Resting pulse rates in a glaucoma clinic: the effect of topical and systemic beta-blocker usage

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Abstract

Introduction Beta-blockers have, for 25 years, been a commonly used agent in the treatment of raised intraocular pressure (IOP). Beta-blockers can also reduce the pulse rate. With no available literature examining a cohort of patients, this study aims to investigate the resting pulse rates in patients attending a specialist glaucoma clinic in order to identify if routine review of ophthalmic medication use is indicated.

Method The resting pulse rates of patients attending a glaucoma clinic were measured using pulseoximetry, with a medical and drug history established for each patient.

Results In all, 205 patients were included in the study. A total of 101 (49%) of patients were using beta-blockers in some form. The mean pulse rate for patients not using beta-blockers (104 patients) was 76 beats per minute (bpm), for topical use only (68 patients) it was 70.3 bpm, for oral use (18 patients) it was 64.7 bpm, and 58 bpm for patients using both topical and oral beta-blockers (15 patients). Groups using beta-blockers (oral, topical, oral and topical) were considered in relation to patients not using beta-blockers. All groups using beta-blockers showed a significant association with causing a bradycardia of less than 60 bpm. Patients with a pulse rate of less than 50 bpm were significantly more likely to be using topical and oral beta-blockers than oral beta-blockers alone ($P = 0.01$).

Conclusion Topical beta-blockers should be used with caution, even in the presence of established systemic beta-blocker use. Routine pulse rate monitoring and review of ophthalmic medication are indicated in patients using beta-blocker therapy.

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Introduction

Topical beta-blockers have a well-established role in the reduction of intraocular pressure;^{1,2} however, their side effects are also well documented, potentially affecting both cardiac^{3–8} and respiratory functions.^{3,4,9–11} In recent years new agents such as prostaglandin analogues have been developed with a better safety profile, as well as comparable efficacy,^{12–15} leading to beta-blockers not now necessarily being the first-line treatment in glaucoma. However, for many ophthalmologists, beta-blockers remain in frequent use, as either a primary treatment or as an adjunct to other agents.

The scientific literature reveals very little with regard to the effect of the concomitant use of topical and oral beta-blockers in relation to resting pulse rates. All studies reviewed used either a very small sample size, were subject to a strict inclusion/exclusion criteria,¹⁶ were reviews,¹⁷ or were individual case reports.^{18,19} We therefore report the results of a study of resting pulse rates in patients attending a hospital-based glaucoma clinic, in order to identify if any individuals required a re-evaluation of their ophthalmic medication based upon resting pulse rate alone.

Method

The routine monitoring of resting pulse rates in glaucoma patients was introduced during August 2003 in one glaucoma clinic. Pulse rates were measured using a hospital maintained handheld pulseoximeter (Nellcor NPB-40) attached to the index finger of patients for at least 3 min. Pulseoximetry was conducted after

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the patient had rested in a seated position for at least 10 min, following an explanation of the procedure. All patients were measured, including those not currently using beta-blockers. Recordings taken during the first 2 months of this new practice were included in the study. Information was elicited from the patient and medical notes, with regard to all medications currently prescribed as well as the patients' medical history. Patients who were found to have a pulse rate of less than 50 bpm were offered an ECG, which was then reviewed by a cardiologist. These patients, along with any patient having a pulse rate of over 100 bpm were referred to their general practitioner.

Results

In all, 208 patients were assessed over a period of 2 months. For analysis, patients were separated into one of four groups, these groups being:

- Patients not using any beta-blockers.
- Patients using topical beta-blockers only.
- Patients using oral beta-blockers only.
- Patients using both topical and oral beta-blockers (dual therapy).

As three patients (1.4%) were taking a pulse rate reducing medication which was not a beta-blocker (Digoxin), these patients were excluded from the study. In all, 205 patients were therefore used in the analysis.

The mean age of all patients was 72.55 (SD 12.2), with no significant difference ($P=0.28$) between the ages of patients on beta-blockers (mean 72.19, SD 10.92) and those not using beta-blockers (mean 72.95, SD 13.37).

