Haemodynamic responses to subconjunctival mydriatic agents (Mydracaine) used for maintenance of perioperative mydriasis in patients undergoing vitreoretinal surgery

D.G.R. JAYAMANNE,
N. RAY-CHAUDHURI,
R. WARIYAR,
D.G. COTTRELL

Abstract

Purpose To assess the systemic effects of subconjunctival mydriatic agents (Mydracaine).

Methods Haemodynamic variables were recorded at baseline and during the first 60 min following subconjunctival injection of Mydracaine and normal saline.

Results Statistical analysis of the change in heart rate showed a highly significant difference between the two groups ($p < 0.001$). There was no significant difference in the effect on systolic or diastolic blood pressure between the two groups.

Conclusions We advise extreme caution when using Mydracaine via the subconjunctival route in patients with compromised cardiac function.

Key words Mydriatic agents, Perioperative monitoring, Cardiovascular effects, Eye surgery

Adverse effects due to systemic absorption of topically administered mydriatic agents are well documented. Unwanted effects due to sympathomimetic and parasympatholytic action can produce tachycardia, hypertension and dysrhythmias leading to coronary ischaemia, myocardial infarction and cerebrovascular accidents.^{1,2} The elderly and those with pre-existing myocardial disease are particularly at risk. An increased incidence of problems in patients taking systemic tricyclic antidepressants and monoamine oxidase inhibitors has also been reported.³

Subconjunctival injections of mydriatic agents are used to achieve and maintain mydriasis perioperatively during prolonged vitreoretinal procedures and to dilate pupils in

uveitic patients with posterior synechiae.⁴ Significant systemic absorption with serious complications can result from these injections,⁵ the risk being enhanced by conjunctival hyperaemia. Isolated adverse reactions have been reported in healthy individuals.^{5,6} The authors are unaware of any published study on the systemic effects of subconjunctival mydriatic agents.

We undertook this prospective clinical study to document the haemodynamic effects of subconjunctival injections of a mixture comprising 1 mg atropine, 0.12 mg adrenaline and 6 mg procaine (Mydracaine No. 2 formulated by Moorfields Eye Hospital) in patients undergoing vitreoretinal surgery.

Patients and methods

All patients over the age of 18 years who underwent vitreoretinal surgery by one surgical team and were anaesthetised by the same senior anaesthetist during the period August 1995 to August 1997 were included in the study. Informed consent was obtained from all patients. Those patients requiring supplementary pupillary dilatation by subconjunctival injection of Mydracaine were included in the study group ($n = 30$) and others were used as controls by injection of the same volume of normal saline at the same stage ($n = 30$). Patients considered unsuitable for the standard anaesthetic technique used and patients who needed intravenous fluids or sympathomimetic agents to treat hypotension were excluded. Pre-operative preparation of the eye was standard, with phenylephrine 2.5% and cyclopentolate 1% eye drops starting 2 h prior to surgery. Baseline heart rate, electrocardiogram, blood pressure and oxygen saturation were

D.G.R. Jayamanne
N. Ray-Chaudhuri
D.G. Cottrell
Department of
Ophthalmology
Royal Victoria Infirmary
Newcastle, UK

R. Wariyar
Department of Anaesthesia
Newcastle General Hospital
Newcastle, UK

Mr D.G.R. Jayamanne,
FRCOphth ✉
Department of
Ophthalmology
Royal Victoria Infirmary
Queen Victoria Road
Newcastle NE1 4LP, UK

recorded prior to induction in the anaesthetic room. Anaesthetic technique was standardised: intravenous induction with fentanyl 1.5 µg/kg, propofol 2–3 mg/kg and vecuronium 0.1 mg/kg; airway maintenance with laryngeal mask; anaesthesia maintained with oxygen, nitrous oxide and isoflurane; muscle paralysis monitored and maintained at one twitch with vecuronium supplements as required.

Time zero readings of systolic and diastolic blood pressure, heart rate and oxygen saturation were recorded when the patient was on the operating table draped and ready. Pupillary size was assessed by the surgeon and 0.5 ml of Mydracaine was injected subconjunctivally if necessary. Patients not needing Mydracaine had 0.5 ml of normal saline injected at the same stage.

Systolic and diastolic blood pressure, heart rate and oxygen saturation were monitored and recorded every 2 min for the next hour. Any changes in rhythm or ST segment were also noted and any anaesthetic or surgical factor contributing to the change at that time were commented on.

For statistical analysis, percentage changes in systolic and diastolic blood pressure, heart rate and oxygen saturation from the baseline were calculated for each 2 min reading and the mean percentage change calculated for each 10 min interval up to 1 h. Procedures lasting less than an hour were excluded. Students's *t*-test was used to compare the results of the study and control groups.

Results

Demographic variables, haemodynamic characteristics measured pre-operatively, incidence of cardiovascular and respiratory diseases, and use of medications were similar between the Mydracaine and normal saline groups (Table 1).

None of the adverse effects noted led to haemodynamic compromise needing treatment. All the adverse effects were self-limiting but in a few patients the tachycardia lasted longer than the 1 h monitored.

There was an increased incidence of abnormal heart rhythms in the study group. These abnormal rhythms were distributed equally amongst all age groups. Three patients with irregular rhythms (25%) had a history of hypertension or heart disease. In all cases the irregular rhythms were self-limiting (Table 2).

