CLINICAL STUDY

The National Survey of Local Anaesthesia for Ocular Surgery. II. Safety profiles of local anaesthesia techniques

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Abstract

Purpose **To describe the adverse events associated with local anaesthesia (LA) for intraocular surgery.**

Methods **An observational study of practice of LA in the whole of the United Kingdom was conducted over 3 months in late 1996. Staff in all ophthalmology theatres in the National Health Service were invited to report every LA given for the purpose of intraocular surgery during the first week, and thereafter to report adverse events only.**

Results **During the first week, the reported incidence of all adverse events within the orbit was 2.7%, and for 'systemic' adverse events it was 0.9%. Serious adverse events were reported in association with all LA techniques. In 3 months, 18 events were described as 'life-threatening' by respondents, and further patients were reported to have had epileptic fits or were transferred directly from the operating theatre to an intensive care unit. The voluntary nature of the survey introduces some bias from under-reporting, making the incidence of these severe events difficult to assess. Reported incidence of severe 'systemic' adverse events was similar for all LA techniques.**

Conclusions **Serious adverse events were reported in association with all LA techniques. This implies that we should be prepared for such events in all patients who have intraocular surgery.**

Key words Anaesthesia, local: adverse effects; Retrobulbar anaesthesia; Peribulbar anaesthesia; Sub-Tenon's anaesthesia; Subconjunctival anaesthesia; Topical anaesthesia

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Local anaesthesia (LA) is frequently used for intraocular surgery in the United Kingdom[1–3] and elsewhere.[4–8] While LA is generally considered to be relatively safe,[9–11] many serious adverse effects have been reported, particularly with periocular injections.

Life-threatening adverse events include brain-stem depression (via presumed injection into cerebrospinal fluid surrounding the optic nerve)[10,12–16] and cardiovascular depression (via presumed systemic absorption of anaesthetic agents or oculocardiac reflex);[17,18] deaths have been reported.[19] Sight-threatening events include globe perforation,[20–22] optic nerve trauma,[23–25] orbital haematoma,[23,26,27] and injections into the ocular blood vessels.[23]

Most adverse events have been reported in association with retrobulbar anaesthesia (RBA), a technique which has been popular for many decades.[3,4,28–30] Incidence of life-threatening adverse events associated with RBA has been estimated at 0.13–0.79%,[10,13–15,31] and that of sight-threatening adverse events is probably somewhat lower.[10,32]

Peribulbar anaesthesia (PBA) was conceived as a safer alternative[33] in the early 1970s and was popularised in the late 1980s.[34] There is some evidence that PBA may indeed be safer than RBA,[10,13,14,35,36] though there has been no large randomised trial to address this issue.

In recent years, subconjunctival anaesthesia (SCA),[37,38] sub-Tenon's (parabulbar) anaesthesia (STA)[39–41] and purely topical anaesthesia (TA)[28,42] have become widely used. There have been many small studies that have demonstrated good results with these newer techniques. Series of several hundred cases each indicate a reasonable safety record,[43–45] though no published series is large enough to assess the incidence of rare, life-threatening adverse events.

There have been no large randomised trials to compare the safety of different LA techniques, or to compare LA with general anaesthesia (GA).

While adverse events with LA are rare, it is important to be prepared when a life-threatening event does occur. Guidelines for safe administration of LA were published in 1993 by the Royal College of Anaesthetists and the College of Ophthalmologists.[46] The Guidelines state that patients scheduled for intraocular surgery under LA should have a

Table 1a. *Orbital Adverse Events during the first week of the Survey*

		Minor Orbital Adverse Events			Major Orbital Adverse Events		
LA technique	No. of reports	Inadequate analgesia, causing surgical difficulty	Inadequate akinesia, causing surgical difficulty	Retrobulbar (periocular) haemorrhage ('minor')	Perforation/ penetration	Retrobulbar (periocular) haemorrhage ('severe', causing proptosis)	Expulsive haemorrhage
Peribulbar	1854	12[a]	12[a,b]	24[b]	1	2[c]	1[c,d]
Retrobulbar	479	1[a]	4[a,b]	6[b]	0	1	0
Sub-Tenon's	190	1	4[b,e]	2[b,e]	0	0	1
Subconjunctival	124	0	0	0	0	0	0
Topical alone	81	1	0	0	0	0	0
Intracameral	2	0	0	0	0	0	0
Combinations	63	3[a]	1[a]	0	0	0	0
Not stated	34	0	0	0	0	0	0
Total	2827	18[a]	21[a,b]	32[b]	1	3[c]	2[c,d]
		71 Minor Orbital Adverse Events[a,b,f]			5 Major Orbital Adverse Events[c]		

