

Comment prolonger une ALR périphérique ?

Fabrice Ferré
CHU Toulouse

Aucun conflit d'intérêt

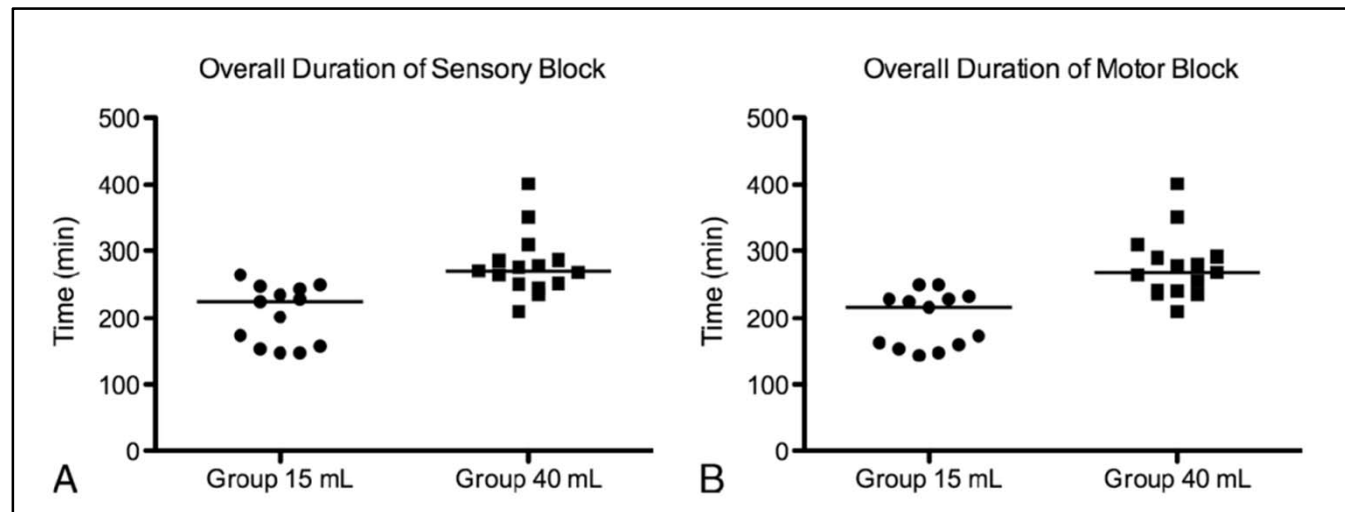
1. Augmenter concentration/dose des AL

2. Adjuvants

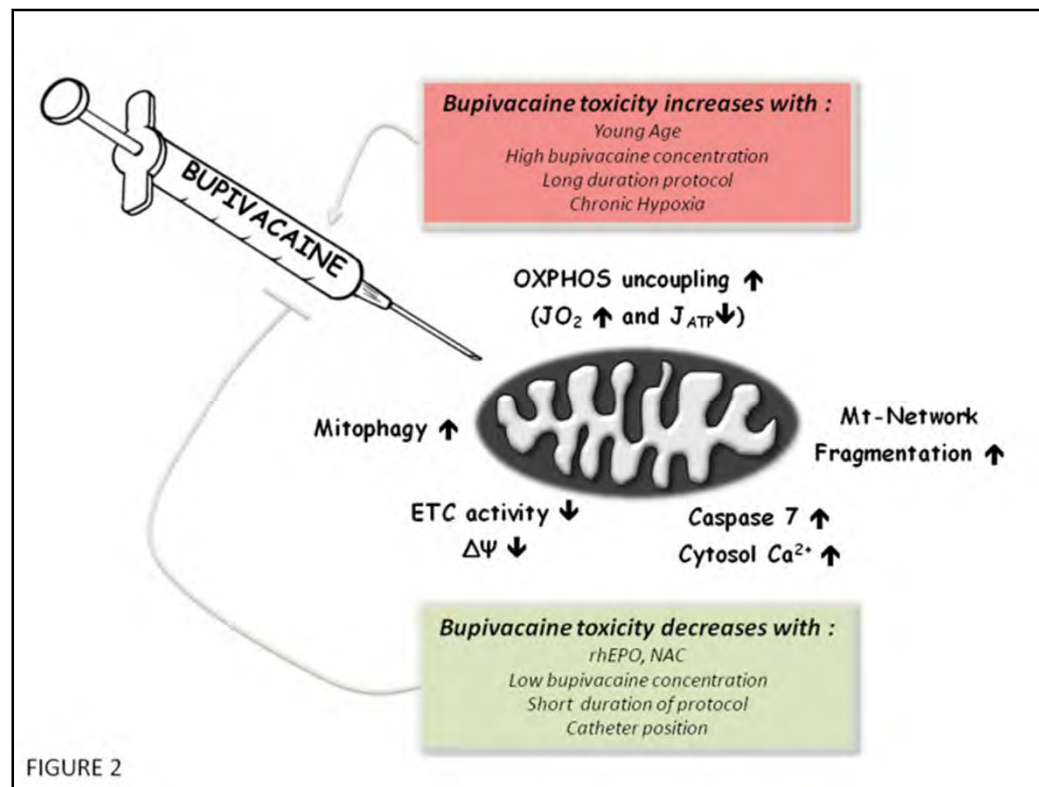
- *Durée du bloc*
- *Mécanismes d'action*
- *Toxicité*
- *Voie d'administration*

