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The air-liquid interface and the pH and PCO₂ of alkalized local anaesthetic solutions

The alkalization of certain local anaesthetics with sodium bicarbonate hastens the onset of epidural analgesia. Increases in both the pH and PCO₂ of the local anaesthetic are necessary to hasten onset. However, carbon dioxide can diffuse from local anaesthetic solutions following alkalization with sodium bicarbonate and change both the pH and PCO₂ of the mixture. This study examined changes in pH and PCO₂ of three local anaesthetics reported to have a faster onset of analgesia following mixture with sodium bicarbonate and examined the effects of time and the local anaesthetic container air/liquid interface on the pH and PCO₂ of the buffered local anaesthetic solutions. Bupivacaine 0.5%, lidocaine 2%, and chloroprocaine 2% were each buffered with sodium bicarbonate. The pH and PCO₂ of each solution were measured at time 0 and at 5, 10, 15, 20, 30, 40, 50 and 60 min intervals. The solutions were placed in containers as follows: 30 ml in 40 ml containers, 10 ml in 40 ml containers, 10 ml in 13 ml containers, and 10 ml in polypropylene syringes. The pH and PCO₂ increased following alkalization but gradually decreased in all containers except in polypropylene syringes.

L'alcalinisation de certains anesthésiques locaux avec bicarbonate de soude accélère le début de l'analgésie épidurale. L'augmentation du pH et de la PCO₂ de l'anesthésique local est nécessaire pour produire cet effet. Cependant, le gaz carbonique peut diffuser hors des solutions d'anesthésique local après l'alcalinisation au bicarbonate de soude et changer ainsi le pH

Key words

ANAESTHETICS, LOCAL: bupivacaine, lidocaine, chloroprocaine.

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et la PCO₂ du mélange. Cette étude étudie les changements de pH et de PCO₂ de trois anesthésiques locaux réputés pour induire un début plus rapide de l'analgésie, une fois mélangés avec du bicarbonate de soude. Les effets du temps et de l'interface air-liquide du contenant sur le pH et la PCO₂ des solutions d'anesthésique local tamponnées ont été examinés. La bupivacaine 0,5%, la lidocaïne 2% et al chloroprocaine 2% ont été tamponnées à l'aide de bicarbonate de soude. Le pH et la PCO₂ de chaque solution ont été mesurés au temps 0 et à des intervalles de 5, 10, 15, 20, 30, 40, 50 et 60 minutes. Les solutions étaient placées dans des contenants comme suit : 30 ml dans des contenants de 40 ml, 10 ml dans des contenants de 40 ml, 10 ml dans des contenants de 13 ml et 10 ml dans des seringues en polypropylène. Le pH et la PCO₂ ont augmenté suite à l'alcalinisation mais ont graduellement diminué dans tous les cas, sauf lorsque les contenants étaient des seringues en polypropylène.

Bupivacaine, chloroprocaine and lidocaine are commonly used in the practice of obstetric anaesthesia. Alkalization of these local anaesthetic solutions with sodium bicarbonate (NaHCO₃) has been reported to hasten the onset of epidural analgesia.¹⁻³ It has been found that increases in both the pH and PCO₂ of the local anaesthetic mixture following buffering with NaHCO₃ are necessary to hasten onset.^{4,5}

When NaHCO₃ is mixed with local anaesthetics, carbon dioxide and water are produced but, carbon dioxide may escape from an alkalized local anaesthetic solution.⁵ The purpose of this study was to determine if the local anaesthetic container air/liquid interface affected the pH and PCO₂ of any of the alkalized local anaesthetic solutions which have been reported to be useful in the practice of obstetric anaesthesia.¹⁻³

Methods

Three different local anaesthetic solutions were studied. Bupivacaine 0.5%, lidocaine 2%, and chloroprocaine 2% were chosen because these were the local anaesthetics and concentrations previously reported to exhibit a hastened onset following alkalization with NaHCO₃ in parturients.¹⁻³

Five bottles of each local anaesthetic were studied and each specific local anaesthetic had the same lot number. Each local anaesthetic solution was alkalized with NaHCO_3 (8.4%) in a preliminary study at our institution to increase the pH to the maximum value that could be obtained without causing precipitation. A volume of unbuffered local anaesthetic equal to the volume of NaHCO_3 mixed with each solution was removed from each container of local anaesthetic prior to the introduction of NaHCO_3 and the pH and PCO_2 of each mixture were measured using an ABL 30 (Radiometer®, Copenhagen) blood gas analyzer. Subsequently each local anaesthetic was buffered with NaHCO_3 as follows:

- 1 0.5% bupivacaine (Sensorcaine®, Astra, Westborough, MA) buffered with sodium bicarbonate (8.4%) (0.03 ml sodium bicarbonate per 10 ml local anaesthetic) (0.09 ml bicarbonate per 30 ml local anaesthetic).
- 2 2.0% lidocaine (Xylocaine®, Astra, Westborough, MA) buffered with sodium bicarbonate (8.4%) (0.5 ml · 10 ml⁻¹) (1.5 ml · 30 ml⁻¹).
- 3 2.0% chloroprocaine (Nesacaine MPR®, Astra, Westborough, MA) buffered with sodium bicarbonate (8.4%) (1 ml · 10 ml⁻¹) (3 ml · 30 ml⁻¹).

