

The efficacy of two bupivacaine hydrochloride injection products

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Objective. The relative efficacy of two bupivacaine hydrochloride injection products was investigated in patients who were undergoing intra-ocular eye surgery.

Design. Patients took part in this double-blind, randomised, parallel-group study and received either Macaine (Keatings) or Regibloc (Intramed), according to the randomisation schedule.

Setting. The study was carried out in the ophthalmology operating theatres of National and Pelonomi Hospitals, Bloemfontein, South Africa.

Patients. Thirty male and 74 female patients who needed extra-capsular lens extraction plus intra-ocular lens implantation, extra-capsular lens extraction, or trabeculectomy were selected for the study.

Outcome measures. Akinesia was evaluated after 10, 15 and 20 minutes. In the event of incomplete akinesia after 20 minutes, an additional injection was administered, and after 5 minutes another evaluation of akinesia was done. Anaesthesia was evaluated at the beginning of surgery.

Results. The proportions of patients who received no additional anaesthesia were 57.7% for Macaine and 70.8% for Regibloc (difference 13.1%, 95% confidence interval (CI) -5.5 - 31.7%). The proportions of patients with adequate akinesia (possibly after additional anaesthesia) were 90.4% for Macaine and 89.6% for Regibloc (difference -0.8%, 95% CI -12.6 - 11.0%).

The proportions of patients experiencing no pain or discomfort at the beginning of surgery were 88.2% for Macaine and 87.5% for Regibloc (difference -0.7%, 95% CI -13.6 - 12.1%).

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Conclusion. The study results indicate that Regibloc is at least as effective as, or superior to, Macaine in achieving adequate akinesia.

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Bupivacaine hydrochloride is a long-acting local anaesthetic of the amide type, with a duration of action of up to 10 hours. Onset of action and depth of anaesthesia depend upon the concentration, dose, route of application, and whether adrenaline is used. Bupivacaine hydrochloride is used mainly for infiltration and regional nerve blocks, particularly epidural block.¹ Mixtures of bupivacaine and hyaluronidase, with or without adrenaline, are used in peribulbar anaesthesia.^{2,3}

Differences in the efficacy of two bupivacaine hydrochloride injection products (Macaine; Keatings and Regibloc; Intramed) available in South Africa were reported, albeit anecdotally. This study was therefore performed to compare the efficacy of Regibloc injection with respect to the reference product, Macaine injection, in ocular surgery.

Methods

Study population

Thirty male and 74 female patients who were undergoing intra-ocular eye surgery took part in this study. For biometric analysis, the data from 100 patients were available. The demographic data are summarised in Table I. Before the operation, the nature, purpose and risk of the procedure involved was explained to all patients. They signed a consent form in the presence of a clinical investigator. The study was approved by the ethics committee of the University of the Orange Free State, Bloemfontein, South Africa, and performed in conformance with Good Clinical Practice guidelines.^{4,5}

Table I. Demographic data

	Macaine (52 patients)	Regibloc (48 patients)
Hospital		
National	28	23
Pelonomi	24	25
Sex		
Male	15	14
Female	37	34
Race		
White	26	21
Black	26	26
Coloured	-	1
Age (yrs)	69	71
(mean and range)	(39 - 90)	(45 - 94)
Type of operation		
ECLI + IOLI	36	26
ECLI	13	18
Trab.	3	4
Eye		
Left	26	20
Right	26	28

ECLI + IOLI = extra-capsular lens extraction plus intra-ocular lens implantation; ECLI = extra-capsular lens extraction; Trab. = trabeculectomy.

Study design

This was a double-blind, randomised, parallel-group study. Patients received an injection of 0.5% bupivacaine hydrochloride, either Macaine or Regibloc according to the randomisation schedule.

Study performance

The study was carried out in the ophthalmology operating theatres of National and Pelonomi Hospitals, Bloemfontein. One of the following operations was carried out: extra-capsular lens extraction plus intra-ocular lens implantation, extra-capsular lens extraction, or trabeculectomy. Each patient received a peribulbar injection of a 10 ml bupivacaine hydrochloride solution, mixed with 150 units of hyaluronidase (Kinetin; Schering), prepared by an assistant within 1 hour of use.^{2,3} Peribulbar anaesthesia was effected with 8 - 9 ml of the solution. The volume depended on the clinical impression of the orbital pressure. Equal volumes of the solution were injected at two different sites with a 22G needle inserted past the equator of the globe: just above the inferior orbital rim in the inferotemporal quadrant (inferior), just lateral to the supratrochlear notch (superior).

