EFFECTS OF CARBON DIOXIDE AND EPINEPHRINE ON SERUM LEVELS OF LIDOCAINE AFTER EPIDURAL ANAESTHESIA

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ABSTRACT

Carbonated lidocaine is believed to penetrate membranes more rapidly than its hydrochloride salt and could possibly cause higher serum levels. To compare serum levels, arterial blood samples drawn at intervals were analyzed in a group of 18 patients under epidural anaesthesia with equivalent doses of lidocaine hydrochloride and lidocaine hydrocarbonate, with and without epinephrine.

Results show that serum levels were significantly higher when lidocaine hydrocarbonate was used for epidural analgesia.

KEYWORDS: ANAESTHETIC TECHNIQUES, Epidural; ANAESTHETICS, LOCAL, Lidocaine, effects of carbon dioxide and epinephrine.

TOXIC REACTIONS to local anaesthetics usually occur when high levels of the agents are reached in the blood.[1] These reactions are mainly neurological and cardiovascular, and represent the most important complications encountered with the use of local anaesthetics.[2]

Lidocaine hydrocarbonate, in a concentration equivalent to lidocaine hydrochloride two per cent, is used in epidural anaesthesia because of its rapidity of onset, quality of sensory block and intensity of motor block.[3] The volume is generally the same as with lidocaine hydrochloride two per cent and the maximum dose suggested by the manufacturer in single dose epidural anaesthesia is 15 ml. If more than 15 ml are to be injected, it is suggested to add epinephrine to the solution.

In a vial, the P_{CO_2} of lidocaine hydrocarbonate is approximately 80 kPa (600 mmHg) and one can imagine that the carbon dioxide should influence the systemic absorption of lidocaine considering the greater penetrability of the lidocaine hydrocarbonate. The present study was undertaken to test that hypothesis.

METHOD

During the course of a larger study including one hundred patients scheduled for surgery under epidural anaesthesia, 18 patients were sampled at random for lidocaine blood levels.

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The study was approved by the ethics committee of the hospital and, in all cases, an informed consent was obtained. The patients were divided into four groups according to a random numbers table. Group I (five patients) received 15 ml of lidocaine hydrochloride two per cent; group II (four patients) received 15 ml of lidocaine hydrochloride two per cent with epinephrine 1:200,000 freshly added; group III (five patients) received 15 ml of lidocaine hydrocarbonate and group IV (four patients) received lidocaine hydrocarbonate 15 ml with epinephrine 1:200,000 freshly added.

An arterial canula was installed in the radial artery under local anaesthesia with procaine and followed by the lumbar epidural block. Arterial blood samples were drawn for measurement of lidocaine serum levels after its injection into the epidural space at 3, 5, 10, 15, 20, 30, 60 and 120 minutes.

Measurement of serum lidocaine levels were carried out with an enzymatic immunoassay technic.[4] The statistical method used for analysis of results is the fitting constants method for non balanced 2 by 2 factorial plan.

RESULTS

When serum levels were studied, no significant interaction between carbon dioxide and epinephrine was found (Table I). There was no antagonism or potentialization between carbon dioxide and epinephrine at any period of sampling; we could therefore evaluate the main effect of epinephrine on lidocaine blood levels in the presence and absence of carbon dioxide and the main effect

TABLE I

INTERACTION BETWEEN CARBON DIOXIDE AND EPINEPHRINE

Experimental Groups	G. I Lidocaine	G. II Lidocaine + EPI	G. III Lidocaine + CO_2	G. IV Lidocaine CO_2 + EPI	Analysis of Variance (interaction effect)	
Statistics	Mean (mg/l)				F	p
3 Min.	1.16	1.42	1.68	1.62	0.58	NS*
5 Min.	2.10	1.78	2.56	2.52	0.16	NS
10 Min.	2.48	2.20	2.98	2.20	0.85	NS
15 Min.	2.36	1.82	2.70	2.38	0.12	NS
20 Min.	2.44	1.80	2.78	2.15	0.001	NS
30 Min.	1.76	1.60	2.08	1.90	0.003	NS
60 Min.	1.36	1.25	1.28	1.45	0.97	NS
120 Min.	0.84	1.12	0.88	1.20	0.02	NS

*NS Not significant at a level of 0.25.

TABLE II

EFFECT OF EPINEPHRINE ON SERUM LEVELS OF LIDOCAINE AFTER EPIDURAL ANAESTHESIA

Experimental Groups	Lidocaine Levels Absence of Epinephrine (with and without CO_2) (N = 10)		Lidocaine Levels Presence of Epinephrine (with and without CO_2) (N = 8)		Analysis of Variance (epinephrine effect)	
Statistics	Mean (mg/l)	S.E.M.	Mean (mg/l)	S.E.M.	F	p
3 Min.	1.42	0.140	1.52	0.165	3.29	<0.10
5 Min.	2.33	0.245	2.15	0.274	2.60	NS
10 Min.	2.73	0.180	2.20	0.202	1.07	NS
15 Min.	2.53	0.201	2.10	0.225	2.09	NS
20 Min.	2.61	0.148	1.98	0.165	2.45	NS
30 Min.	1.92	0.115	1.75	0.129	3.28	<0.10
60 Min.	1.32	0.095	1.35	0.106	0.10	NS
120 Min.	0.86	0.075	1.16	0.084	0.25	NS

of carbon dioxide in the presence and absence of epinephrine.