Because 2% lidocaine (Xylocaine®) and 0.5% bupivacaine (Sensorcaine®) are commercially available from Astra in 13 ml containers and in 40 ml glass containers, the pH and PCO_2 measurements were measured with buffered local anaesthetics placed in 13 ml and 40 ml containers. Furthermore, 10 ml of each of the local anaesthetics were buffered with NaHCO_3 in 12 ml Monoject® (Sherwood Medical, St. Louis, MO) polypropylene syringes. All the local anaesthetics were buffered with NaHCO_3 in each of the containers studied. The study was done in the anaesthesia laboratory where the ambient temperature was kept constant (21°).

After mixing NaHCO_3 with each local anaesthetic solution, the resulting mixtures were left undisturbed in their respective commercial containers without their stoppers with the exception of the syringes. The solutions in the syringes were left with capped 1.5" #22 gauge needles. The pH and PCO_2 of the solutions were measured prior to, immediately after, and at 5, 10, 15, 20, 30, 40, 50, and 60 min after the alkalization. The mean temperatures of the study solutions were as follows: bupivacaine 21.2° C (± 0.1), chloroprocaine 21.0° C (± 0.1), lidocaine 21.2° C (± 0.2) and sodium bicarbonate (21.0° C (± 0.1)). The surface area of the 13 ml containers was 8.9 ± 0.04 cm² while that of the 40 ml container was 7.1 ± 0.06 cm² at the air-liquid interface. The values obtained for the mean pH and PCO_2 for each solution at each time interval were analyzed using one-way analysis of variance followed by the Scheffe' critical value test for multiple

TABLE I Characteristics of the local anaesthetic solutions (mean $\pm$ SD)

	Bupivacaine	Lidocaine	Chloroprocaine
Initial pH	5.86 $\pm$ 0.13	6.18 $\pm$ 0.10	4.23 $\pm$ 0.14
Final pH	6.75 $\pm$ 0.14	7.01 $\pm$ 0.05	7.56 $\pm$ 0.03
Initial PCO_2 (mmHg)	7.6 $\pm$ 0.6	6.5 $\pm$ 0.9	11.08 $\pm$ 1.37
Final PCO_2 (mmHg)	59.1 $\pm$ 8	183.0 $\pm$ 21.4	97.3 $\pm$ 6.3

TABLE II Stability of pH and PCO_2 of alkalized local anaesthetics over 60 min

<i>Local anaesthetic</i>	<i>Time of significant change of pH and/or PCO₂ (min)</i>	
<i>30 ml of local anaesthetic in 40 ml container</i>		
Bupivacaine	pH: no change	PCO ₂ : no change
Lidocaine	pH: 50 min	PCO ₂ : 60 min
Chloroprocaine	pH: 5 min	PCO ₂ : 50 min
<i>10 ml of local anaesthetic in 40 ml container</i>		
Bupivacaine	pH: 10 min	PCO ₂ : 10 min
Lidocaine	pH: 30 min	PCO ₂ : 30 min
Chloroprocaine	pH: 15 min	PCO ₂ : 20 min
<i>10 ml of local anaesthetic in 13 ml container</i>		
Bupivacaine	pH: no change	PCO ₂ : 30 min
Lidocaine	pH: 30 min	PCO ₂ : 40 min
Chloroprocaine	pH: no change	PCO ₂ : 20 min
<i>10 ml of local anaesthetic in syringe</i>		
Bupivacaine	pH: no change	PCO ₂ : no change
Lidocaine	pH: no change	PCO ₂ : no change
Chloroprocaine	pH: no change	PCO ₂ : no change

comparisons. A *P* value < 0.05 was considered necessary to reject the null hypothesis.

Results

The pH and PCO_2 of the local anaesthetics prior to pH adjustment with NaHCO_3 and at 60 min following alkalization are presented in Table I. The pH of each of the local anaesthetics with respect to volumes and sizes of their respective containers, as well as the time when a change occurred in pH and/or PCO_2 are presented in Table II. The containers with no air-liquid interface (polypropylene syringes) exhibited no changes in pH or PCO_2 over 60 min (Tables II, III).