[a]Inadequate analgesia and akinesia coexisted with 2 PBA, 1 RBA and 1 combination (PBA + RBA).
[b]'Minor' retrobulbar haemorrhage (without proptosis) coexisted with inadequate akinesia with 1 PBA, 1 RBA and 1 STA.
[c]In one case of retrobulbar haemorrhage, the operation took place on the same day and was complicated by expulsive haemorrhage.
[d]There were 2 further reports of choroidal haemorrhage with PBA during this week.
[e]Sub-Tenon's anaesthesia and periocular haemorrhage: one patient had 'subconjunctival haemorrhage ++'; the other had periocular haemorrhage and inadequate akinesia
[f] Seven further 'miscellaneous' Minor Orbital Adverse Events were reported, but do not appear in the table.

pre-operative medical evaluation, including blood pressure and urinalysis, and further tests as appropriate. Vital signs should be monitored during the operation, an intravenous cannula should be inserted, and an anaesthetist should be available in case resuscitation is required. These recommendations have not been universally accepted, partly due to the shortage of anaesthetists in some hospitals,[1] and partly due to the perception that LA is generally safe. To provide a background for a review of these Guidelines, an assessment of the current status of LA was required. The National Survey of Local Anaesthesia for Ocular Surgery was therefore designed to assess the usage of LA, compliance with the safety guidelines, and the incidence and severity of adverse events.

Method

The methodology for the Survey has already been described in detail.[1] It was designed as a prospective observational study, involving all National Health Service (NHS) operating theatres where intraocular surgery is performed. Introductory questionnaires were sent to all consultant ophthalmologists, and heads of department of anaesthesia in hospitals with an ophthalmology unit. Participants were asked to report every LA administered for intraocular surgery during the first week of the Survey, then to report adverse events only for the remainder of the 3-month period. All aspects of the Survey, including the validation protocol, were designed to ensure anonymity for those respondents who did not wish to be identified. For the purposes of the Survey, an Adverse Event was defined as 'something which made you observe the patient more closely, or take action'.

Results

Response rates were good at all stages of the Survey. An estimated 65 100 LAs were administered during the 3-month period (95% confidence interval: 48 500–81 700); 65.6% of these LAs were administered by the peribulbar technique, 16.9% were retrobulbar, 6.7% sub-Tenon's, 4.4% subconjunctival, 2.9% topical, 0.07% intracameral, and 2.3% used a combination of techniques. Oral premedication or intravenous sedation was given to 8% of LA patients. Further detail can be found in our companion paper.[1]

Adverse Events were categorised as 'Orbital' (i.e. occurring within the anatomical confines of the orbit) or 'Systemic' (i.e. having a more generalised effect on the patient's physiology). The most commonly reported Orbital Adverse Events were 'retrobulbar' haemorrhage (orbital haematoma), inadequate akinesia and inadequate analgesia. Systemic Adverse Events included brain-stem and cardiovascular depression, angina, fainting, epileptic fits, confusion and panic attacks.

A total of 76 Orbital Adverse Events were reported in the first week, and are summarised in Table 1a. This gives an overall reported incidence of 76/2827 or 2.7% for Orbital Adverse Events.

There were 92 reports of Systemic Adverse Events during the 3-month Survey, 26 of which took place in the initial week. These events are summarised in Tables 2a–c. Reported incidence of Systemic Adverse Events in the first week was 26/2827, or 0.9%.

