Clinical Reports

Epidural anaesthesia with mixtures of bupivicaine and lidocaine

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In a randomized double-blind trial in 30 patients receiving lumbar epidural anaesthesia, the onset and duration of sensory blockade with 0.375 per cent bupivicaine was compared with a mixture of 0.375 per cent bupivicaine and one per cent lidocaine hydrochloride and a mixture of 0.375 per cent bupivicaine and one per cent carbonated lidocaine. Onset (9.3 ± 1.16 minutes) and complete spread (23.3 ± 4.8 minutes) for bupivicaine was significantly slower than in the mixtures containing carbonated lidocaine (onset 4.7 ± 0.48 minutes, complete spread 14.8 ± 2.49 minutes) and lidocaine hydrochloride (onset 5.0 ± 0.67 minutes, complete spread 16.3 ± 3.2 minutes). There was no significant difference in times of onset and complete spread between the two mixtures. The duration of sensory blockade for bupivicaine alone (165 ± 20 minutes) was not significantly different from the duration in either the mixture containing carbonated lidocaine (161 ± 51.24 minutes) or lidocaine hydrochloride (143 ± 33.7 minutes).

The results indicate a clinical advantage in speed of onset without significant shortening of duration of action for mixtures of carbonated lidocaine or lidocaine hydrochloride with bupivicaine as compared to bupivicaine alone.

Key words
ANAESTHETIC TECHNIQUES, REGIONAL: epidural; ANAESTHETICS LOCAL: lidocaine, carbonated lidocaine, bupivicaine, compounding.

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In clinical practice an ideal local anaesthetic might combine the properties of rapid onset with long duration of action.[1] No single agent suitable for routine clinical use combining these properties is available.[2,3] As a result there is considerable interest in compounding of local anaesthetics in order to obtain the benefit of the rapid action of one agent combined with the long duration of the other agent.

Clinical studies of such mixtures have produced varied results. When used for brachial plexus blockade, both chloroprocaine[1] and carbonated lidocaine[4] have been shown to shorten the latency of onset of block of the long acting local anaesthetic bupivicaine, while retaining a moderately long duration of action. However, in the epidural space one study has shown that the latent periods of mixtures of bupivicaine and lidocaine hydrochloride was similar to that of bupivicaine alone.[3] In a previous study we demonstrated that mixtures of carbonated lidocaine and bupivicaine and of lidocaine hydrochloride and bupivicaine had a duration of action equal to bupivicaine alone, when used for intradermal analgesia.[5]

The present study was designed to compare the rates of onset of mixtures of carbonated lidocaine and bupivicaine and of lidocaine hydrochloride and bupivicaine with bupivicaine alone for epidural blockade, and to confirm that the duration of action of such mixtures was comparable to that of bupivicaine in clinical situations.

Methods

A double-blind study was undertaken on 30 ASA physical status I patients presenting for routine

TABLE I Patient characteristics

	Age (yrs)	*Height (cm)*	*Weight (kg)*	*Sex*	
				Male	*Female*
B	43 ± 18.12	165.5 ± 7.43	68.3 ± 7.24	6	4
B + CO_2	40 ± 16.7	172.25 ± 4.63	72.5 ± 5.1	5	5
B + HCL	44.8 ± 18.3	169.5 ± 7.62	72.9 ± 6.12	6	4

Mean ± standard deviation.
B = 0.375% bupivicaine.
B + CO_2 = 0.375% bupivicaine and 1 per cent carbonated lidocaine.
B + HCL = 0.375% bupivicaine and 1 per cent plain lidocaine hydrochloride.

TABLE II Onset and duration of epidural block

	Initial Onset	*Time to reach maximal extent*	*Duration of Block*
B	9.3 ± 1.16*	23.2 ± 4.76*	165 ± 20
B + CO_2	4.7 ± 0.48	14.8 ± 2.49	161 ± 51.24
B + HCL	5 ± 0.67	16.3 ± 3.2	143 ± 33.68

Times in minutes. Mean ± standard deviation.
B = 0.375% bupivicaine.
B + CO_2 = 0.375% bupivicaine and 1 per cent carbonated lidocaine.
B + HCL = 0.375% bupivicaine and 1 per cent plain lidocaine hydrochloride.
*Significant difference between groups ($p < 0.01$).

lower abdominal or perineal operations. Informed consent was obtained from each patient, and the procedure was approved by the hospital ethics committee.

