Pain perception with pH buffered peribulbar anaesthesia: a pilot study

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Abstract

***Aims*—To determine the relation between pH of anaesthetic solutions and patient perception of pain with peribulbar injection of local anaesthesia.**

***Methods*—This prospective randomised controlled double blind pilot study involved 60 consecutive patients who received a peribulbar block with either a standard acidic local anaesthetic of 5 ml 2% lignocaine and 5 ml of 0.5% bupivacaine (solution A), or an alkalinised solution composed of the same anaesthetic agents but with a pH of 7.44 (solution B). Before surgery patients were asked to grade the pain of both the preoperative dilating drops and the peribulbar injection using a visual analogue scale.**

***Results*—The mean pain scores were similar in the two treatment groups—slightly higher (4.97) in group B who received the buffered solution, compared with group A (4.84) who received the plain solution. The small difference (−0.13, 95% confidence limits −1.6 and +1.3) was not significant. There was, however, a highly significant association between pain threshold ("drop pain") and injection pain levels ($p<0.0001$).**

***Conclusion*—This study showed no difference in the reduction in the pain experienced by patients undergoing peribulbar anaesthesia with pH buffered local anaesthetic. The study suggests the importance of "pain threshold" as a confounder and also showed the considerable pain felt by some patients on instillation of the preoperative dilating drops.**

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Local anaesthetic is the commonest form of anaesthesia for patients undergoing cataract surgery in the UK.[1–3] Different techniques have been described for administering the anaesthesia[4–9] and different solutions have been suggested.[10–14] Modification of local anaesthetics by the addition of agents to reduce the onset time or to prolong duration of blockade has been practised and investigated extensively.[15–21] The pain often experienced on injection of local anaesthetic solutions is in part related to pH[22] and this is particularly true for solutions with added adrenaline (epinephrine).[23] There is some evidence to suggest that adding preservative free sodium bicarbonate to local anaesthetic solutions results in less discomfort on injection.[24–26] We have therefore investigated the use of a buffered solution of lignocaine (lidocaine) and bupivacaine in peribulbar anaesthesia to study the effect on pain perception in patients undergoing cataract surgery.

Patients and methods

Sixty patients (35 female, 25 male) admitted for elective cataract surgery were randomised to receive either a standard solution of local anaesthetic (solution A) or an alkalinised solution (solution B). Patients who did not have a good understanding of spoken English were excluded. Solution A was prepared using 5 ml of 2% lignocaine and 5 ml of 0.5% bupivacaine (total 10 ml, both manufactured by Antigen Pharmaceuticals Ltd) with a resultant pH of 4.87. Solution B was prepared as above with the addition of 1ml of 8.4% preservative free sodium bicarbonate with a resultant pH of 7.44 (1 ml of solution B was discarded to achieve an equal volume to solution A).

To ensure stability of pH, the solutions were prepared in polypropylene syringes at the beginning of each operating list. The pH of each solution was tested using a Corning 240 pH meter (subjected to a two point calibration using commercially available buffered pH solutions).

Preoperative pupil dilatation using phenylephrine 10% eyedrops (2.5% in hypertensives) and cyclopentolate 1.0% eyedrops were given topically at 60, 45, 30, and 15 minutes before surgery and proxymetacaine 0.5% eyedrops were given topically before peribulbar anaesthesia. All peribulbar injections were given by two ophthalmologists who were unaware of the choice of solution (AI or MM). The peribulbar anaesthetic was administered at the junction of the middle and lateral thirds of the lower lid using a 1¼ (15/16″) 25 gauge needle (0.25×24 mm). Before surgery the patients were asked to grade the pain of both the preoperative dilating drops and the peribulbar injection on a standard visual analogue scale[5 14] which was enlarged to A4 size to facilitate reading in these visually impaired patients—0 represents no pain and 10 the most severe pain imaginable. The

Table 1 Distribution of the possible prognostic factors in the two treatment groups

	Number (%)	
	Group A (n=31)	*Group B (n=29)*
Sex:		
Males	12 (39)	13 (45)
First eye	23 (74)	19 (68)
Injector:		
AI	24 (77)	17 (59)
MM	7 (23)	12 (41)
Drop pain		
mean	3.23	2.69
SD	2.59	2.02

None of the differences were significant, all p values >0.05.