Table 1b. *Major Orbital Adverse Events during the whole of the Survey*

LA Technique	No. of reports	Perforation/ penetration	Retrobulbar (periocular) haemorrhage (severe, causing proptosis)	Expulsive haemorrhage[a]
Peribulbar	42 700 (33 000–55 100)	6	18	2
Retrobulbar	11 000 (8400–14 400)	1	8	1
Sub-Tenon's	4380 (3280–5840)	0	0	1
Subconjunctival	2860 (2100–3880)	0	0	0
Topical alone	1870 (1340–2600)	0	0	0
Intracameral	46 (11–188)	0	0	0
Combinations	1450 (1020–2060)	1[b]	0	0
Not stated	780 (510–1190)	0	0	0
Total	65 100 (48 500–81 700)	8	26	4[a]

[a]Data on expulsive haemorrhage were specifically requested for patients who had LA in the first week, resulting in two of the four reports. As LA is not generally agreed to be a risk factor for expulsive haemorrhage, we did not expect many reports thereafter.
[b]Occurred with combined retrobulbar + peribulbar anaesthesia (RBA + PBA). Total number of RBA + PBA in the 3 months was calculated to be 830 (95% CI: 550–1250).

Orbital Adverse Events are summarised in Tables 1a and 1b. As would be expected from the Survey design, most reports of 'Minor' Adverse Events were from the first week. The tables therefore show the reported incidence of minor Adverse Events for the first week only (Table 1a), but severe Adverse Events for the whole 3-month period (Tables 1a, 1b).

The major Orbital Adverse Events associated with LA are globe perforation and retrobulbar haemorrhage. Expulsive haemorrhage (acute intraoperative suprachoroidal haemorrhage), while frequently associated with a poor outcome, is not generally agreed to be a complication of LA itself.[47,48] For the first week of the Survey, the Report Form contained a specific request for each of these three Orbital events to be reported. Thereafter, reporting of adverse events relied on the respondent recognising an adverse event to be related to the LA itself. We therefore did not expect many reports of expulsive haemorrhage after the first week.

The reported incidence of globe perforation with retrobulbar anaesthesia was 1:11 000, or 0.9 per 10 000 (95% confidence intervals (CI): 0.1–6.6 per 10 000). With peribulbar injections the incidence was 6:42 700, or 1.4 per 10 000 (95% CI: 0.6–3.3 per 10 000) and with combined retrobulbar + peribulbar it was 1:830 or 12.0 per 10 000 (95% CI: 1.6–89.4 per 10 000).

'Retrobulbar' (periocular) haemorrhage was defined as 'Severe' if there was associated proptosis. Calculated incidence of reported 'Severe' retrobulbar haemorrhage (RBH) after retrobulbar injection was 8:11 000 or 7.3 per 10 000 (95% CI: 3.5–15.2 per 10 000), and after peribulbar injection the incidence was 18:42 700 or 4.2 per 10 000 (95% CI: 2.5–7.2 per 10 000). Less severe RBH was

Table 2a. *Systemic Adverse Events reported during the first week of the Survey. Patients given oral pre-medication or intravenous sedation are indicated in italics. Criteria for definition of an Adverse Event as 'Severe' are summarised in Box 1*

LA		Less severe Systemic Adverse Events		'Severe' Systemic Adverse Events	
Technique	No. of reports	No. of reports	Description	No. of reports	Description
Peribulbar	1854	17	3 hypertension (1 with ventricular ectopics; *had pre-med.*) 3 bradycardias (1 with pulsus bigemini, 1 with panic, *1 sedated pre-op.*) 2 tachycardias (2 supraventricular, *1 sedated pre-op.*) 1 palpitations 1 vasovagal faint 1 unspecified cardiovascular system problem (*had pre-med.*) 1 'totally uncooperative' 2 panic only (*both sedated pre-op.*) 2 deoxygenation (1 with claustrophobia, *1 sedated pre-op.*) 1 urinary incontinence	2	see Table 2c: lines 5 and 7
Retrobulbar	479	2	1 panic/tremor 1 panic/confusion	1	see Table 2c: line 17
Sub-Tenon's	190	3	1 hypertension 1 panic/claustrophobia 1 confused/hyperventilating	0	
Subconjunctival	124	0		0	
Topical alone	81	0		0	
Intracameral	2	0		0	
Combinations	63	1	Hypotension (*sedated pre-op.*) after RBA + PBA	0	
Not stated	34	0		0	
Total	2827	23		3	

Table 2b. *Frequency and incidence of reported Systemic Adverse Events during the whole of the Survey. Criteria for definition of an Adverse Event as 'Severe' are summarised in Box 1*