In all, 101 (49%) of patients were using beta-blockers in some form. Of these 68 were using topical only, 18 used oral only, and 15 used dual therapy. In patients using topical medication, the breakdown of use was as follows: 83 (48.5%) of patients were using a topical beta-blocker, with 122 (71%) using a Prostaglandin Analogue. In all, 43 (25%) of patients were using both agents (Figure 1).

The mean pulse rate for patients not using beta-blockers was 76 beats per minute (bpm) (SD 13), for topical use only it was 70.3 bpm (SD 11), for oral use it was 64.7 bpm (SD 10.6), and 58 bpm (SD 10) for patients using dual therapy. The spread of pulse rate values are shown as a boxplot in Figure 2.

Groups were compared, using a one-way ANOVA test in order to identify any significant differences in pulse rates between the groups. This proved highly significant ($P<0.0001$). Following this result, the significance between the individual groups using beta-blockers when compared to the group with no beta-blockers was assessed using an unpaired *t*-test (Table 1).

Figure 1 All topical medication used in the cohort (count).

Figure 2 Pulse rates.

Table 1 Differences between heart rates (*t*-test)

No beta-blockers vs	Significance (P)
Topical only	0.003
Oral only	0.0007
Dual therapy	<0.0001

Taking an accepted value for bradycardia as below 60 bpm,²⁰ Fisher's test was used in order to identify any association between bradycardia and each specific group. Groups using beta-blockers (oral, topical, dual) were considered individually in relation to patients not using beta-blockers. All groups using beta-blockers showed a significant association with bradycardia (Table 2).

Table 2 Association with bradycardia <60 bpm (Fisher's test)

No beta-blocker vs	Significance (P)
Topical only	0.0008
Oral only	0.0007
Dual therapy	0.0001

Table 3 Comparison with dual therapy (Fisher's test)

	P-value at <60 bpm	P-value at <50 bpm
Topical only	0.02	0.0006
Oral only	0.5	0.01

As the only group whose mean pulse rate was below 60 bpm was the dual therapy group, the concomitant effect of topical and oral beta-blockers was considered. Fisher's test was employed to examine whether an association with bradycardia existed when comparing the use of dual beta-blockers *vs* oral only and topical only. When dual therapy was compared to topical only there existed, as expected, a significant association with bradycardia at both the <60 and <50 bpm levels of pulse rate. A highly important result however was that significance was shown in comparing oral only to dual therapy at the <50 bpm level, showing the influence of topical medication at this level of bradycardia (Table 3).

All patients ($n=5$) who showed a pulse rate of less than 50 bpm accepted the offer of an ECG. In three of the five patients a bradycardia of 50 bpm or less was confirmed. One of these five patients was considered to have evidence of borderline 1st degree A-V block in which beta-blocker use may have been a contributory factor. In this case, the patient's GP opted to discontinue the systemic beta-blocker.

Discussion

Topical beta-blocker use is on the decline, due primarily to the introduction of prostaglandin analogues in the mid 1990s, which have a proven efficacy and a different side effect profile.^{12–15} In 1997 Gottfredsdottir *et al*²¹ showed that in the United States 91% of topical medications were beta-blockers during the period 1992–1994. In our study, topical beta-blocker use had reduced to 48.5% of those patients using antiglaucoma medication. It is unlikely however that beta-blocker use will discontinue, as they are very effective agents for pressure reduction. In our cohort 43 (25%) of patients using topical medication required the use of both a beta-blocker and a prostaglandin analogue for intraocular pressure control.