3. Cathéters périmerveux

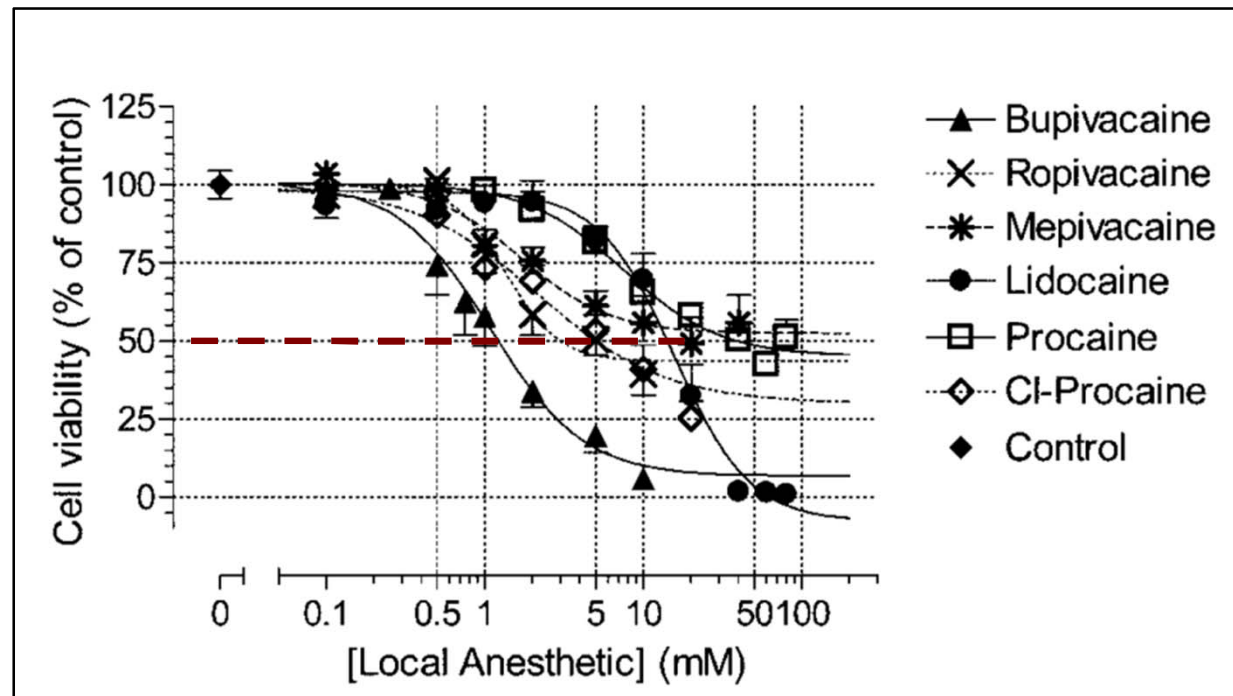
Effect of Local Anesthetic Volume (15 vs 40 mL) on the Duration of Ultrasound-Guided Single Shot Axillary Brachial Plexus Block



Local anesthetic 'in-situ' toxicity during peripheral nerve blocks: update on mechanisms and prevention.