LA		'Severe' Systemic Adverse Events		Total Systemic Adverse Events	
Technique	Estimated no. given in 3 months	No. of reports	Reported incidence (95% CI)	No. of reports	Reported incidence (95% CI)
Peribulbar	42 700	15	3.5 per 10 000 (2.0–6.2)	64	15.0 per 10 000 (10.5–21.4)
Retrobulbar	11 000	2	1.8 per 10 000 (0.4–7.4)	8	7.3 per 10 000 (3.5–15.2)
Sub-Tenon's	4380	0		6	13.7 per 10 000 (5.9–32.1)
Subconjunctival	2860	0		2	7.0 per 10 000 (1.7–29.0)
Topical alone	1870	1	5.4 per 10 000 (0.7–39.1)	4	21.4 per 10 000 (7.6–60.4)
Intracameral	46	1	217 per 10 000 (19–2400)	1	217 per 10 000 (19–2400)
Retro- + peribulbar	830	1	12.1 per 10 000 (1.6–89.4)	3	36.2 per 10 000 (10.9–120)
LA not stated		2		4	
Total	65 100	22	3.4 per 10 000 (2.1–5.5)	92	14.1 per 10 000 (10.2–19.6)

reported to occur about 10 times as frequently (data from the first week, Table 1a). Of the 26 reported cases of 'Severe' RBH, surgery went ahead on the same day in four cases. In one of these patients, surgery was complicated by an expulsive haemorrhage, with a poor outcome. Follow-up data were obtained for 11 of the other 25 cases of Severe RBH, and 19 cases of RBH without associated proptosis. There were no further reports of long-term problems associated with RBH.

The most serious Systemic Adverse Events were classified as 'Severe' if they fulfilled at least one of the following criteria: (i) the person reporting the event described it as 'life-threatening' (18 cases), (ii) the patient had an epileptic fit (excludes those already on anti-epileptic drugs) (3 cases), (iii) the patient was transferred from theatre to an Intensive Therapy Unit (ITU) (3 cases), (iv) on follow-up of a Systemic Adverse Event, subsequent death was attributed to the Adverse Event itself (1 case). These criteria are summarised in Box 1. A total of 22 Severe Systemic Adverse Events were reported, and are summarised in Table 2c. There were no reports of fatalities while in the operating theatre. Other reported Adverse Events, not fulfilling the criteria for classification as Severe, included bradycardia, tachycardia, other dysrhythmias, deoxygenation, unresponsiveness to speech, panic, confusion and vomiting.

Severe Systemic Adverse Events were reported 3 times in the first week, and 19 times in the remainder of the 3-month period. This second figure does fall within the range of uncertainty of prediction, based on the first-week returns. Incidence of reported Severe Systemic Adverse Events in the 3-month period was 22/65, 100, or 3.4 per 10 000 (95% CI: 2.1–5.5 per 10 000).

Box 1. *Summary of criteria for definition as Severe Systemic Adverse Events (see text)*
Severe Systemic Adverse Events
(i) Described by respondent as 'life-threatening'
(ii) Epileptic fit
(iii) Transferred from theatre to an Intensive Therapy Unit
(iv) Subsequent death attributed to the Adverse Event

Tables 2a–c demonstrate that Systemic Adverse Events were seen in association with all LA techniques. 'Severe' events were reported with peribulbar, retrobulbar, topical and intracameral techniques. Serious Adverse Events were also reported in association with sub-Tenon's and subconjunctival LA, though they did not fulfil our strict criteria for classification as Severe. Of the six reports associated with sub-Tenon's anaesthesia, one patient became bradycardic and unresponsive to command, three became hypertensive and one confused; the other suffered panic and claustrophobia. The two reports with subconjunctival anaesthesia were a hypotension/bradycardia and a panic/claustrophobia attack.

We looked at the characteristics of the 22 patients who had Severe Systemic Adverse Events, to see whether there were any features common to this group (Table 3). Because of the design of the Survey, we did not have data on the ASA grade, exact LA mixture or timing of intravenous access in the 'control' group who had uncomplicated LA. We therefore chose as our comparison group those patients who had Minor Orbital Adverse Events (comprising 67 patients with inadequate anaesthesia or analgesia, or 'minor' periocular haemorrhage). As most (15) of the reported Severe Systemic Adverse Events occurred after peribulbar anaesthesia, we made a separate analysis for this LA technique (see Table 3). Mann-Whitney, chi-squared and Fisher's exact tests were used as appropriate. No significant differences were found between the two adverse event groups, with the single exception of lignocaine use. Lignocaine was used more commonly in the Minor Orbital Adverse Events group ($p = 0.02$; chi-squared test).

