favoured over pharmacological management as medication is expensive, treatment is often life-long and may have unpleasant local and systemic side-effects whereas the disease is painless and asymptomatic, medication regimens may be confusing and compliance is often poor [1]. If used, pharmacological management should be instituted following successful trabeculectomy in eyes in which IOP control is inadequate and then the recommended order of preference is 1) topical beta blocker, 2) topical parasympathomimetic and 3) oral carbonic anhydrase inhibitor. Chronic glaucoma is difficult to manage successfully as explained earlier but also for a number of further reasons: in persons of African descent there is an earlier age of onset, late presentation and irreversibility of visual loss [1].

The National Guidelines [1] recommend 500 trabeculectomy operations per million of the population annually using the formula for trabeculectomy surgery rate (TSR) as:

$$\frac{\text{Number of trabeculectomy operations per year} \times 1 \text{ million}}{\text{Area population}}$$

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The TSR for the George Region with a population of 250 000 in 2006 should have been 125. For the purpose of this study chronic glaucoma was defined as primary open angle glaucoma (POAG).

Methods

A descriptive design using retrospective record review was undertaken. The objectives of the study were 1) to establish the number of patients who had trabeculectomy with cytotoxic adjunct as the first line of treatment for POAG between 2002 and 2006; and 2) to compare baseline clinical data about the condition of the affected eye (visual acuity, Cup/Disc ratio and IOP) at the time of diagnosis and at the time of surgery to determine the efficacy of pharmacological management. We anticipated the unavailability of operating room time and the need for pharmacological management in the interim. In addition demographic data (age and gender) were described to establish trends including race because of the strong genetic link between chronic glaucoma and black persons of African origin.

The Research Ethics Committee of the Faculty of Health Sciences at the University of Cape Town approved the study and all study procedures adhered to the Declaration of Helsinki [5]. The Hospital Management team granted access to patient documents. Confidentiality was maintained by using code numbers for patient records. In South African legislation (Section 16 (2)) a health care provider may examine a client's health records for research purposes without authorization if the information does not identify the client [6] The Mayo Clinic has a long tradition of patient record review to improve patient care [7] Debates concerning the waiving of patient consent for quality-improvement research initiatives in hospitals, are well documented [8,9] provided stringent conditions are met, and if these studies are not done, may well be more harmful than helpful [10].

The study population comprised the total number of patients attending the eye clinic during the period under review. This time frame was purposively selected to coincide with the appointment of the only ophthalmologist at the hospital who also performed all surgical procedures. Inclusion criteria were: 1) a diagnosis of POAG during the period under review, 2) excavated appearance of the optic disc (increased Cup/Disc ratio), 3) IOP ≥ 21 mmHg, 4) rim haemorrhage, 5) notching of the cup (loss of nerve fibre layer), 6) bayonetting of vessels in the cup and 7) worsening of Cup/Disc ratio in patients with apparently good IOP control (Stempels). Visual field testing, also diagnostic for chronic glaucoma [1], was not considered in this study because the hospital did not have a visual field analyzer.

Exclusion criteria included patients diagnosed with POAG before 1 March 2002 even if operated on during the period under review.

The design of a record review form was guided by the study objectives and examined for content validity by the ophthalmologist at the clinic and an ophthalmic trained nurse and for construct validity by a nurse researcher. The review form was pilot tested at the clinic on three medical records selected consecutively for trabeculectomy with cytotoxic adjunct in POAG as planned for the actual study. These records were not included in the study as patients had been diagnosed with POAG before 1 March 2002. A second reviewer established reliability of the instrument and the quality of record review. The form did not need revision. The first line of treatment was interpreted as trabeculectomy with cytotoxic adjunct if patients had been given a date for surgery at the time of diagnosis and were operated on within one month even if medication was prescribed. Medical management included eye drops. Surgery was performed under local anaesthetic.

The cytotoxic adjunct used was mitomycin-C. After surgery Spersadex Comp eye drops were prescribed for administration four times a day. Glaucoma medication was often reinstated at a later stage. For binocular raised IOP monocular surgery was performed while continuing with pharmacological management of the un-operated eye until surgery was needed.

All IOP measurements were made by Goldmann applanation tonometry by the same ophthalmologist who measured Cup/Disc ratio. Nurses measured visual acuity using the Snellen chart.