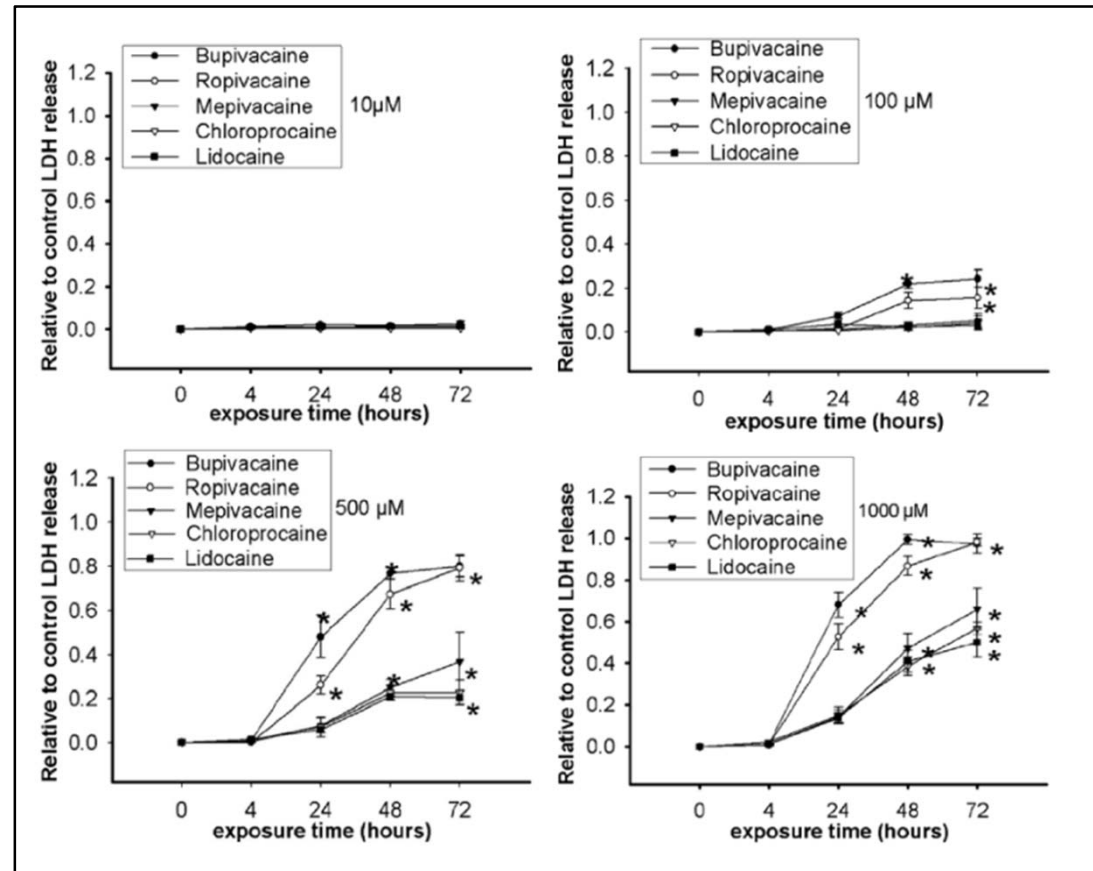


Cytotoxicity of Local Anesthetics in Human Neuronal Cells



Local Anesthetic Schwann Cell Toxicity is Time and Concentration-Dependent

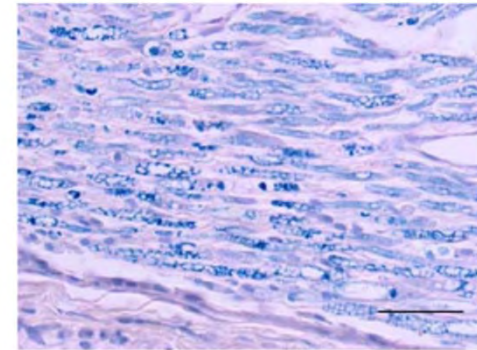
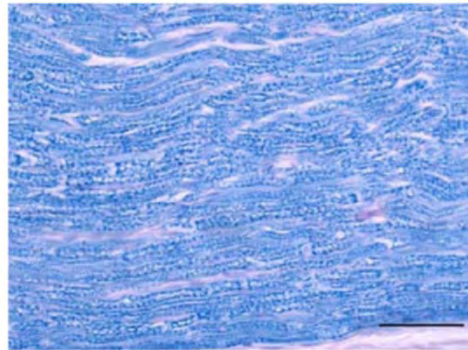
- Cellules de Schwann (NS rats)
- [C] croissantes AL
- Durée d'exposition croissantes
- L, M, C, R et B
- LDH = mort cellulaire



