TITLE: INFLUENCE OF DIFFERENT LIPOSOMAL FORMULATIONS ON PHARMACOKINETICS OF ENCAPSULATED BUPIVACAIN.

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Bupivacain (BP) was encapsulated into multilamellar (MLV) and small unilamellar (SUV) liposomes in order to obtain a low prolonged plasma level after epidural administration to rabbits.

60 Mg liposomes, MLV or SUV, made of egg phosphatidylcholine and cholesterol in a molar ration 4:3, both containing 3.6 mg BP and 8 µCi ^{3}H-BP were injected epidurally at the sacral level with or without adrenalin. 3.6 Mg free drug and 8 µCi ^{3}H-BP were administered to an other series of animals. Plasma arterial levels of anesthetic were determined during 3 days by counting radioactivity. Alternatively, ^{99m}Tc-labeled liposomes or free $^{99m}TcO_4$ were injected epidurally and followed by scintigraphy.

The Table indicates that plasma level of free BP peaked 15 to 20 minutes after injection with or without adrenalin. Encapsulation of BP into SUV led to a lower and constant plasma level during 3 hours; this level dropped after 1 day. Addition of adrenalin did not modify the pharmacokinetics of BP encapsulated into SUV. When MLV-BP were injected without adrenalin, the plasma level was low and constant during 3 days. The lowest plasma concentration was observed during the 3 hours following injection of MLV and adrenalin, but after 1 day, it was raised to the same concentration as when no adrenalin was added and was constant during the next 2 days. Scintigraphic studies demonstrated that ^{99m}Tc-MLV remained as a spot at the epidural injection site for 2 days without diffusion into the blood and liver labelling. Oppositely, ^{99m}TC-SUV were captured by the liver 4 hours after epidural injection and diffused into the epidural space. When free ^{99m}TcO4 was given epidurally, it immediately diffused into the whole body without specific labelling of any organ.

These results raise the hope of reducing bupivacain systemic toxicity and of prolonging the duration of local action through a slow release from the epidural MLV liposomal depot.

	15 Min	1h	3h	1day	3days
Free BP	1.10±0.07	1.04±0.03	0.80±0.01		
FreeBP +Adr.	0.66±0.01	0.56±0.01	0.42±0.01		
MLV	0.00±0.01	0.30±0.03	0.28±0.03	0.24±0.09	0.30±0.08
MLV+ Adr.	0.04±0.02	0.06±0.02	0.08±0.01	0.31±0.02	0.22±0.03
SUV	0.3±0.1	0.4±0.2	0.37±0.06	0.11±0.08	0.11±0.07
SUV+ Adr.	0.3±0.1	0.4±0.2	0.39±0.09	0.2±0.1	0.10±0.05

Plasma levels of bupivacain at different times after epidural injection. (Mean ±S.D.)

TITLE : **INFLUENCE OF DURATION OF THE LATERAL POSITION DURING SPINAL ANESTHESIA ON DISTRIBUTION OF HYPERBARIC TETRACAINE**

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INTRODUCTION : It is admitted that the distribution of hyperbaric local anesthetics during spinal anesthesia (SA) is influenced by the patients' position[1]. Theoritically, an unilateral anesthesia can be obtained on the dependent side, if the patient is left long enough in lateral decubitus position (LDP). However, there is no report on the optimal duration of LDP necessary to obtain unilateral anesthesia, which could be clinically advantageous, since with the same dosage of local anesthetic, it could provide more profound and longer anesthesia with less sympathetic blockade. The purpose of this study was to determine how the duration of LDP influences the anesthetic characteristics of tetracaine hyperbaric SA.

METHODS : After institutional approval, 60 patients undergoing lower limb surgery under SA were randomized into 4 groups, according to the duration of LDP following the spinal injection; Group O: patients immediately turned supine after spinal injection; Group 6 : 6 min in LDP, then supine; Group 12 : 12 min in LDP, then supine; Group 18 : 18 min in LDP, then supine. While the patients were placed in the LDP, with the operative side dependent, lumbar puncture was performed via the L2-L3 or L3-L4 interspace with a 25 G needle, and each patient received 12 mg lyophilized tetracaine and 0.2 mg epinephrine in 2.5 ml dextrose 10%. The cephalad sensory level and quality ot motor blockade (modified Bromage scale) on the operative (OP) and non operative (NOP) sides were assessed by a person unaware of duration of LDP, at 20, 25, 30 min, then every 15 min during surgery, and every 30 min until recovery. Mean arterial pressure (MAP) and heart rate were recorded every 5 min during the entire procedure. The regression time of sensory level to L2 was considered as the duration of SA. The four groups were compared with an ANOVA, and each variable was compared with a paired t-test between OP and NOP side.

RESULTS : The most important data are indicated in table 1. When the data of the different groups are compared, the only significant differences between group O and 18 are a later onset of maximal motor blockade on the NOP side and a longer duration of sensory blockade on the OP side. However, when the different data are compared between OP and NOP side, similar sensory levels are obtained, but the duration of anesthesia increases on the OP side with the duration of LDP. On the NOP side the onset of maximal motor blockade is delayed and its quality decreases as the duration of LDP increases.

CONCLUSION : Although 18 min LDP does not produce unilateral anesthesia during hyperbaric SA, a longer duration of sensory blockade can be obtained on the dependent side. The major clinical implication of this study is that the distribution of local anesthetics during SA can still be influenced by changing patients' position 18 min after administration of hyperbaric tetracaine.

Reference : 1. Anesth Analg 64:715-30, 1985

Table 1 : Anesthesia Characteristics (X±SD)

	Max sensory level (obtained after min)		Max degree of motor block (obtained after min)		Regression of sensory level to L2 (min)		Max Decrease in MAP(%)
	OP	NOP	OP	NOP	OP	NOP	(observed after min)
Group O (n = 15)	T 4.5±2.1 (28±9)	T 4.6±2.3 (33±17)	3.9±0.3 (20±0)	3.9±0.5 (23±9)	243±36—••—233±43		30±11 (41±45)
Group 6 (n = 15)	T 5.3±3.4 (35±18)	T 5.5±3.4 (36±18)	4±0 (21±3)—•—(29±13)	3.5±1	269±38—•—223±52		27±14 (43±35)
Group 12 (n = 15)	T 6.8±3.5 (41±23)	T 7±4.1 (41±17)	4±0 (23±9)—•—(32±13)	4±0 —•—3.3±1.2	277±48—••—223±52		26±11 (56±36)
Group 18 (n = 15)	T 7.3±2.9 (39±18)	T 6.9±3 (40±15)	4±0 (21±2)—••—(44±19)*	—•—3.2±1.3	* 291±51—••—227±60		21±13 (42±35)

* Significantly different from group O ($p < 0.05$) / • $p < 0.05$, •• $p < 0.01$ comparison between OP and NOP