Table 2c. *Brief description of each Severe Systemic Adverse Event reported for the period September-November 1996. Criteria for definition of an Adverse Event as Severe are summarised in Box 1*

Gender Decade of birth ASA grade Chronic illnesses	LA technique Volume Mixture Sedatives	Time to Adverse Event	Description of event	Action taken; immediate outcome	Reason for classification as Severe	Follow-up
Male 1920s Grade II	Peribulbar 8 ml Lignocaine, bupivacaine, hyaluronidase	5 min	Confusion, contralateral amaurosis, bradycardia, respiratory depression, epileptic fit	Given oxygen, glycopyrrolate, diazepam; operation postponed	Epileptic fit	No lasting effects; uneventful surgery under GA
Male 1930s Grade II HT	Peribulbar 8 ml Lignocaine, bupivacaine, hyaluronidase	30 min	Bradycardia (P = 36), hypotension, nausea and retching	Given atropine; operation completed	'Life-threatening'	No lasting effects
Female 1910s Grade II	Peribulbar 5 ml Lignocaine, bupivacaine, hyaluronidase	1–2 min	Bradycardia (P = 33), hypotension, unresponsive to speech for 1 min	Given oxygen, atropine; operation commenced when patient stabilised	'Life-threatening'	No lasting effects
Female 1910s Grade III HT, IHD	Peribulbar 10 ml Prilocaine, hyaluronidase	20 min	Deoxygenation, unresponsive to speech	Given oxygen, cyclizine	'Life-threatening'	n/a
Male 1920s Grade III NIDDM, IHD	Peribulbar 10 ml Lignocaine, bupivacaine, hyaluronidase IV midazolam	Occurred in theatre before LA was given	Bradycardia, atrial fibrillation	Given oxygen, atropine	'Life-threatening'	n/a
Male 1900s Grade II	Peribulbar 6 ml Lignocaine, hyaluronidase	15 min	Agitation, poorly responsive to speech, P = 80, BP = 200/110	Given oxygen, atropine; operation not started	'Life-threatening'; transfer to ITU	No lasting effects; subsequent surgery (LA) uneventful
Female 1900s Grade II Hypothyroidism	Peribulbar 8 ml Prilocaine, hyaluronidase IV midazolam and fentanyl	Initial (uneventful) injection to wrong side. Event occurred 1 min after second peribulbar	Oxygenation 85%, patient unresponsive for 20 s	Given flumazenil; operation proceeded	'Life-threatening'	No lasting effects
Male 1910s Grade II NIDDM, Leukaemia	Peribulbar 10 ml Lignocaine, bupivacaine, adrenaline, hyaluronidase	10 min	Anaphylaxis (attributed to platelet infusion)	Anaphylaxis treated; operation not started	'Life-threatening'; transfer to ITU	Patient died of pulmonary embolism (not related to LA)
Male 1910s Grade I	Peribulbar 6 ml Bupivacaine	20 min	Bradycardia (P < 30)	Management not stated; operation completed	'Life-threatening'	No lasting effects
Male 1920s Grade II IDDM, IHD, epilepsy	Peribulbar 8 ml Lignocaine, bupivacaine, hyaluronidase	3 min	Hypoglycaemia, deoxygenation, unresponsive to speech	Given oxygen, ephedrine, dextrose; operation not started	'Life-threatening'	n/a