The patients were randomly allocated to three groups of ten patients each, and each group received a different local anaesthetic solution. The first solution was 0.375 per cent bupivicaine, obtained by diluting 0.75 per cent bupivicaine with an equal volume of normal saline. The second solution was a mixture of equal volumes of 0.75 per cent bupivicaine and two per cent lidocaine hydrochloride to give a final equivalent of 0.375 per cent bupivicaine and one per cent lidocaine. The third solution was a mixture of equal volumes of 0.75 per cent bupivicaine and carbonated lidocaine to give a final equivalent of 0.375 per cent bupivicaine and one per cent carbonated lidocaine.

Each patient received diazepam 10 mg orally two hours before the operation. One litre of a balanced electrolyte solution was given intravenously before epidural blockade. The epidural injection was carried out with the patient sitting, and the epidural space was identified by loss of resistance to air. Fifteen ml of the local anaesthetic solution was administered over 20 seconds via a 17 S.W.G. Tuohy needle, with the bevel of the needle facing caudally. Following injection, the patient was immediately placed in the supine position, and a separate assessor, who was unaware which drug combination had been injected, started clinical observations. All patients were assessed by the same observer. The following information was recorded:

(a) The upper level of sensory analgesia was determined bilaterally by the loss of sensation of sharpness to a pinprick every two minutes for the first 30 minutes and subsequently every 15 minutes until complete regression of the sensory block.

(b) The degree of motor blockade was assessed using a score described by Bromage.[6] This was measured every five minutes for the first 30 minutes, and subsequently at 15-minutes intervals.

(c) Pulse and blood pressure were recorded every five minutes for the duration of the operation, and subsequently at fifteen-minute intervals in the recovery room.

Statistical analysis was by Student's t test.

Results

There were no significant differences in the mean height, age, weight or sex distribution between the groups (Table I).

Table II shows the mean time for first appearance of analgesia (initial onset), time to reach the highest level of analgesia (maximal extent) and duration of sensory block (defined as time from reaching level of maximal extent to regression of four sensory segments).[7] The mean initial onset time for 0.375

per cent bupivicaine was 9.3 minutes, which was significantly longer ($p < 0.01$) than the initial onset time for the mixtures containing plain lidocaine (five minutes) or carbonated lidocaine (4.7 minutes). The mean time to reach maximal extent for 0.375 per cent bupivicaine was 23.2 minutes, which was significantly longer ($p < 0.01$) than for the groups which received mixtures containing lidocaine hydrochloride (16.3 minutes) or carbonated lidocaine (14.8 minutes). There were no statistical differences between the times of onset of the two mixtures.

The mean duration of sensory blockade was 165 minutes for the group receiving 0.375 per cent bupivicaine, with the mixture of bupivicaine and lidocaine hydrochloride 143 minutes and with the mixture of bupivicaine and carbonated lidocaine 161 minutes. These differences are not statistically significant. Using a scaled score of 0–2,[7] the mean score for motor blockade for the bupivicaine group was 0.4. This was significantly less ($p < 0.05$) than the mean score of 0.8 for the group which had received lidocaine hydrochloride and bupivicaine and the mean score of 1.1 for the group which had received carbonated lidocaine and bupivicaine. There was no significant difference between these two latter groups.

Two patients in the bupivicaine only group had insufficient depth of analgesia with resulting discomfort to the patient. Both were undergoing inguinal herniorrhaphy and local injection with two per cent lidocaine hydrochloride was needed for satisfactory completion of the operation. They are, however, included in the statistics, measurements being confined to the side which was not operated on.

There were no significant alterations in either blood pressure or pulse rate in any of the patients throughout the procedure.

Discussion

There has been considerable interest in mixing short and long lasting local anaesthetics in order to achieve rapid onset and long duration of analgesia.

Epidural administration of mixtures of local anaesthetics has been shown to be safe in man.[8] Pharmacokinetic studies of mixtures of bupivicaine and lidocaine hydrochloride have demonstrated blood concentrations below the toxic range and in fact blood concentrations are in the same range as if the components had been injected singly.[3]

This approach to shortening the latent period of bupivicaine assumes that there is no interaction between the two agents injected, and that both behave as if the other agent were not present. However, mixtures of chloroprocaine and bupivicaine have been demonstrated to have a duration of action only slightly longer than chloroprocaine alone and significantly shorter than bupivicaine alone.[9] This might be due to various factors, including differences between pH and pKa of the two agents,[10] and perhaps due to competitive binding to nonspecific receptor sites in the infiltrated tissues.[11] The pH and pKa of bupivicaine and lidocaine are similar[10] and therefore are less likely to interfere with each other's action.