Our study indicates that patients using topical beta-blockers have significantly lower resting pulse rates than those not using beta-blockers ($P=0.003$), and is similar to previous studies.^{3–8} This is probably due to the good bioavailability of topical beta-blockers²² therefore easily affecting the body systemically. An aspect of beta-blocker therapy, not widely considered in the literature, is the effect of combining oral and topical beta-blockers. Schuman¹⁶ indicated that caution is required in combining topical and oral beta-blockers; however, this sample was taken from a randomised controlled trial and was not a cohort. Some studies have examined the use of multiple prescriptions. Gottfredsdottir *et al*²¹ showed that 84% of glaucoma patients in their practice were receiving one or more medications for systemic disease, with 8% using Atenolol, a systemic beta-blocker. Valuck *et al*²³ showed that between 4.3 and 25.1% of glaucoma patients were prescribed systemic medication for a heart condition. Our cohort showed that the group combining the two medications was the only group in which the mean pulse rate was below that defined as bradycardic (mean 58 bpm, SD 10).

Unsurprisingly, there was an association to bradycardia if an oral beta-blocker is used in combination with a topical beta-blocker ($P=0.02$) when compared to topical alone. However, the group using both topical and oral beta-blockers was also shown to be strongly associated with a bradycardia of below 50 bpm when compared to the use of oral medication alone ($P=0.01$). In our cohort, 27% of patients using both topical and oral beta-blockers were prescribed topical beta-blockers when already taking oral beta-blockers. There was however no association between hospital ophthalmologists or general practitioners commencing a concomitant beta-blocker and subsequent bradycardia, at 60 bpm ($P=0.57$) or 50 bpm ($P=0.56$). However, this highlights an important aspect of patient care, and without routine pulse rate monitoring, an up to date drug history, or knowledge of the concomitant effect of these drugs, ophthalmic and systemic beta-blocker use in patients appears potentially hazardous.

In order to clarify current practice, an anonymous questionnaire concerning pulse rate monitoring was given to a group of practicing consultant ophthalmologists, all with a special interest in glaucoma (Figure 3). The questionnaire was completed in 79% of cases ($n=11$). Results indicate that 46% ($n=5$) of respondents measure pulse rates in glaucoma patients as part of their routine practice, with three stating 'before prescribing a beta-blocker', one stating 'at every visit', and one 'only if concerned'. All respondents stated that they routinely record the systemic medications taken by their glaucoma patients, but vary in their practice of this: 64% ($n=7$) 'at first visit only', 27% ($n=3$) 'every visit',

Heart rate monitoring in glaucoma patients - questionnaire

- 1a** Do you measure heart rates in your glaucoma patients as part of your practice?
- Yes / No
- 1b** If Yes do you measure:
- On all new patients.**
- On all patients at every visit**
- On all patients using beta-blockers at every visit.**
- Before prescribing a beta-blocker.**
- Only if concerned with cardiovascular function.**
- Other (please state) _____**
-
- 2a** Do you routinely review and record systemic medications in patients' medical records?
- Yes / No
- 2b** If Yes, when:
- At first visit only**
- Every visit**
- Annually**
- Other (please state) _____**
-
- 3** Do you consider that the addition of a topical beta-blocker to an existing systemic beta-blocker may adversely affect the patients heart rate?
- Yes / No

Figure 3 Current practice questionnaire.

and 9% ($n=1$) 'annually'. When questioned as to their opinion whether the addition of a topical beta-blocker to an existing oral beta-blocker might adversely affect the patients' pulse rate 46% ($n=5$) stated 'no'.

It is of note that none of the patients not taking beta-blockers had a resting pulse rate of less than 50 bpm, and that the five patients with severe bradycardia were asymptomatic. Even so a clinically significant finding in one patient was found. Therefore routine pulse rate testing is advisable in patients using beta-blockers.

Recent advances in ophthalmology, such as the introduction of electronic patient management systems²⁴ may well aid prescribers in the future by highlighting possible drug interactions, and therefore reduce the potential for harm to patients. However, despite new electronic management aids, and the reduction in topical beta-blocker usage, it remains crucial that the dangers of the concomitant use of topical and oral beta-blockers are

born in mind when prescribing beta-blockers. Pulse rate monitoring and a review of ophthalmic medication is indicated in patients using beta-blocker therapy, as is good communication with the patients' general practitioner, to ensure that the health of patients is not compromised.

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