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Table 2 Frequency distribution of injected pain

Injection pain	*Group A*	*Group B*	*Total*
0.0	1	2	3
	3.2%	6.9%	5.0%
1.0	2	3	5
	6.5%	10.3%	8.3%
2.0	4	3	7
	12.9%	10.3%	11.7%
3.0	2	3	5
	6.5%	10.3%	8.3%
4.0	3	0	3
	9.7%	0%	5.0%
5.0	8	5	13
	25.8%	17.2%	21.7%
6.0	3	3	6
	9.7%	10.3%	10%
7.0	3	1	4
	9.7%	3.4%	6.7%
8.0	3	6	9
	9.7%	20.7%	15.0%
9.0	1	2	3
	3.2%	6.9%	5.0%
10.0	1	1	2
	3.2%	3.4%	3.3%
Total	31	29	60
	51.7%	48.3%	

questions were phrased identically in all patients. The recording of "drop pain" served as an assessment of the individual patient's pain threshold.

A *t* test was used to compare the mean pain scores in the two treatment groups, together with Levene's test for equality of variances to validate the *t* test. An equivalent non-parametric test (Mann–Whitney) was also used to complement the *t* test. To adjust for confounding effects of possible prognostic factors (pain threshold and injector) a general multifactor ANOVA (SPSS statistical software) was performed, using the "drop pain" scores as a covariate for "injection pain".

Results

Table 1 shows the baseline characteristics for the two treatment groups. They were assessed according to the following four criteria; sex of the patient, whether or not they had previously undergone cataract surgery under local anaesthesia, which of the injectors administered the anaesthetic and, finally, pain threshold. None of the differences was statistically significant (all p values >0.05). Table 2 shows the frequency distribution of injection pain between the two groups and Table 3 gives a further analysis of the injection pain mean scores in the two treatment groups. The mean pain scores were similar in the two groups—only slightly higher (4.97) in group B who received the buffered solution of anaesthetic, compared with group A (4.84) who received the plain solution. The small difference (−0.13, 95% confidence limits −1.6 and +1.3) was not significant (*t* test, two tailed p=0.86). Taking into account the pain threshold and the injector and adjusting for their possible confounding effects made no material difference to the findings (general ANOVA, p=0.85). As expected, the ANOVA model showed a highly significant association between pain threshold ("drop pain") and injection pain levels (p<0.0001). Figure 1 shows the pain experienced from the injection in the two groups before and after adjustment for the patients with high and low pain thresholds. The initial difference in the pain experienced is seen to even out after the adjustments have been made.

Table 3 Comparison of injection pain mean scores in the two treatment groups

				Significance tests p values		
Treatment group	*No of patients*	*Mean injection pain score (SD)*	*Mean difference*	*t test*	*Non-parametric Mann-Whitney test*	*Multifactor ANOVA with adjustment for pain threshold and injector*
A	31	4.84 (2.49)	−0.13	p=0.86	p=0.77	p=0.85
B	29	4.97 (3.02)				
Totals	60	4.90 (2.74)				

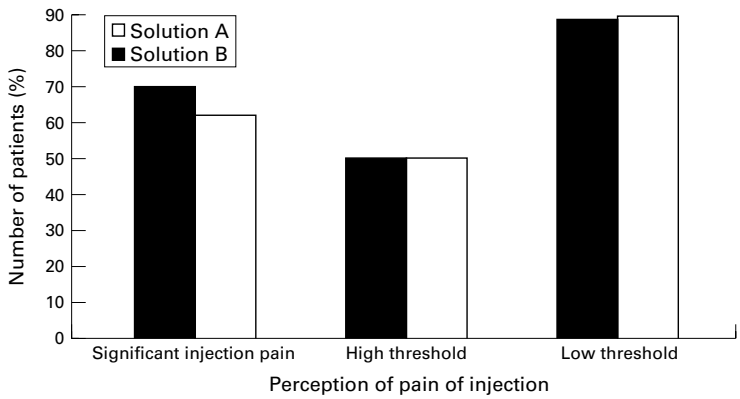

Figure 1 Pain perception adjusted for patient pain threshold.

DROP PAIN

A substantial number of patients experienced considerable pain on instillation of the preoperative dilating drops.

COMMENTS ON THE POWER OF THE STUDY

The study had reasonable power (90% probability) to detect a reduction in the mean pain score from about 5.0 to 2.5. The results of the trial, therefore, may be interpreted to suggest that the treatment effect (if any) was likely to be smaller than the level of reduction mentioned above. The study provided useful data on levels of mean pain score and the standard deviation that can be expected and used to design future larger studies. A more sensitive study with 90% power to detect a relatively small reduction in pain score of 1.0 unit (from 5.0 to 4.0) would require 314 patients to be randomised.