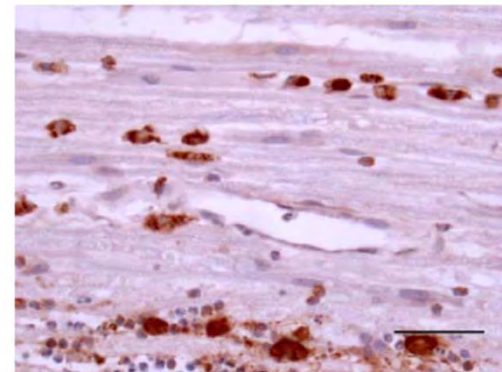
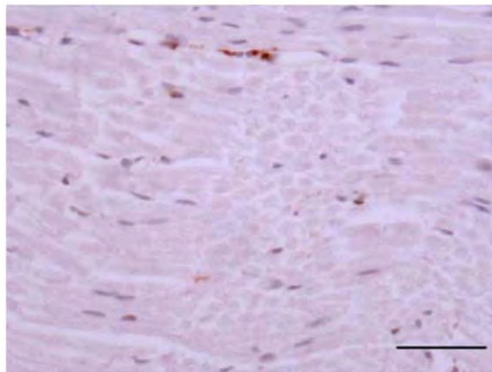
SSI

Bupivacaine 0,5%

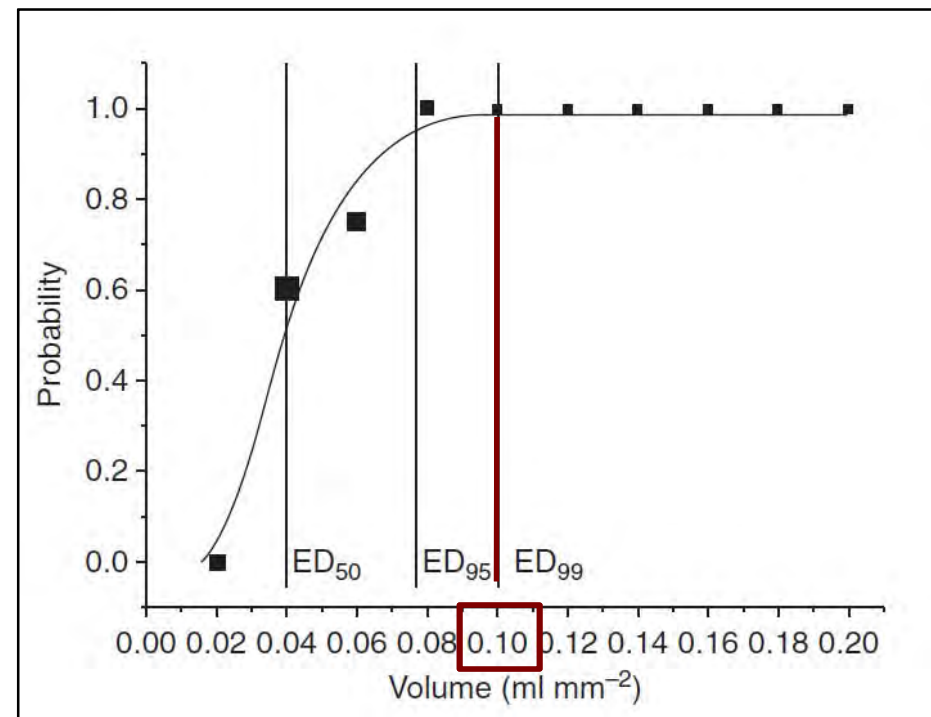
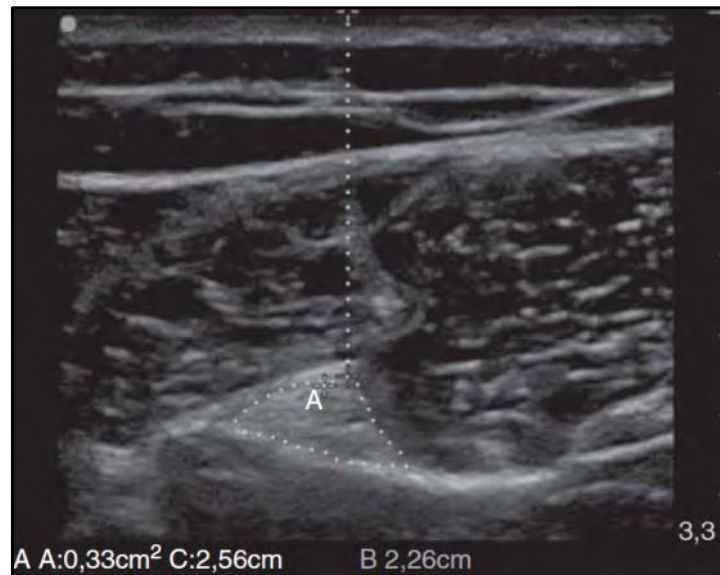
Myéline