Male 1920s Grade III HT	Peribulbar 7 ml Lignocaine, bupivacaine, hyaluronidase	Noted before LA given	Hypertension, tachycardia (blamed on stress of having LA surgery)	Hypertension treated	Subsequent death blamed on this this event	MI next day; patient died 4 days later
Female 1920s Grade I	Peribulbar 8 ml Prilocaine, hyaluronidase	10 min	Grand mal fit	Given oxygen, thiopentone; operation postponed	Epileptic fit	No lasting effects; uneventful surgery under GA
Male 1920s Grade II HT	Peribulbar 10 ml Lignocaine, bupivacaine, hyaluronidase	7 min	Confusion, apnoea, P = 30, BP = 98/30	Given oxygen, glycopyrrolate, ephidrine; operation postponed	'Life-threatening'	No lasting effects; uneventful surgery under GA
Female 1930s Grade I	Peribulbar 5 ml Prilocaine, hyaluronidase	10–12 min	Hypertension, tachycardia, epileptic fit	Given oxygen, manual respiration with bag	Epileptic fit	Residual scotoma in this eye (presumed intraneural injection)
Male 1950s Grade I	Peribulbar 4 ml Bupivacaine, hyaluronidase	20 min	Bradycardia (P = 38), panic hyperventilation	Given atropine; operation abandoned	'Life-threatening'	No lasting effects; uneventful re-operation with sedation, 3 days later
Female 1920s Grade II Osteoarthritis	Retrobulbar 9 ml Lignocaine, adrenaline, hyaluronidase Oral temazepam	5 min	Bradycardia (P = 24), unresponsive to speech	Given atropine	'Life-threatening'	No lasting effects
Male 1930s Grade I	Retrobulbar 7 ml Bupivacaine, hyaluronidase	5 min	Confused and unresponsive, slow breathing, poor oxygenation, P = 75; BP = 115/63	Given oxygen, converted to GA; operation proceeded	'Life-threatening'	No lasting effects
Female 1910s Gade II IHD	Topical Amethocaine 1%	25 min (2 min after g. carbachol 3%)	Hypotension, bradycardia and myocardial ischaemia	Given oxygen, atropine	'Life-threatening'; transfer to ITU	n/a
Male 1920s Grade IV NIDDM, IHD, SA	Topical Amethocaine, topped up with intracameral 1 ml lignocaine IV fentanyl/midazolam	Following top-up and IV sedation	Brief apnoea, unresponsive to speech	Ventilated with facemask and bag; operation completed	'Life-threatening'	No lasting effects
Female 1910s Grade II	Retrobulbar + Peribulbar 10 ml Lignocaine, bupivacaine, adrenaline, hyaluronidase	3 min	Shallow breathing, deoxygenation, unresponsive to speech, transient VII nerve palsy	Given oxygen; operation not started	'Life-threatening'	No lasting effects; uneventful surgery under GA
Female 1910s Grade II HT, IHD	LA technique not stated 10 ml Lignocaine, bupivacaine, adrenaline, hyaluronidase	30 min	Angina, sinus tachycardia with ectopics	Given oxygen, glyceryl trinitrate; operation proceeded	'Life-threatening'	n/a
Female 1910s Grade II IDDM	LA technique not stated 8 ml Lignocaine, bupivacaine, adrenaline, hyaluronidase	15 min	Sinus tachycardia	Given esmolol; operation proceeded	'Life-threatening'	n/a