Statistical Analysis

Raw data were captured onto a password-protected Excel® spreadsheet (Microsoft Office 2007). Statistical analyses were undertaken with IBM SPSS Statistics version 19. The probability value $p.05$ was accepted as the level of significance [11]. Standard deviation (SD) was set at 95% Confidence Intervals. Means were calculated from frequency tables for age for each race group, visual acuity, Cup/Disk ratio and IOP.

For the purpose of analyzing data, visual acuity measurements are given as LogMAR [12] Table 1 including count fingers and hand motion [13] except for light perception which is noted in descriptive terms as this simply detects a stimulus [13].

Tests of normality of distribution of variables for visual acuity, Cup/Disc ratio and IOP followed the convention of using the Shapiro-Wilk test for a sample size smaller than 50 [11], showing data were not normally distributed therefore non-parametric tests were used to compare readings.

Results

The study population comprised the total number of eye clinic outpatients (N=2580) during the period under review, of whom 965 (37.4%) were treated for glaucoma. Purposive sampling for the period March 2002 to 2006 resulted in review of 64 (6.6%) of 965 records of patients diagnosed with POAG comprising 34 females and 30 males with a mean age of 59.7 years representing a population profile of 40 (62.5%) Coloured, 15 (23.4%) White, seven Black African (10.9%) and two (3.1%) Indians.

Of the 64 patients, 24 (37.5%) had trabeculectomy with cytotoxic adjunct. Only these results are reported. Demographic data for the sample are presented in Table 2.

The mean number of operations performed annually was 4.8 (range 2 to 9) with a waiting time of between 3 days and 2 years 7 months (Table 3).

Five patients (20.8%) had drainage surgery within one month

Snellen equivalent	LogMAR
No Light Perception (NLP)	Descriptive text
Hand movement at 0.61 metres (HM)	+3.0
Count Fingers at 0.61 metres (CF)	+2.0
6/60	+1.0
6/36	+0.8
6/24	+0.6
6/18	+0.5
6/12	+0.3
6/9	+0.176
6/6	0.0

Table 1: Snellen equivalent of LogMar visual acuity measurement.

of diagnosis of POAG meeting the criterion of having surgery as the first line of treatment. The majority of patients (16/24; 66.7%) had surgery within six months. For all patients surgery was preceded by pharmacological management.

A comparison of visual acuity, Cup/Disc ratio and IOP in operative eyes at diagnosis of POAG and at the time of trabeculectomy with cytotoxic adjunct following pharmacological management is presented in Table 4.

The mean pre-treatment visual acuity LogMAR of 0.81 (6/36 on the Snellen chart) (Table 4) had decreased to 1.15 (6/60 or worse on the Snellen chart) at the time of trabeculectomy, but the difference was not statistically significant ($p=0.128$). The difference between the mean pre- and post-treatment Cup/Disc ratio was not statistically significant ($p=0.438$). The mean pre-treatment IOP improved from 30.8 mm Hg to 28.08 mm Hg at the time of trabeculectomy, but the difference was not statistically significant ($p=0.232$).

Coloured patients were younger (mean age 55.1 years) and had better vision (mean LogMAR 0.5) than Black Africans (58.7 years; mean LogMAR 1.5) at the time of diagnosis. White patients were the oldest (mean age 59.7 years) with the same visual acuity as the Coloured patients.

Discussion

In 2002 Government guidelines recommended trabeculectomy as the first line of treatment for chronic glaucoma in South Africa [1]. Study results showed that the majority of patients with POAG (40/64, 62.5%) only had pharmacological intervention and the patients having surgery were all commenced on a medication regimen. Only 20.8% (5/24) of these patients had surgery within one month of diagnosis.

Age (years)	56.1 ± 13.53 (range 30 to 85)
Gender (M:F)	12 (22.6%): 12 (22.6%)
Race (coloured:black:white)*	18 (34.0%): 3 (5.7%): 3 (5.7%)

*South African classification

Data is presented as Mean, Standard Deviation (±) or Number (%)

Table 2: Patient Demographics (n=24).

Time period	Number of patients (n=24)
3-6 days	2
7-14 days	1
15-days-1 month	2
2 months	3
3-4 months	4
5-6 months	4
7-11 months	2
≤1 yr 2 months	2
<1 yr 10 months	2
≤2 yrs 7 months	2

Table 3: Waiting time for surgery.

	Pre-trabeculectomy	At time of surgery
Visual acuity (LogMAR)	†0.81 ± 0.76	†1.15 ± 1.09
Cup/Disc ratio	0.70 ± 0.20	0.71 ± 0.19
Intraocular pressure	30.79 ± 8.48 (range 17 to 56)	28.08 ± 7.00 (range 12 to 46)

†Corresponds to mean visual acuity of approximately 6/36 on Snellen chart and †6/60 respectively

Data is presented as Mean and Standard Deviation (±)

Table 4: Comparison of clinical characteristics of operative eyes.