The containers that were exposed to ambient air with the smaller surface areas (13 ml) with an equal volume of local anaesthetic (10 ml) as the 40 ml containers exhibited less change in pH and PCO_2 from their respective baseline alkalized measurements than 10 ml in 40 ml containers. The 40 ml containers which contained 30 ml of buffered local anaesthetic solution exhibited the least change in pH

TABLE III PCO₂ (mmHg) stability of alkalinized local anaesthetic solutions in various commercial containers following alkalinization with sodium bicarbonate

	Minutes								
	0	5	10	15	20	30	40	50	60
<i>Bupivacaine</i>									
10 ml · 40 ml ⁻¹	53.4(10.3)	49.0(7.2)	47.3(9.4)*	46.4(9.4)*	46.0(9.7)*	42.9(8.4)*	41.0(8.3)*	37.2(6.3)*	33.5(6.8)*
30 ml · 40 ml ⁻¹	56.6(2.2)	54.8(5.5)	56.3(2.3)	53.0(3.2)	53.2(3.8)	53.1(4.6)	54.3(2.8)	52.4(3.7)	51.7(5.8)
10 ml · 13 ml ⁻¹	59.3(7.2)	59.1(7.6)	58.4(7.6)	56.2(7.6)	57.3(7.6)	53.5(7.7)*	53.6(8.3)*	50.3(7.4)*	48.2(7.4)*
10 ml syringe	67.0(4.0) ^a	68.0(3.3) ^a	68.0(4.1) ^a	67.8(3.6) ^a	67.8(3.7) ^a	67.6(4.1) ^a	67.6(3.4) ^a	66.8(3.9)	68.2(3.9)
<i>Lidocaine</i>									
10 ml · 40 ml ⁻¹	150.8(8.0)	150.3(7.9)	148.5(8.3)	145.9(8.7)	142.8(7.8)	135.0(10.4)*	121.5(8.4)*	104.9(9.6)*	88.8(7.8)*
30 ml · 40 ml ⁻¹	190.0(11.4)	190.0(14.4)	188.2(15.2)	190.3(14.5)	184.9(10.9)	181.5(10.1)	175.9(9.8)	168.7(12.1)	165.1(14.7)*
10 ml · 13 ml ⁻¹	188.5(8.1)	184.6(10.8)	181.6(9.8)	183.2(7.1)	176.3(8.6)	168.9(8.2)	157.6(7.4)*	151.8(11.0)*	144.9(10.1)*
10 ml syringe	203.3(2.4) ^a	204.2(3.2) ^a	205.8(2.7) ^a	206.1(2.6) ^a	206.1(2.1) ^a	205.1(3.0) ^a	206.0(2.7) ^a	205.1(2.7) ^a	205.8(2.5) ^a
<i>Chloroprocaine</i>									
10 ml · 40 ml ⁻¹	92.7(4.2)	89.5(3.4)	87.5(3.4)	83.2(5.9)	81.2(5.2)*	75.5(3.5)*	64.4(5.4)*	59.0(2.6)*	53.0(1.3)*
30 ml · 40 ml ⁻¹	98.6(1.9)	95.8(2.5)	96.5(2.7)	96.1(2.5)	95.7(4.3)	93.8(2.5)	92.9(3.7)	92.2(3.9)	90.9(2.5)*
10 ml · 13 ml ⁻¹	92.9(3.8)	89.5(2.0)	88.1(1.7)	85.9(1.7)*	83.0(2.7)*	79.6(5.4)*	73.9(5.2)*	66.1(4.4)*	62.3(4.3)*
10 ml syringe	105.1(5.3)	104.3(4.2) ^a	104.6(3.6) ^a	105.1(3.6) ^a	104.9(3.7) ^a	104.3(4.1) ^a	104.5(2.9) ^a	104.9(3.3) ^a	105.5(3.2) ^a

Mean ± SD.

*P < 0.05 (within group analysis).^a*P* < 0.05 (between group analyses).

and/or PCO₂ with ambient air exposure when compared to the other open bottles.

Discussion

This study demonstrated that there were no changes in pH or PCO₂ following alkalinization with NaHCO₃ when exposure to ambient air was eliminated and the local anaesthetic was buffered in a polypropylene syringe. No changes were noted in pH or PCO₂ when the buffered local anaesthetic mixtures were placed in capped polypropylene syringes indicating that CO₂ did not diffuse from the syringe within 60 min. Because carbon dioxide can escape from alkalinized local anaesthetic solutions, Ikuta *et al.* have recommended that NaHCO₃ be mixed with local anaesthetic immediately before performing regional anaesthesia.⁵ The results of our study demonstrate that not only should one consider the interval from the time of alkalinization with NaHCO₃ but that also one should take into consideration the size of the air-liquid interface which subsequently can be affected by the volume of local anaesthetic relative to the local anaesthetic container volume.

In conclusion, the results of this investigation suggest that local anaesthetic buffered with NaHCO₃ be placed in a container that minimizes the air-liquid interface prior to administration.

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