ASA grade, American Society of Anesthesiologists' classification of physical status; IDDM, insulin-dependent diabetes mellitus; NIDDM, non-insulin-dependent diabetes mellitus; HT, hypertension; IHD, ischaemic heart disease;

Discussion

The Survey results confirm the widely held view that serious adverse events associated with LA are rare. However, we have shown that adverse events are seen with all LA techniques, thus demonstrating that no LA is totally safe.

It is likely that the actual incidence of adverse events was higher than estimated in this paper. In calculating the number of LAs actually given during the Survey, we made a correction for the 72.8% participation rate in the initial week. In calculating the incidence of Adverse Events, we assumed that all such events had been reported (i.e. 100% participation for adverse events). Table 2a shows that 23 non-severe Systemic Adverse Events were reported in the first week: if incidence and reporting had continued at the same rate, we would have expected a further 362 reports for the remainder of the Survey: the actual figure was 47, about one-eighth of that predicted. We suspect that there was also significant under-reporting of the more serious adverse events.

Causes of low-response bias could include: lack of awareness of the Survey, failure to recognise that the event had taken place or was eligible, not considering an adverse event to be severe enough for inclusion, forgetting that the Survey was still running, unwillingness to spend time completing an Adverse Event Form, concern that the report may engender further time-consuming correspondence, embarrassment if safety Guidelines had not been followed, overwork, apathy, suspicion of an underlying motive for the Survey, and fear of being 'policed' by the Royal Colleges. We tried to minimise non-response bias from these causes by offering complete anonymity to respondents,

Table 3. *Features of the patients who had Severe Systemic Adverse Events associated with local anaesthesia. The comparison group comprises patients who had Minor Orbital Adverse Events. Most Adverse Events were reported to occur in patients who were given peribulbar anaesthesia (the most common LA technique). We have therefore made comparisons for the groups as a whole, and also for the subgroups of patients who had peribulbar anaesthesia. Criteria for definition of an Adverse Event as Severe are summarised in Box 1*

	All LA techniques			Peribulbar LA only		
Characteristic	Severe Systemic Adverse Events group (all 22 patients)	Minor Orbital Adverse Events group (all 67 patients)	Significance of comparison	Severe Systemic Adverse Events group (15 patients)	Minor Orbital Adverse Events group (47 patients)	Significance of comparison
Gender (Male:female)	12:10	27:38 (2 not stated)	$p = 0.29$	10:5	19:26 (2 not stated)	$p = 0.10$
Age:						
Born 1900s	2	5		2	3	
Born 1910s	8	21		4	18	
Born 1920s	8	22		6	16	
Born 1930s	3	9	$p = 0.42$	2	2	$p = 0.73$
Born 1940s	0	6		0	5	
Born 1950s	1	2		1	2	
Born 1960s	0	1		0	0	
		(1 not stated)		0	(1 not stated)	
ASA grade:						
I	5	14		4	8	
II	13	40		8	31	
III	3	11	$p = 0.95$	3	6	$p = 0.71$
IV	1	0		0	0	
Not stated	0	2		0	2	
LA mix included:						
Lignocaine	14	58	$p = 0.02$*	9	41	$p = 0.02$*
Bupivacaine	14	46	$p = 0.66$	10	33	$p = 0.80$
Prilocaine	4	10	$p = 0.72$	4	7	$p = 0.30$
Adrenaline	5	20	$p = 0.42$	1	15	$p = 0.09$
Hyaluronidase	19	50	$p = 0.25$	14	35	$p = 0.22$
Sedation used	3	3	$p = 0.32$	2	2	$p = 0.49$
Premedication used	1	3	$p = 0.94$	0	1	$p = 0.76$
IV cannula sited before adverse event occurred	12	40	$p = 0.67$	8	30	$p = 0.47$
Availability of anaesthetist						
Dedicated for this list	15	48		10	33	
Elsewhere in theatres	5	10	$p = 0.17$	5	10	$p = 0.64$
Available only in dire emergency	0 (2 not stated)	9		0	4	

Tests of significance used: Mann-Whitney, chi-squared and Fisher's exact test, as appropriate.

*Lignocaine was used significantly less frequently in the group who had Severe Systemic Adverse Events when compared with the group who had the Minor Orbital Adverse Events of inadequate block or minor periocular haemorrhage.

and providing simple forms with a reminder poster that carried the eligibility criteria.[1] During the first week of the Survey, when all LAs were to be reported, there were 3 reports of Severe Systemic Adverse Events, as defined in Box 1. Multiplying this by our workload factor of 16.76, this would predict around 50 reports in the 3 months, or 70 if we assume that the overall participation rate of 72.8% also applied. The actual number of Severe Systemic Adverse Events reported in the 3-month period was 22, which does fall within the wide range of uncertainty of prediction based on the first week's returns. Thus it appears that there is probably less under-reporting for the more severe adverse events. From the incidents reported, we calculate that the number of life-threatening adverse events occurring annually in the United Kingdom is at least 100. Depending on the degree of under-reporting, the true figure may be in the order of a few hundred.

