

[2003 Fall A34] Alkalinization and precipitation characteristics of levobupivacaine

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Introduction: pH adjustment of local anesthetics has been used to reduce the latency of conduction nerve blocks (1), reduce pain on injection as well as prolong (2) and possibly intensify them (3). However, alkalinization of local anesthetic solutions may cause precipitation, thereby decreasing bioavailability and anesthetic activity. Alkalinization of levobupivacaine has not been described. This laboratory study assessed the alkalinization and precipitation characteristics of levobupivacaine.

Methods: Aliquots (5ml) of commercially available levobupivacaine (Chirocaine, 0.25, 0.5 and 0.75%; Purdue Pharma L.P. Stamford, CT) were alkalinized with increasing amounts (0.01, 0.02, 0.05 ml) of sodium bicarbonate (8.4%) and immediately monitored for pH change and onset of visible precipitation at 4°C, room temperature and at 37°C. We then alkalinized levobupivacaine with sodium bicarbonate and measured the amount of precipitate that accumulated after various incubation times at room temperature.

Results: The pH of levobupivacaine increases with addition of small amounts of bicarbonate. The calculated percentage of nonionized levobupivacaine increased from 0.2% to only slightly greater than 6% with alkalinization from pH of 5.32 to 7.11 (table). Drug loss to precipitation increased with higher doses of bicarbonate, reaching 30-35% of the total levobupivacaine. Even with a low dose of bicarbonate (0.05 ml bicarbonate/20 ml of levobupivacaine), precipitation increased with time of incubation reaching a maximum at 15 minutes. Addition of sodium bicarbonate to levobupivacaine at room and body temperature resulted in reduced time to precipitate and increased amount of precipitate compared to levobupivacaine at 4°C.

Conclusion: In our experiment, low doses of bicarbonate produced only moderate increase in the proportion of nonionized levobupivacaine with immediate and marked precipitation. There is high likelihood of substantial drug precipitation even if the mixture was administered within 5-10 minutes after alkalinization. This is first report to reveal significant precipitation of levobupivacaine with addition of minimal volume of sodium bicarbonate and hence alkalinization of levobupivacaine cannot be recommended for clinical use or laboratory studies.

References:

1. Canadian Anaesthetists' Society Journal 1986;33:537-41.
2. Regional Anesthesia & Pain Medicine 2001;26:357-62.
3. Regional Anesthesia 1983;8A:35-6.

Table

Levobupivacaine	pH/precipitation characteristics before and after addition of Sodium Bicarbonate			
	0.00 ml	0.01 ml	0.02 ml	0.05 ml
0.25%	5.32 ± 0.05/NA	6.65 ± 0.04/+	6.86 ± 0.09/++	7.11±0.07/++
0.5%	5.37 ± 0.07/NA	6.51 ± 0.11/+	6.53± 0.08/++	6.55±0.10/++
0.75%	5.35 ± 0.09/NA	6.41 ± 0.07/++	6.46± 0.06/++	6.51±0.08/++

Table Legend.

NA not applicable, no precipitation before addition of Sodium Bicarbonate

+ precipitate visible immediately on mixing

++ precipitate visible immediately on addition of Sodium Bicarbonate

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