Title : BUPIVACAINE PHARMACOKINETICS DURING AXILLARY BRACHIAL PLEXUS BLOCK IN RENAL FAILURE

Authors : M. Chauvin, M.D., J.X. Mazoit, M.D., F. Andrivon, M.D., O. Goeau, M.D., P. Duvaldestin, M.D.

Affiliation : Département d'Anesthésie-Réanimation, Hôpital Ambroise-Paré, 92100 BOULOGNE, FRANCE
et Département d'Anesthésie-Réanimation, Hôpital Bicêtre, 94270 LE KREMLIN BICETRE, FRANCE

Introduction. Cardiac arrhythmias due to bupivacaïne (B) have been reported in patients suffering from chronic renal failure (RF) (1,2). Although B is almost completely metabolized in the liver (3), RF may alter B kinetics. Decreased drug protein binding is a frequent finding in patients with RF (4). An increase in free fraction (FF) may modify the distribution and the elimination of drugs which are extensively bound to plasma proteins and also increase the systemic effects. Bupivacaïne which is a weak base is 96 % bound to plasma proteins and especially to alpha 1-acid glycoprotein (alpha 1-AGP) (5) and it is questionable how RF may affect the protein binding of B and its pharmacokinetics. The purpose of this study was to determine the pharmacokinetics and the plasma protein binding of B after axillary brachial plexus block in patients with RF.

Methods. After obtaining informed consent and institutional approval, 11 patients with RF aged 59 ± 15 yrs (mean ± SD) and weighing 66 ± 10 kg and 6 normal patients (NL) aged 40 ± 13 yrs and weighing 69 ± 9 kg were studied. RF patients had a creatinine clearance of below 10 ml/min and normal hepatic function. All patients had normal serum K^+ levels and near normal CO_2 content. Serum albumin (SA), alpha 1-AGP and hematocrit (Ht) values are reported in table I. RF patients were scheduled for creation of arteriovenous fistulas and NL patients for minor orthopaedic surgery of the arm. Patients were premedicated with oral lorazepam 2.5 mg, 2 h before anesthesia. Axillary brachial plexus block was performed using 2.8 mg/kg of B 0.5 percent with adrenaline 1:200 000. Peripheral venous blood samples were collected from the arm opposite the site of injection just before, and 2, 5, 10, 15, 30 min and 1, 2, 3, 4, 6, 8, 10, 12 hours following the block. Serum B concentration was measured using gas chromatography with a nitrogen specific detector. The area under the serum concentration-time curve from injection to 10 hours (AUC 0-10) was calculated using the trapezoidal rule. Peak serum concentration (C_{max}) and the time to reach the peak (T_{max}) were calculated on individual observed data. The free concentration (free) of B was also measured by ultrafiltration using the sample collected at 30 min (5). The free fraction (FF) was calculated by dividing the free concentration by the total concentration. All data are reported as mean ± SD. The Mann and Whitney U-test was used to compare the values between the two groups.

Results. The biochemical data are presented in table I. SA was not significantly different between the two groups. C_{max} was significantly ($P < 0.05$) lower in patients with RF (table II). The free B and the FF were similar in the two groups.

Table I. Major biochemical data+

	HT (%)	SA ($g.dl^{-1}$)	alpha 1-AGP ($mg.dl^{-1}$)
NL	39 ± 3	4.3 ± 0.3	89 ± 30
RF	29 ± 5*	4.4 ± 0.8	101 ± 47

* $P < 0.05$ +mean ± SD

Table II. Pharmacokinetic parameters+

	NL	RF
C_{max} ($\mu g.ml^{-1}$)	1.78 ± 0.52	1.12 ± 0.59
T_{max} (min)	43 ± 15	44 ± 17
AUC 0-10 ($\mu g.ml^{-1}.min^{-1}$)	498 ± 233	412 ± 212
free ($\mu g/ml$)	0.12 ± 0.04	0.9 ± 0.05
FF (%)	6.8 ± 0.8	8.2 + 3.0

* $P < 0.05$ +mean ± SD

Discussion. This study indicates that the mean plasma level of B remains much below the toxic level in both groups. The C_{max} was much lower in RF patients which can be explained either by a larger volume of distribution or by a slower rate of absorbtion from the site of injection of B in patients with RF. The unbound fraction of B was not increased in patients with RF. This result is not surprising since B is mainly bound at low concentration to alpha 1-AGP (5) which was found unchanged in RF. Therefore an increased toxicity of B explained by altered pharmacokinetics or increased free fraction appears unlikely in patients with RF after axillary block.

References.

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