Ac anti macrophages
(CD68)



Minimal local anaesthetic volumes for sciatic nerve block: evaluation of ED₉₉ in volunteers



1. Augmenter concentration/dose des AL

2. Adjuvants

- *Durée du bloc*
- *Mécanismes d'action*
- *Toxicité*
- *Voie d'administration*

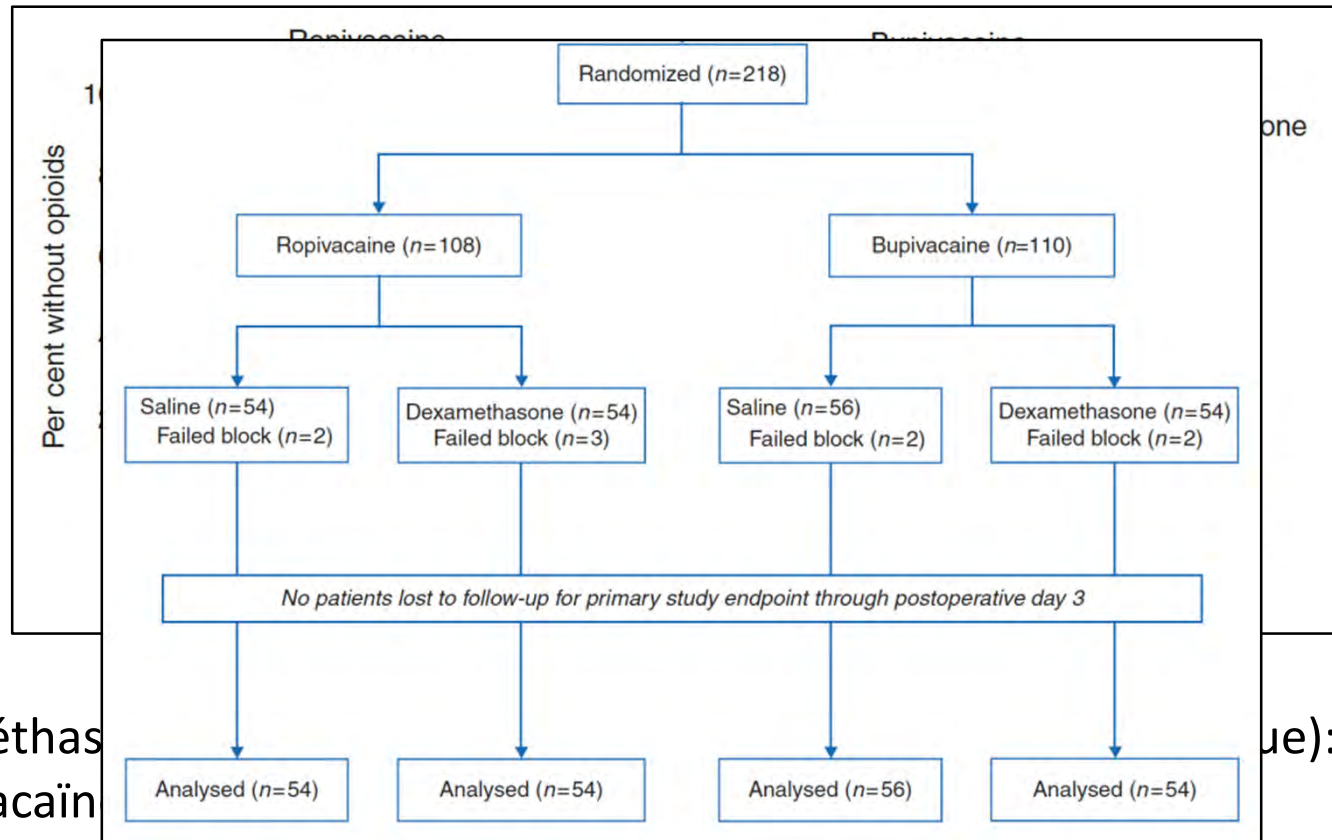
3. Cathéters périnerveux

Equivalence anti-inflammatoire des corticoïdes

	Activité anti-inflammatoire	Activité minéralo-corticoïde	Equivalence de doses	Demi-vie biologique (heures)
Hydrocortisone	1	1	20 mg	8-12
Cortisone	0.8	0.8	25 mg	8-12
Prednisolone*	4	0.8	5 mg	12-36
Méthylprednisolone	5	0.5	4 mg	12-36
Triamcinolone	5	0	4 mg	12-36
Bétaméthasone	25	0	0.75 mg	36-54
Dexaméthasone	25	0	0.75 mg	36-54