Epinephrine lowered the serum levels at every period of sampling, except at the first (at 3 min) and at the last two (60 and 120 min) (Table II). At 30 minutes the difference was significant. Consequently, the "epinephrine" curve is flattened and widely spread compared to that of controls without epinephrine (Figure 1).

Carbon dioxide increased serum levels of lidocaine; they were higher at every period of sampling with a significant difference at 10, 20 and 120 minutes (Table III and Figure 2).

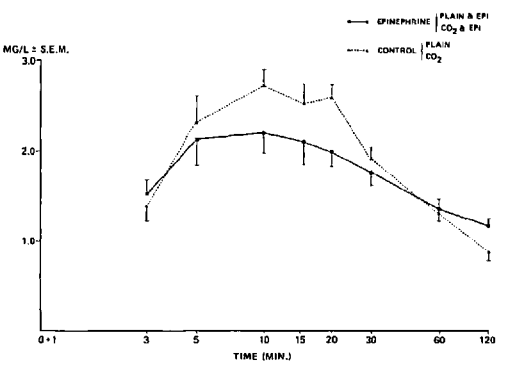

FIGURE 1 Effect of epinephrine on serum levels of lidocaine after epidural injection of lidocaine hydrocarbonate or lidocaine hydrochloride, 15 ml. (Semilogarithmic paper.)

DISCUSSION

Toxic levels of lidocaine are reached near 5 mg/l in venous blood and probably at more than

TABLE III

EFFECT OF CARBON DIOXIDE ON SERUM LEVELS OF LIDOCAINE AFTER EPIDURAL ANAESTHESIA

Experimental Groups	Lidocaine Levels Absence of CO_2 with and without Epinephrine (N = 9)		Lidocaine Levels Presence of CO_2 with and without Epinephrine (N = 9)		Analysis of Variance (CO_2 effect)	
Statistics	Mean (mg/l)	S.E.M.	Mean (mg/l)	S.E.M.	F CO_2	p
3 Min.	1.28	0.147	1.66	0.147	0.25	NS
5 Min.	1.96	0.258	2.54	0.258	0.24	NS
10 Min.	2.36	0.190	2.63	0.190	3.84	<0.10
15 Min.	2.12	0.212	2.56	0.212	2.03	NS
20 Min.	2.16	0.156	2.50	0.156	8.23	<0.02
30 Min.	1.69	0.122	2.00	0.122	0.96	NS
60 Min.	1.31	0.100	1.36	0.100	0.04	NS
120 Min.	0.97	0.079	1.02	0.079	7.23	<0.02

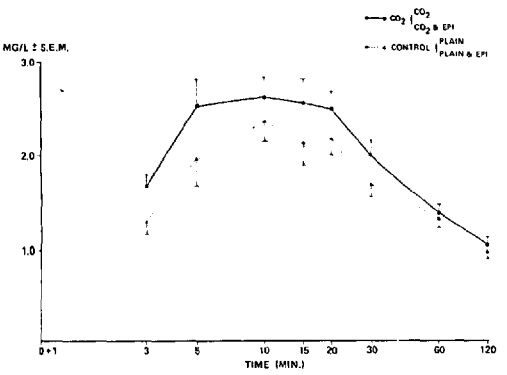

FIGURE 2 Effect of carbon dioxide on serum levels of lidocaine after epidural injection of lidocaine hydrocarbonate or lidocaine hydrochloride, 15 ml with or without epinephrine. (Semi-logarithmic paper.)

6 mg/l[5] in arterial blood, while therapeutic levels for treatment of cardiac arrythmias are in the range of 1 to 2 mg/l. The highest serum concentration of lidocaine extrapolated to the population, in accordance with the confidence interval calculated from our data, would be less than 4 mg/l 99.9 per cent of the time. So lidocaine used under the conditions described in this study is unlikely to produce toxic concentrations in the blood.

Nevertheless, the present study leads us to the following points: first, we did not find interaction (potentiation or antagonism) between carbon dioxide and epinephrine with regard to serum levels of lidocaine in patients who had received 15 ml of lidocaine hydrocarbonate or hydrochloride in equivalent concentrations, with or without epinephrine, in epidural anaesthesia. Carbon dioxide and epinephrine maintain their own effects, which are additive. Secondly, epinephrine abolishes the serum peaks of lidocaine and promotes more constant levels. Finally, the hypothesis of greater absorption of lidocaine hydrocarbonate is retained.

Consequently, it can be concluded that despite the fact that carbon dioxide in lidocaine solutions facilitates diffusion and absorption of the agent, serum levels are in the non-toxic range when 15 ml of solution are used for epidural anaesthesia. If higher dosages of lidocaine hydrocarbonate are to be injected in the epidural space or in more vascular regions, the addition of epinephrine to the solution would appear mandatory.

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RÉSUMÉ

Dix-huit patients soumis à une chirurgie sous anesthésie épidurale ont été étudiés dans le but de vérifier l'hypothèse d'une plus grande diffusion de la lidocaïne carbonatée avec production de taux sériques plus élevés. Des dosages artériels ont été faits à périodes fixes après l'injection épidurale de 15 ml d'hydrochlorure de lidocaïne 2% ou de lidocaïne carbonatée avec ou sans épinéphrine. L'étude a confirmé l'hypothèse d'une plus grande diffusion de la lidocaïne carbonatée avec des taux sériques plus élevés.