PHARMACY PRACTICE

Is Lidocaine Hydrocarbonate More Effective Than Lidocaine Hydrochloride in Epidural Anaesthesia for Caesarean Section?

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Caesarean section is commonly performed under regional anaesthesia because it enables the mother to be conscious of the birth of her baby and it avoids the risks of failed tracheal intubation and inhalation of gastric contents. The onset, duration, and quality of sensory blockade are determined by the intrinsic properties and dose of the local anaesthetic and the addition of epinephrine or narcotics.

To achieve solubility, local anaesthetics are prepared as salts in an acidic solution, in which most of the drug is ionized. After injection, tissue buffering increases the pH and a percentage of the drug associates into an nonionized form, which penetrates the axon membrane to reach the interior of the axon. Once inside, the cellular acidity causes the drug to reionize. It is this form which blocks the sodium channels, preventing the entry of sodium into the cell and the propagation of the action potential.

Alkalinization increases the proportion of nonionized drug and enhances its diffusion across the axon membrane. Carbonation increases the proportion of the ionized form in the axon by lowering the intracellular pH.[1] *In vitro* studies on isolated nerve preparations have shown that potency is increased by either alkalinization or addition of carbon dioxide to a lidocaine solution.[2] However, clinical trials designed to define and compare the characteristics of local anaesthetics have given inconclusive and sometimes conflicting results.

Lidocaine hydrocarbonate (CO2) has been used extensively because of superior effectiveness over the hydrochloride (HCl) salt, as demonstrated in nonrandomized, nonblinded studies conducted by Bromage.[3] Subsequent randomized and blinded trials in patients undergoing various surgeries, have not shown significant differences in the onset of maximum analgesia between lidocaine HCl and lidocaine CO2. One study did report improved motor blockade with lidocaine CO2[4] and improved quality of sensory blockade was reported in another.[5] Moreover, Bromage was able to confirm his results in a later randomized, blinded trial.[6]

Comparative trials of lidocaine HCl, lidocaine CO2 and alkalinized lidocaine solutions in caesarean section are equally contradictory. A critical analysis of this literature was undertaken to determine the role of lidocaine CO2 in caesarean section.

Lidocaine CO2 versus Lidocaine HCl in Caesarean Section

Two randomized-controlled, double-blind studies have compared lidocaine CO2 with lidocaine HCl in elective caesarean section. In a study by Hemmings et al,[7] forty patients received an initial bolus dose of 12mL lidocaine CO2 or lidocaine HCl with epinephrine, followed by an 8 mL dose five minutes later. Sensory loss to pin prick was determined every three minutes until sensory block to the sixth thoracic segment of the spinal chord was obtained. Spread of block was significantly faster with lidocaine CO2. Sensory block from the fifth lumbar to the first sacral dermatone took an average of 8.8 minutes for lidocaine CO2 versus 12 minutes for lidocaine HCl. Spread from the second to the fourth sacral dermatone averaged 10 minutes for lidocaine CO2 versus 12.5 minutes for lidocaine HCl. There was no difference in latency of block to the sixth thoracic dermatone.

These results were not confirmed in a study by Cole,[8] where 20 patients received either lidocaine CO2 or HCl without epinephrine, as a 2 mL test dose, followed by 6 mL every three minutes to a maximum of 20 mL. Both groups were reported to be similar for maternal age, weight, and parity. The onset and spread of sensory block was evaluated by analgesia to pin prick and ice every two minutes until anaesthesia was extended to the second, third and fourth sacral, and fourth thoracic segments, and the furthest dermatone. Motor block was assessed using the Bromage scale.[3] No statistically

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significant difference in any index was reported between the groups. However, the use of incremental doses, as opposed to the single bolus doses used by Hemmings et al,[7] may have masked differences in onset of block between the two lidocaine solutions.

Lidocaine HCl versus Alkalinized Lidocaine in Caesarean Section

Comparisons between alkalinized and plain lidocaine solutions have consistently shown a faster onset with alkalinized lidocaine. In one study,[9] 148 patients undergoing epidural anaesthesia for various surgeries, including caesarean section, were randomly assigned to five groups. Sodium bicarbonate or saline (which served as a control) was added to lidocaine solutions with epinephrine and the anaesthetic given in 5 mL increments every 20-30 seconds. The time of onset of sensory blockade to the second lumbar dermatone and the level of analgesia were assessed at 5,10,15 and 30 minutes by loss of scratch sensation. The time of onset of sensory analgesia decreased as the pH of the lidocaine solution increased. Greater spread of analgesia at 5,10 and 15 minutes was documented with the pH-adjusted solution, but at 30 minutes the sensory level was not significantly different among the groups.

A recent study conducted by Capogna et al[10] randomized 116 women undergoing elective caesarean section to receive lidocaine buffered with sodium bicarbonate or with saline as a control. The addition of bicarbonate resulted in an increase of pH from 6.6 to 7.1. After a 3 mL test dose, patients received fentanyl, then incremental doses of 5 mL of lidocaine every two to three minutes. Patient age, weight, height, and gestational age did not differ among the groups. Onset of sensory analgesia to the first sacral segment was significantly shorter in the bicarbonate group (15 minutes) than in the plain lidocaine group (19 minutes). No differences in motor block as assessed by the Bromage scale were noted. Fewer patients experienced pain in the alkalinized group, but serum fentanyl levels were higher in this group.

All Three Lidocaine Solutions Compared in Caesarean Section

A comparison of all three types of lidocaine was conducted by Liepert et al.[11] In his study, 60 patients presenting for elective caesarean section received lidocaine HCl or lidocaine CO2 or pH-adjusted lidocaine (sodium bicarbonate added for pH >7) in 3 mL incremental doses injected every one to two minutes. Sensory loss to temperature and pin prick was assessed every 30 seconds. The time to onset of sensory block to the first lumbar and the second sacral segments from the time of injection was determined. Motor block was not assessed. The groups were similar in height, weight, parity, volume of lidocaine, and supplemental fentanyl. There was no statistical difference in onset of sensory block or maximum spread and in duration of block among any of the groups. However, as no normal saline control was added to the non-alkalinized lidocaine solutions, it is possible that the lack of a faster onset time with alkalinized lidocaine may have been due to its lower concentration.

In conclusion, it is important to note that the practice of epidural anaesthesia depends on the skill and experience of the individual anaesthetist. Therefore, many confounding biases existed in the administration and assessment of anaesthesia. In addition to the method of injection (bolus versus incremental), other factors included: the lumbar interspace selected, variations in the frequency and extent of evaluation of block, and the use of nonstandard scales for the assessment of quality of analgesia.

Our review of the literature suggests that lidocaine CO2 is no more effective than lidocaine HCl. A more important question, however, is the clinical relevence of a statistically significant faster onset of sensory block of one to three minutes in elective caesarean section. It is therefore concluded, that the use of the CO2 formulation in elective caesarean secion is not warranted and, as its cost is four-fold higher than lidocaine HCl, is wasteful. In emergency situations, where time of onset is critical, lidocaine CO2 may be appropriate. The addition of bicarbonate to lidocaine HCl solutions may be a useful therapeutic alternative.

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