The novel design of the Survey makes it difficult to compare incidence of adverse events with other studies. Large case-series are often produced in centres with a special interest in LA safety, and as such their results may be better than average. As discussed above, we expect that the Survey suffered from a degree of under-reporting of serious adverse events. There is also the problem that severity of adverse events is not well defined in all studies. In this Survey, the 22 cases that fulfilled our strict criteria as Severe Systemic Adverse Events gave a calculated incidence of 0.034% (95% confidence intervals: 0.021–0.055%), though the true figure is likely to be higher due to presumed bias from under-reporting. A study of 6000 consecutive retrobulbar blocks[13] found 'life-threatening' complications in 0.13% of patients when given 'appropriate premedication' and a 2% lignocaine/0.5% bupivacaine/hyaluronidase mixture. Most of these patients exhibited the classical features of 'brain-stem anaesthesia': respiratory depression, hypotension and bradycardia. Another series of 3123 retrobulbar blocks[14] found the incidence of respiratory arrest to be 0.79% when using 4% lignocaine, and 0.09% when using 2% lignocaine, in patients who were also given oral or intravenous sedation. Another series describes using a 2% lignocaine/0.75% bupivacaine/hyaluronidase/adrenaline mixture; less than 5% of patients were sedated. Brain-stem anaesthesia was recorded in 0.15% of 5235 retrobulbar blocks and 0 of 5704 peribulbar blocks.[10] A multi-centre, prospective study of 16 224 consecutive peribulbar blocks, many of which were supplemented by sedation, identified one epileptic fit (0.006%) and no cases of cardiac or respiratory depression.[35] A series of 3000 sub-Tenon's blocks with 2% lignocaine found no systemic or orbital complications.[44] In our Survey, the incidence of adverse events was of similar order to these published figures, but the limitations of the Survey design preclude any critical comparison.

An observational study of this type cannot answer the question of which LA technique is safest: this would require a prospective randomised trial so large that it could probably never be performed. However, it is interesting to compare the incidence of Severe Adverse Events with the different LA techniques used in the Survey (Table 2b). Serious Adverse Events were seen with all LA techniques, though not all of these fulfilled our strict criteria for classification as 'Severe'. We did not show any LA technique to be obviously more or less safe than any other.

Despite the large size of the Survey, there were not enough reports of Serious Adverse Events to allow us to compare safety of the different LA techniques. For the Survey to have sufficient power to allow such a comparison, we would have needed a data collection period of about a year. There were several reasons why we felt that this would not be appropriate, the main ones being that a longer period of data collection could adversely affect participation, and that there is a wide range of LA injection techniques, some of which may be described as 'retrobulbar' by one clinician and 'peribulbar' by another. As discussed above, the observational design of the Survey does not permit direct comparisons to be made.

In Table 3, we attempted to find any common features in the group of patients who had Severe Systemic Adverse Events, by comparing them with a group who had minor complications within the orbit. The proportion of patients with intravenous access or a dedicated anaesthetist was similar in both groups, implying that the Severe events had not been predicted in individual cases. Patient age, ASA grade and use of sedation were similar in the two groups. The only significant difference was in the use of lignocaine: when the components of the LA mixture were compared separately, lignocaine was used significantly less in the group who had Severe Systemic Adverse Events. Numbers were too small for us to make a useful multivariate analysis for the overall LA mixture. The lower prevalence of lignocaine use in the Severe Systemic Adverse Events group may reflect a higher incidence of Minor Orbital events with lignocaine, a higher incidence of Systemic events with the other LA agents, or a random effect. Because this was not a prospective randomised study, Table 3 should not be considered as a direct comparison of safety. Thus, it cannot be used to argue for the safety or otherwise of any particular LA agent or of sedation.

There were no reports of death in the operating theatre for the 3-month Survey, though one patient suffered hypertension and tachycardia prior to his LA injection, and his death due to a myocardial infarction the following day was attributed to the stress of having LA. Our initial questionnaire to consultant ophthalmologists identified 10 cases of patient death attributed to LA,[1] which is equivalent to one LA-associated death per twenty 25-year consultant careers. A questionnaire to UK ophthalmologists, published in 1994, identified 12 cases of LA-associated death,[19] all but one of which occurred 'on the operating table' (S.A. Haider, personal communication). In view of the severity of some of the adverse events reported during our

Survey, it is possible that timely intervention by anaesthetists prevented a number of deaths during the 3-month period.

Serious Systemic Adverse Events were reported in association with all LA techniques. Many of the events summarised in Table 3 could be explained by the 'classical' routes of intraneural injection or systemic absorption of LA agents. Other events could be attributed to stress reaction, oculocardiac reflex, systemic effects of topical mydriatics, ocular hypotensive agents or sedatives, or causes unrelated to the LA or surgery. However these events were caused, the fact that they were seen with all LA techniques implies that we should be prepared for serious adverse events in all patients who have intraocular surgery.

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