Discussion

Local anaesthetics used in nerve blockade must cross the perineural sheath and nerve membrane; these structures are only permeable to the drug in its non-ionised form.[18] Most local anaesthetics are weak bases with pKa values varying from 7.7 to 8.9, although they are supplied as acidic solutions[18] to improve stability. In this form the local anaesthetic agent exists mainly in the ionised form. Therefore it probably achieves nerve blockade more slowly than a solution with a pH that more closely approximates the pKa and contains more of the non-ionised, lipid soluble form. It has been shown that the active form of the drug is the ionised or cation form.[21 27] Alkalinisation of a local anaesthetic solution with bicarbonate

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should increase the amount of the non-ionised form. Despite the ionised form being active, it had been postulated that the non-ionised lipid soluble form diffuses through the soft tissues and nerve membrane faster.[17 28]

A number of studies have reported comparisons between alkalinised and plain anaesthetic solutions.[15–18 20–26] Previous studies looking at modification of discomfort with alkalinised local anaesthetics report a statistically significant reduction in pain of injection with alkalinised solutions.[23–26] However, these studies investigated this effect in intradermal, not peribulbar, anaesthesia. It is difficult to compare the results of these studies as different anatomical sites of local anaesthetic neural blockade were used. Although studies have investigated both the pain of infiltration and onset of action, the effect of alkalinisation on the pain of peribulbar injections has not been previously described. The only study looking at the peribulbar model investigated onset time of anaesthesia and not pain of injection.[15] This study reported a statistically significant faster onset time with alkalinised local anaesthetics in a sample of 80 patients.

A number of reasons for the reduction in pain with alkalinisation of the anaesthetic have been suggested. Firstly, the adjustment of local anaesthetic pH towards the physiological range of 7.0–7.4 reduces the direct tissue irritation caused by infiltration of a more acidic compound; it has been found that commercial lignocaine with adrenaline (pH 4.15) has a lower pH and is more painful than lignocaine with added adrenaline (pH 6.4).[23–26] Secondly, the increased relative concentration of the non-ionised form allows for a more rapid diffusion through tissues and might result in almost immediate sensory nerve blockade.[23 24 27] Thirdly, it is conceivable that nociceptor receptors may be less sensitive to the non-ionised form.[24] Conversely, the greater diffusibility of the non-ionised form may result in greater inhibition of pain transmission, thereby preventing nociceptive impulses from being fully appreciated.

Caution must be taken when alkalinising local anaesthetic solutions so as not to cause precipitation or denaturing of the compound. The exact pH at which this can occur is not clear and values vary in the literature; this in part must reflect the variation in standard pH of solutions from different manufacturers. Bupivacaine can be safely alkalinised to a pH of 7.0–7.4 without risk of precipitation,[23] lignocaine is stable at a slightly higher pH of 7.54.[25] We did not experience any problems with precipitation at the pH levels used in our solutions. In addition to the risk of precipitation there is also a cost implication in the addition of a buffer to the plain solution.

A reduction in the time of onset of neural blockade with alkalinised solutions has been questioned by some investigators.[15] This may be attributed to work on carbonated lignocaine.[29] Carbonated salts of local anaesthetics release carbon dioxide, which is believed to reduce intracellular pH and promote the diffusion of intraneural local anaesthetic.[29] Difficulties in needle placement for brachial block may well account for different results among investigators. It may be that the peribulbar anaesthetic block is a more useful model for studying pH adjusted local anaesthetics, because the onset time of neural blockade depends mainly on diffusion, as the injection does not penetrate the muscle cone.

The pain experienced during an injection is of course also related to the temperature of the injectate and speed of delivery of the solution.[7 23] These variables were standardised as much as possible. All solutions were used at room temperature; however, the variability between the two injectors, and indeed the same injector on different days, could not be completely eliminated.

This study found no significant difference in the pain of peribulbar injection with an alkalinised anaesthetic solution. A larger trial with more patients might yield a significant difference. In addition, the study highlighted the pain experienced by patients on instillation of preoperative dilating drops.