This study has confirmed our previous findings[5] that the duration of action of bupivicaine is not impaired by the compounding with either lidocaine hydrochloride or carbonated lidocaine.

It has been suggested that when mixtures of carbonated lidocaine and bupivicaine are used for brachial plexus blockade, the latent period approaches that of the carbonated lidocaine alone, and that the duration of action of the mixture is not different from bupivicaine alone.[4] This trial was neither randomized nor double-blind, and no comments on the statistical significance of these findings were made. Other authors[12] have demonstrated similar findings when mixtures of bupivicaine and lidocaine hydrochloride were used for epidural blockade, and concluded that such mixtures produced less motor block than bupivicaine alone; this finding can probably be explained by the fact that the concentration of the bupivicaine in the mixture was 0.375 per cent but the control concentration of bupivicaine was 0.5 per cent. More recently, the results of a comprehensive study of mixtures of lidocaine hydrochloride and bupivicaine hydrochloride using a single dose epidural technique have been reported by Seow *et al.*[3] The results of this study are similar to the present study, though a number of differences are present. Seow *et al.* reported that for mixtures of lidocaine hydrochloride and bupivicaine the duration of action correlated closely with the fractional dose of bupivicaine in the solution, but that the latency of onset was similar to that of bupivicaine alone. These

authors were also unable to demonstrate any difference in onset time between lidocaine hydrochloride alone and bupivicaine alone. A possible explanation of these differences may lie in different concentrations of local anaesthetic solutions used and also in the addition of epinephrine to the solutions used.

Carbonated lidocaine has been shown to have a considerably faster onset of action than lidocaine hydrochloride for brachial plexus blockade.[4,13] In comparison, when used for epidural blockade no difference has been demonstrated in comparative speed of onset of the block.[7,14] We have also been unable to demonstrate any statistically significant difference in speed of onset between mixtures containing carbonated lidocaine and lidocaine hydrochloride. Some authors[7] have demonstrated significantly enhanced motor blockade when carbonated lidocaine is used, but this is not generally agreed.[14] Our results have not shown any statistically significant difference between the intensity of motor blockade when mixtures containing carbonated lidocaine are compared to those containing lidocaine hydrochloride. However, both mixtures produced significantly greater motor blockade than bupivicaine alone. This finding is not surprising in view of the control concentration of bupivicaine (0.375 per cent).

This study has demonstrated a clinical advantage in terms of speed of onset without significant shortening of duration of action, when bupivicaine is mixed with either carbonated lidocaine or lidocaine hydrochloride for epidural blockade.

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Résumé

On a fait une étude randomisée, à double inconnue sur le début et la durée du bloc sensoriel chez 30 patients ayant reçu l'anesthésie épidurale lombaire. On administra 0.375 pour cent de bupivicaine qu'on compara avec un mélange de 0.375 pour cent de bupivicaine et un pour cent de lidocaine chlorhydrate et avec un autre mélange de 0.375 pour cent du bupivicaine et un pour cent de lidocaine hydrocarbonate. Le début (9.3 ± 1.16 minutes) et la diffusion complète (23.3 ± 4.8 minutes) avec la

bupivicaine étaient significativement plus lents que ceux obtenus avec des mélanges contenant de la lidocaine hydrocarbonate (début 4.7 ± 0.48 minutes, diffusion complète 14.8 ± 2.49 minutes) et de la lidocaine chlorhydrate (début 5.0 ± 0.67 minutes, diffusion complète 16.3 ± 3.2 minutes). On n'observa pas de différence significative au début de la diffusion, ni pendant la diffusion complète entre les deux mélanges. La durée du bloc sensoriel avec la bupivicaine seule (165 ± 20 minutes) n'était pas significativement différente de la durée observée avec chaque mélange contenant de la lidocaine hydrocarbonate (161 ± 51.24 minutes) ou de la lidocaine chlorhydrate (143 ± 33.7 minutes). Ces résultats ont un avantage clinique dû à la rapidité du début du bloc sans diminution significative de la durée de son action, soit avec les mélanges de lidocaine hydrocarbonate ou de lidocaine chlorhydrate avec bupivicaine, par opposition à la bupivicaine seule.