After the block, the patient received digital massage of the eyelids for 2 minutes. Extra-ocular pressure was applied with a Honan balloon for 20 minutes. The akinesia was evaluated by the surgeon 10, 15 and 20 minutes after the injection. In the event of incomplete akinesia after 20 minutes, an additional injection of 1 - 2 ml of the same solution was administered either at the superior or the inferior position. The total volume administered did not exceed 10 ml. After 5 minutes, another evaluation of akinesia was done. If akinesia had not occurred after an additional injection was given, the block was considered to have failed. The evaluation of anaesthesia was done at the beginning of surgery.

Efficacy variables

Evaluation of akinesia. The following muscle movements were recorded: medial rectus (MR), lateral rectus (LR), superior rectus (SR), inferior rectus (IR), eyelid.

Full movement was recorded as 0, partial movement as 1 and total paralysis as 2. The total score was recorded as the sum of the five individual scores, and graded as follows:² 8, 9 and 10 — akinesia suitable for operation (adequate akinesia), except in cases where only one of the muscles was responsible for a score of 8 (i.e. one muscle scored 0); 5, 6 and 7 — partial akinesia that requires additional anaesthetic; 4 and lower — akinesia not suitable for operation.

If additional local anaesthetic was needed, the position of injection (superior or inferior) was recorded, as well as the volume of the solution injected.

Evaluation of anaesthesia. The evaluation of anaesthesia at the beginning of surgery was recorded as follows: pain = 0; discomfort = 1; no pain or discomfort = 2.

Biometric methods

The two treatments were compared by calculating point estimates and 95% confidence intervals (CIs) for the

Table II. Evaluation of akinesia, need for additional anaesthesia, and pain score (dose injection of solution containing 5 mg bupivacaine hydrochloride per ml)

	Macaine (reference)		Regibloc (test)		Difference (%)*	95% CI (%)†
	No.	%	No.	%		
Adequate akinesia after 10 min	25/52	48.1	32/48	66.7	18.6	-0.4 - 37.6
Adequate akinesia after 15 min	30/52	57.7	33/48	68.8	11.1	-7.7 - 29.8
Adequate akinesia after 20 min	31/52	59.6	34/48	70.8	11.2	-7.3 - 29.7
No additional anaesthesia	30/52	57.7	34/48	70.8	13.1	-5.5 - 31.7
Adequate akinesia (poss. after add. anaesthesia)‡	47/52	90.4	43/48	89.6	-0.8	-12.6 - 11.0
No pain or discomfort at beginning of surgery	45/51	88.2	42/48	87.5	-0.7	-13.6 - 12.1

* Point estimates for the 'test-reference' difference between treatments.

† 95% CI for the difference between treatments.

‡ Missing pain scores were replaced by a pain score of 0 (pain).

differences between the treatments in the following proportions: (i) the proportions of patients with adequate akinesia after 10, 15 and 20 minutes after injection, respectively; (ii) the proportions of patients requiring no additional anaesthesia; (iii) the proportions of patients with adequate akinesia, 5 minutes after additional anaesthesia; and (iv) the proportions of patients with no pain or discomfort at the beginning of the operation. The CIs were calculated as described by Gardner and Altman.⁶

Results

The point estimates and CIs for the true 'test-reference' differences in the proportions are given in Table II.

The proportions of patients who received no additional anaesthesia were 57.7% for Macaine and 70.8% for Regibloc (difference 13.1%, 95% CI -5.5 - 31.7%). The proportions of patients with adequate akinesia (possibly after additional anaesthesia) were 90.4% for Macaine and 89.6% for Regibloc (difference -0.8%, 95% CI -12.6 - 11.0%).

In 10 cases of block failure, the patients were given additional anaesthetic and the planned operations were successfully performed. The following were recorded: 4 patients received an additional injection of Macaine, 5 patients received an additional injection of Remicane (2% solution), and 1 patient, with a score of 8 but with inadequate anaesthesia, received local drops of amethocaine during the operation. In all cases of block failure (i.e. inadequate akinesia), anaesthesia was not evaluated and a score of 0 was used for statistical analysis.

The proportions of patients experiencing no pain or discomfort at the beginning of surgery were 88.2% for Macaine and 87.5% for Regibloc (difference -0.7%, 95% CI -13.6 - 12.1%).

Discussion

The point estimates and CIs for the 'test-reference' difference in the proportions of patients with adequate akinesia at 10, 15 and 20 minutes after the first injection

indicate that Regibloc is at least as effective as, or is superior to, Macaine in achieving adequate akinesia. After additional injections in cases of inadequate akinesia, both products appear equally effective.

The point estimates and CIs for the test-reference difference in the proportions of patients with adequate akinesia (possibly after additional anaesthesia), and in the proportions of patients with no pain or discomfort at the beginning of surgery, indicate that the two treatments were equally effective with respect to those efficacy variables.

Regibloc is therefore at least as effective as Macaine in achieving adequate anaesthesia for intra-ocular eye surgery.

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