Anecdotal reasons (personal communication Dr Stempels) for the delay in surgery for up to 2 years 7 months included a backlog of patients and a shortage of staff as the only public health sector ophthalmologist in the region had been newly appointed to the post in 2002 and there was no ophthalmic nurse practitioner. In addition there was a high cancellation rate of operations due to the unavailability of beds at the hospital. Financial constraints and few employment opportunities may have played a part as the median annual income of working adults aged 15-65 in the George local municipality was \$2,439 in 2001 [14]. Furthermore, poor adherence to pharmacological regimes and to keeping follow-up appointments meant that patients only returned to the hospital when their vision had deteriorated considerably. Afrikaans is the dominant language (67.1%) [14] in the region of the 11 official languages in South Africa but the role of language differences in non-adherence to the medical regimen was not established.

Although it is reported [15] that age-related prevalence of POAG is four to five times higher in African Americans and Afro Caribbeans than in Caucasians [16] the demographic profile of the sample reflects the local population demographics of this rural area. In 2001 the racial makeup of the George local municipality was Coloured 50.38%, Black African 27.28%, White 22.08% and Indian/Asian 0.26% [14]. The South African Glaucoma Society reported that the prevalence of glaucoma is around 5 to 7% in the black population and 3 to 5% in the white population of South Africa [17]. As race is a complex and controversial concept 'racial' difference may be due to factors other than genetics such as differences in social, behavioural and environmental exposure [15]. In the study Black Africans with chronic glaucoma were detected at a late stage when they had severe vision loss.

The key role of ophthalmic nurse practitioners (ONPs), in its broadest sense, is prevention of avoidable blindness [18]. Since the completion of the study one author (NO) has commenced an ONP-led eye screening programme in the region under the supervision of the ophthalmologist to fulfil the global imperative to collect data on the prevalence and types of glaucoma and the availability and use of services [2] amongst other responsibilities. This includes annual eye screening of close relatives of a person who has chronic glaucoma, particularly if over the age of 40 years.

There appears to be no South African published literature on the implementation of the DoH Guidelines (2002) and limited international literature on the pro's and con's of trabeculectomy with mitomycin-Cas the first line of treatment for chronic glaucoma. Prescribed medication, usually eye drops, was effective in reducing intraocular pressure but not sufficiently to bring pressures to within normal ranges (<21 mm Hg). Cup/Disc ratio was unchanged between the time of diagnosis and trabeculectomy. The South African Glaucoma Society recommends prostaglandin derivatives or fixed combination drugs or laser surgery as first line treatment for open angle glaucoma [17].

The feasibility of sustaining the recommended protocol is questionable. Nevertheless, drainage surgery may be the only solution for successful management of chronic glaucoma in a developing country such as South Africa for four reasons. First, we have an adult illiteracy rate of around 18% of adults over 15 years old (about 9million adults are not functionally literate) [19] and second, only 17% of the Coloured population and 14% of Black Africans have a high school or higher qualification while this figure is 65% for Whites over 20 years old and 40% for Indians [19]. Illiteracy may be associated with reported non-adherence to medication regimes [1] and with the finding that Black Africans were diagnosed with advanced POAG and severe visual impairment. Third, in a resource poor country medication is expensive

and patients have reported anecdotally that eye drops are not always available at the clinics and that public transport is too expensive to return as there is no guarantee there will be a supply next time. Finally, elderly patients find it difficult to administer eye drops when eyesight is poor and other debilitating comorbid conditions such as arthritis are present.

A further compelling reason for drainage surgery as first line treatment in South Africa as in some parts of the world, including England, is the prevention of visual field loss but not so in the United States in the near or distant future until maximal medical treatment is inadequate [20]. Concerns of safety are a deterrent to the use of incisional surgery in the United States [20]. Discussion of a combined approach such as phacoemulsification for mild glaucoma is beyond the scope of this study. Trabeculectomy may therefore have to continue as the first line of treatment but a field analyzer, operating room time and ward beds are prerequisites for successful outcomes.

This study of limited scope described trabeculectomy surgical rate and patient data from the time of diagnosis of POAG to the time of surgery at one rural public health sector hospital (George Provincial Hospital) in one Health District (Southern Cape Karoo District) in one Province (Western Cape Province). No such published data was found in South Africa.

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