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1 Eke T, Thomson JR. The National Survey of Local Anaesthesia for Ocular Surgery. I. Survey methodology and current practice. *Eye* 1999;**13**:189–95.
2 Courtney (Desai) P. The National Cataract Surgery Survey. I. Method and descriptive features. *Eye* 1992;**6**:487–92.
3 Hodgkins PR, Luff AJ, Morrell AJ, *et al.* Current practice of cataract extraction and anaesthesia. *Br J Ophthalmol* 1992; **76**:323–6.
4 Murdoch IE. Peribulbar versus retrobulbar anaesthesia. *Eye* 1990;**4**:445–9.
5 Duguid IG, Claoué CM, Thamby-Rajah Y, *et al.* Topical anaesthesia for phacoemulsification surgery. *Eye* 1995;**9**: 456–9.
6 Khurana AK, Sachdeva RK, Gombar KK, *et al.* Evaluation of subconjuctival vs peribulbar anaesthesia in cataract surgery. *Acta Ophthalmol Copenh* 1994;**72**:727–30.
7 Gillart T, Bazin JE, Montetagaud M, *et al.* The effects of volume and speed of injection in peribulbar anaesthesia. *Anaesthesia* 1998;**53**:486–91.
8 Verghese I, Sivaraj R, Lai YK. The effectiveness of sub-Tenon's infiltration of local anaesthesia for cataract surgery. *Aust NZ J Ophthalmol* 1996;**24**:117–20.
9 Stevens JD. A new local anaesthesia technique for cataract extraction by one quadrant sub-Tenon's infiltration. *Br J Ophthalmol* 1992;**76**:670–4.
10 Thomson I. Addition of hyaluronidase to lignocaine with with adrenaline for retrobulbar anaesthesia in the surgery of senile cataract. *Br J Ophthalmol* 1998;**72**:700–2.
11 Brydon CW, Basler M, Kerr WJ. An evaluation of two concentrations of hyaluronidase for supplementation of peribulbar anaesthesia. *Anaesthesia* 1995;**50**:998–1000.
12 Crawford M, Kerr WJ. The effect of hyaluronidase on peribulbar block. *Anaesthesia* 1994;**49**:907–8.
13 Reah G, Bodenham A, Braithewaite J, *et al.* Peribulbar anaesthesia using a mixture of local anaesthetic and vecuronium. *Anaesthesia* 1998;**53**:551–4.
14 Henderson TR, Franks W. Peribulbar anaesthesia for cataract surgery: prilocaine versus lignocaine and bupivacaine. *Eye* 1996;**10**:497–500.
15 Zahl K, Jordan A, McGroaty J, *et al.* Peribulbar anaesthesia. Effect of bicarbonate on mixtures of lidocaine, bupivacaine and hyaluronidase with or without epinephrine. *Ophthalmology* 1991;**98**:239–42.
16 Roberts J, Macleod B, Hollands R. Improved peribulbar anaesthesia with alkalinisation and hyalurionidase. *Can J Ophthalmol* 1993;**40**:835–8.
17 Fernando R, Jones H. Comparison of plain and alkalinised local anaesthetic mixtures of lignocaine and bupivacaine for elective extradural caesarean section. *Br J Anaesth* 1991;**67**:699–703.
18 Morrison D. Alkalinisation of local anaesthetics (Editorial). *Can J Anaesth* 1995;**42**:1076–9.
19 Lewis P, Hamilton R, Loken R, *et al.* Comparison of plain with pH-adjusted bupivicaine with hyaluronidase for peribulbar block. *Can J Anaesth* 1992;**39**:555–9.
20 Capogna G, Celleno D, Constantina P, *et al.* Alkalinisation improves the quality of lidocaine-fentanyl epidural anaesthesia for elective Caesarean section. *Can J Anaesth* 1993;**40**:425–30.

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21 Gaggero G, Meyer O, van Gessel E, *et al.* Alkalinisation of lidocaine 2% does not influence the quality of epidural anaesthesia for elective Caesarean section. *Can J Anaesth* 1995;**42**:1080–4.
22 Shafi T, Koay P. Randomised prospective masked study comparing patient comfort following the instillation of topical proxymetacaine and amethocaine. *Br J Ophthalmol* 1998;**82**:1285–7.
23 Christoph R, Buchanan L, Schwartz S. Pain reduction in local anaesthetic administration through pH buffering. *Ann Emerg Med* 1998;**17**:117–20.
24 Mackay W, Morris R, Mushlin P. Sodium bicarbonate attenuates pain on skin infiltration with lidocaine, with or without epinephrine. *Anaesth Analg* 1987;**66**:572–4.
25 Martin A. pH adjustment and discomfort caused by the intradermal injection of lignocaine. *Anaesthesia* 1990;**45**: 975–8.
26 Korban G, Hurley D, Gaylord W. pH-adjusted lidocaine does not 'sting'. *Anaesthesia* 1987;**66**:855–6.
27 Ritchie JM, Ritchie B, Greenford P. The active structure of local anaesthetics. *J Pharmacol Exp Ther* 1965;**150**:152–9.
28 Ritchie JM, Ritchie B, Greenford P. The effect of the nerve sheath on the action of local anaesthetics. *J Pharmacol Exp Ther* 1965;**150**:160–4.
29 Sukhani R, Winnie AP. Clinical pharmacokinetics of carbonated local anaesthetics I; subclavian perivascular brachial block model. *Anaesth Analg* 1987;**66**:749–54.

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