Table 1. Patient demographics

	Mydracaine group	Control group
No. of patients (male/female)	30 (22/8)	30 (16/14)
Age range (mean), years	23–78 (48.2)	22–86 (53.7)
Patients (n):		
With hypertension	5	5
With diabetes	6	5
With heart disease	3	6
With lung disease	4	5
Taking beta-blockers	4	5
Taking Ca ²⁺ blockers	4	7
Taking inhalers and/or steroids	4	5
Taking ACE inhibitors	1	1

Table 2. Number of patients with dysrhythmias

	Mydracaine group	Control group
Ventricular ectopics	4	1
Supraventricular ectopics	2	0
Nodal rhythm	6	2

Change in heart rate

Percentage change in heart rate over the first 60 min varied from +93.2% to –1.3% with a mean of +32.1% in the Mydracaine group and from +34.4% to –19.2% with a mean of –1.6% (Figs. 1, 2) in the normal saline group as compared with baseline. Statistical analysis showed a highly significant difference in the percentage change in heart rate between the two groups (*p* < 0.001). No relationship was demonstrated between the age of the patient, pre-operative use of cardiovascular medication, history of systemic disease and the percentage change in heart rate.

Change in blood pressure

Figs. 3–6 summarise the percentage changes in systolic and diastolic blood pressure during the first 60 min in the Mydracaine and normal saline groups. There was no significant difference in the percentage change in systolic or diastolic blood pressure between the two study groups.

Change in oxygen saturation

All patients maintained oxygen saturation levels above 98% at all times.

Discussion

Mydracaine No. 2 is a drug formulation containing atropine sulphate 1 mg, adrenaline 0.12 ml of 1:1000, procaine hydrochloride 6 mg, boric acid 5 mg, sodium metabisulphite 0.1%, sodium chloride 0.32% and water for injection. It is given by subconjunctival injection when maximal pupil dilatation is required.

Atropine is an anticholinergic drug, systemic absorption of which can result in adverse side effects.^{5,7} Cardiac dysrhythmias such as atrial fibrillation and supraventricular tachycardias⁷ are particularly dangerous potential reactions.

Adrenaline is a potent, alpha-1 adrenergic agonist. Stimulation of these receptors can cause constriction of the systemic, pulmonary and coronary arteries. This can lead to severe hypertension, arrhythmias and myocardial infarction.⁵ Procaine blocks uptake in the adrenergic system and produces a tachycardia in its own right. However, its effect is significantly less than that produced by cocaine.⁸

Isolated case reports have been published in medical journals discussing the possible role of atropine and adrenaline in subconjunctival preparations as a cause of myocardial ischaemia in previously healthy subjects. Systemic absorption of these drugs may be enhanced by inflamed periocular tissues.⁹ This prospective study was

Fig. 1. Percentage change in heart rate in the first 60 min in the Mydracaine group.

Fig. 2. Percentage change in heart rate in the first 60 min in the normal saline group.

Fig. 3. Percentage change in systolic blood pressure in the first 60 min in the Mydracaine group.

Fig. 4. Percentage change in systolic blood pressure in the first 60 min in the normal saline group.

Fig. 5. Percentage change in diastolic blood pressure in the first 60 min in the Mydracaine group.

Fig. 6. Percentage change in diastolic blood pressure in the first 60 min in the normal saline group.

undertaken to monitor the haemodynamic effects of subconjunctival Mydracaine. The results of the present study fail to confirm previous reports of severe hypertensive reactions but do show a significant effect on heart rate.

We advise extreme caution when using Mydracaine via the subconjunctival route in patients with compromised cardiac function. These patients are often sensitive to alterations in cardiac rhythm and careful patient selection should minimise severe cardiac complications.

References

1. Fraunfelder FT, Scafadi M. Possible adverse effects from topical ocular 10% phenylephrine. *Am J Ophthalmol* 1978;4:447-53.
2. Jayamanne DGR, Fitt AWD, Wariyar R, Cottrell DG. Persistent tachycardia following subconjunctival injections of mydriatic agents (Mydracaine) used for maintenance of perioperative mydriasis in vitreo-retinal surgery. *Eye* 1995;9:530-1.
3. McGoldrick K. Ocular drugs and anesthesia. *Int Anesthesiol Clin* 1990;28:73-8.
4. Duane TD. *Clinical ophthalmology*, vol 4. Revised ed. Philadelphia: Lippincott, 1988:chapter 43:3.
5. Hartstein I, Deutsch N. Adverse effects of subconjunctival injections of mydriatic agents [letter]. *Br J Ophthalmol* 1991;75:253.
6. Pandit JC. Tachycardia and myocardial ischaemia following subconjunctival injection of Mydracaine No. 2. *Eye* 1994;8:599.
7. Merli GJ, Weitz H, Martin JH, *et al*. Cardiac dysrhythmias associated with ophthalmic atropine. *Arch Intern Med* 1986;146:45-7.
8. Jones LF, Tackett RL. Central mechanisms of action involved in cocaine induced tachycardia. *Life Sci* 1990;46:723-8.
9. Fernandes A, Rato Q, Pinto LS. Taquidistritmia supraventricular complicada por isquemia aguda do miocardio desencadeada pela injeccao de atropina: a proposito de um caso clinico. *Rev Port Cardiol* 1992;11:1095-9.