CLINICAL STUDY

The incidence of systemic side-effects following subconjunctival Mydricaine No. 1 injection

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Abstract

Purpose **To investigate the cardiovascular response to the subconjunctival injection of 0.25 ml of Mydricaine No. 1 during vitrectomy surgery.**

Methods **Pulse and blood pressure were recorded at 5 min intervals before and following the subconjunctival injection of Mydricaine No. 1 in a group of 49 sequential patients undergoing vitrectomy surgery under general anaesthetic during a 6 month period. These responses were compared with a sequential and similar group of 35 patients during the following 6 months.**

Results **Ten patients in the group administered Mydricaine, but no patients in the control group, developed a sinus tachycardia of >100 beats/min for more than 10 min which was attributable to the mydriatic regime used. The occurrence of this response was not predictable based on the patients' age, weight or the presence of conjunctival erythema. The magnitude and temporal course of the tachycardia observed were variable. Blood pressure recordings showed no clinically significant changes during the tachycardias.**

Conclusion **Twenty per cent of patients administered 0.25 ml of Mydricaine No. 1 subconjunctivally develop a significant sinus tachycardia following injection. This response is unpredictable and all patients given Mydricaine should be monitored carefully after injection.**

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

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The occurrence of adverse systemic side-effects following the administration of subconjunctival mydriatics is well known. Severe hypertension, cardiac arrhythmias, myocardial infarction as well as prolonged sinus tachycardias have all been reported.[1–3] Mydricaine is a frequently used preparation and is formulated by Moorfields Eye Hospital in two types: No. 1 and No. 2. Mydricaine No. 2 contains 1 mg of atropine, 0.12 mg of adrenaline and 6 mg of procaine hydrochloride. Mydricaine No. 1 contains half the quantity of atropine and procaine. Mydricaine is widely used in the UK to achieve pupillary dilatation in patients with uveitis as well as prior to vitreoretinal surgery. Following two reports describing adverse cardiovascular side-effects from Mydricaine No. 2,[2,3] we began to administer only half a vial of Mydricaine No. 1 immediately prior to vitreoretinal surgery in the belief that this would reduce and perhaps eliminate significant systemic side-effects. To test this hypothesis we carried out a prospective study and compared the cardiovascular responses to this reduced dose of Mydricaine in a series of consecutive patients undergoing vitrectomy with a sequential and similar group of patients in whom no Mydricaine was used.

Method

Forty-nine consecutive patients undergoing a pars plana vitrectomy between March 1996 and September 1996 formed the 'Mydricaine group'. Patients' age, sex and weight were recorded. The presence of significant conjunctival injection was also recorded. Relevant systemic co-morbidity and medications were recorded and consent obtained. The Mydricaine group were given half a vial of Mydricaine No. 1 subconjunctivally adjacent to the limbus after induction of anaesthesia and before surgery was commenced. The subconjunctival injection was generally given in two divided doses superior to and inferior to the limbus. Pulse and blood pressure were recorded at 5 min intervals.

A further 35 sequential and consecutive patients between October 1996 and April 1997 formed the second arm of the study without Mydricaine: the 'no Mydricaine group'. As with the Mydricaine group these patients had one

Table 1. *Patient characteristics*

	Mydricaine group (n = 49)	No Mydricaine group (n = 35)
Age (years)	55.4 (SD 20.7)	57.9 (SD 19.1)
Sex (M:F)	26:23	20:15
Weight (kg)	69 (SD 15.7)	66.7 (SD 12.5)
% with 'significant inflammation'	24%	23%
Systemic co-morbidity:		
Hypertension	14%	14%
Diabetes mellitus	18%	14%
Atrial fibrillation	4%	6%
Ischaemic heart disease	10%	9%

drop of atropine given 2–3 h pre-operatively and for further mydriasis adrenaline was added to the vitreous infusion fluid (0.5 ml of 1:1000 adrenaline in 500 ml of balanced salt solution). Again pulse and blood pressure were monitored at 5 min intervals from the induction of anaesthesia. Anaesthetic technique was standardised and was common to both groups.

The occurrence of a sustained tachycardia at a pre-defined level of greater than 100 beats/min for greater than 10 min during surgery was noted. Events resulting in abnormal cardiovascular responses other than those attributable to the mydriatic agents were recorded.

Statistical analysis was carried out using non-paired t-tests and chi-squared tests.

Results

The compositions of the Mydricaine and no Mydricaine groups were broadly similar in respect of age, sex and weight as well as the proportion of the patients in each group with significant inflammation. Systemic co-morbidity was broadly similar between the two groups (Table 1).

There were 14 patients in the Mydricaine group and 4 in the no Mydricaine group who developed a sinus tachycardia of greater than 100 beats/min for 10 min during surgery. Four patients in each of these two groups had clear reasons other than the systemic effects of Mydricaine for the tachycardia. Four patients developed sinus tachycardias with intubation, 2 during laser treatment, 1 patient went into fast atrial fibrillation with intubation and 1 patient developed a tachycardia after the administration of intravenous phentolamine for hypertension. These patients were excluded from further study. There were therefore 10 patients in the Mydricaine group but no patients in the no Mydricaine group who developed significant tachycardias that we considered to be related to the mydriatic regime. This difference was significant ($p<0.001$). There were no clinically significant changes in blood pressure in these 10 patients who developed a tachycardia and this was not analysed further. There were no other dysrhythmias observed.

A comparison between the patients within the Mydricaine group who developed a tachycardia and those who did not is shown in Table 2. There was a significant difference in age between the two groups although the age range was large. There were no other significant differences between the other parameters studied. No patient developed a significant systemic complication as a result of the tachycardia induced.

The magnitude and temporal course of the tachycardia following the Mydricaine injection are shown in Table 3.

Intraoperative pupillary dilation was subjectively judged to be similar between the two groups although this was not objectively measured.

Table 3. *Magnitude and temporal course of the tachycardia following the Mydricaine injection*

	Mean	SD
Maximum heart rate recorded	118 beats/min	7.8
Increase in heart rate from rate prior to induction	40 beats/min	7.5
Time from Mydricaine injection to heart rate rising to >100 beats/min	10 min	9.9
Time from Mydricaine injection to maximum recorded heart rate	37.5 min	20.3
Duration of heart rate >100 beats/min	75 min	46.8

Discussion

Ten of the 49 patients given subconjunctival Mydricaine developed a sinus tachycardia of greater than 100 beats/min that could not be explained by any other agent or event. A recent prospective trial of the haemodynamic responses to subconjunctival Mydricaine No. 2 by Jayamanne *et al.*[4] found a similar significant rise in heart rate following injection. The important significant finding from our study is that patients still experience significant tachycardias despite the fact we used only

Table 2. *Patient characteristics of the group given Mydricaine*

	Tachycardia with Mydricaine (n = 10)			No tachycardia (n = 35)			
	Mean	Range	SD	Mean	Range	SD	p value
Age (years)	37	(7–74)	22.7	56.3	(17–83)	17.3	p = 0.02 (t-test)
Weight (kg)	66.6	(34–136)	30.7	69.6	(55–89)	9.2	p = 0.76 (t-test)
% with significant inflammation	30%			23%			p = 0.81 (x^2 test)
Co-morbidity:	3			6			
Hypertension							
Diabetes mellitus	3			5			
Atrial fibrillation	0			2			
Ischaemic heart disease	0			5			

one-quarter of the dosage of Mydricaine commonly used, i.e. one-half of one vial of Mydricaine No. 1 as opposed to one whole vial of Mydricaine No. 2.

The study was not randomised but the patients were recruited consecutively and the two groups were of similar composition in terms of age, weight and the amount of conjunctival injection present. Bias could have been introduced into the study as the anaesthetist was not masked to the mydriatic regime used. Similarly the factors which were considered to cause a tachycardia, other than the mydriatic regime used, were not pre-planned and were identified at the time of surgery. However, despite these reservations we believe the results showed a clear difference between the two mydriatic regimes which can not be fully accounted for by bias.

All three major components of Mydricaine are capable of producing a sinus tachycardia. Analysis of the temporal relationship of the tachycardias to the timing of the Mydricaine injection as well as the duration of the effect and the relative stability of the blood pressure, as also found by Jayamanne *et al.*,[4] suggest that atropine was the causal agent.[5]

The 10 patients who developed a sinus tachycardia with Mydricaine were significantly younger in age as a group than those who did not, possibly relating to the increased vagal tone in youth.[6] However, the age range was from 7 to 74 years and age alone was not predictive of an adverse response. There was no relationship of response with weight or with the presence of ocular inflammation that has previously been noted to be associated with an adverse response. The occurrence of a tachycardia was therefore unpredictable and furthermore the extent, duration and timing of the peak of the tachycardia were also variable and unpredictable.

There were no patients in the study on monoamine oxidase inhibitors, tricyclic antidepressants, beta stimulants or any other agents which would have placed them at an increased risk of developing a tachycardia. None of the patients developed adverse sequelae resulting from the tachycardia. Patients who may be at increased risk of these include those with known ischaemic heart disease and diabetics who may have silent ischaemia, patients with cerebrovascular disease and those in atrial fibrillation or with other dysrhythmias such as paroxysmal atrial tachycardia including Wolff-Parkinson-White syndrome.

In conclusion, this study found an approximately 20% incidence of significant sinus tachycardias after subconjunctival injection of one-half of one vial of Mydricaine No. 1. The occurrence of the tachycardia was not predictable. We would suggest that if any form of Mydricaine is administered patients should be monitored closely, especially those with risk factors for adverse systemic effects.

References

1. Hartstein I, Deutsch N. Adverse effects of subconjunctival injections of mydriatic agents [letter]. Br J Ophthalmol 1991;75;253.
2. Jayamanne DGR, Fitt AWD, Wariyer R, Cottrell DG. Persistent tachycardia following subconjunctival injections of mydriatic agents (Mydricaine) used for maintenance of perioperative mydriasis in vitreoretinal surgery. Eye 1995;9:530–1.
3. Pandit JC. Tachycardia and myocardial ischaemia following subconjunctival injection of Mydricaine No. 2. Eye 1994;8:599.
4. Jayamanne DGR, Ray-Chaudhuri N, Wariyar R, Cottrell DG. Haemodynamic responses to subconjunctival mydriatic agents (Mydricaine) used for maintenance of perioperative mydriasis in patients undergoing vitreretinal surgery. Eye 1998;12:792–4.
5. Goodman LS, Gilman A. The pharmacological basis of therapeutics. 6th ed. New York: McGraw-Hill, 1975:518.
6. Barash PG, Cullen BF, Stoelting RK. Clinical anaesthesia. 1st ed. Philadelphia: JB Lippincott. 1989:193.