Cortivazol	60	0	0.3 mg	> 60

Durée du bloc ?

Effect of dexamethasone on the duration of interscalene nerve blocks with ropivacaine or bupivacaine

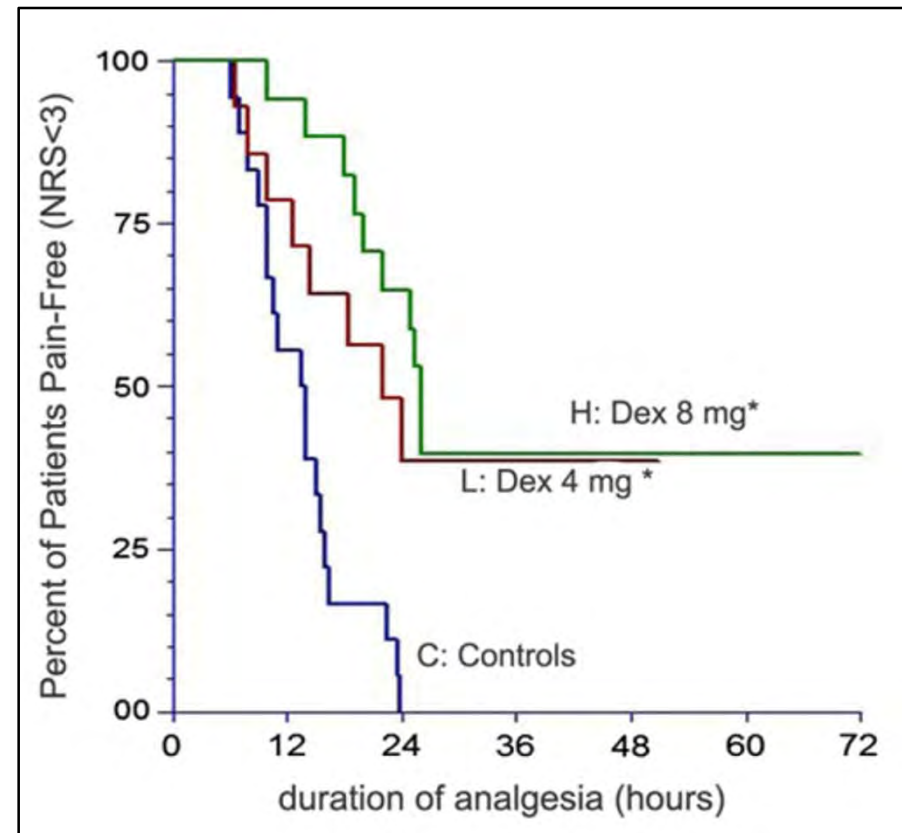


Dexaméthasone

- Ropivacaine
- Bupivacaine (n=110): 14.8 vs 22.4 heures; $p < 0,001$
- L'amplitude de l'effet diffère entre les AL

Adjuvant dexamethasone with bupivacaine prolongs the duration of interscalene block: a prospective randomized trial

- BIS pour chir ambu épaule
- 90 patients, 3 groupes (C, L, H)
- 40 ml Bupi 0,5%
- Durée analgésie (ENS < 3) prolongée L (21.6 h) et H (25.2 h) vs C (13.3 h)
- DXM: diminution antalgiques
- Satisfaction des patients/enquête téléphonique J14 et J28

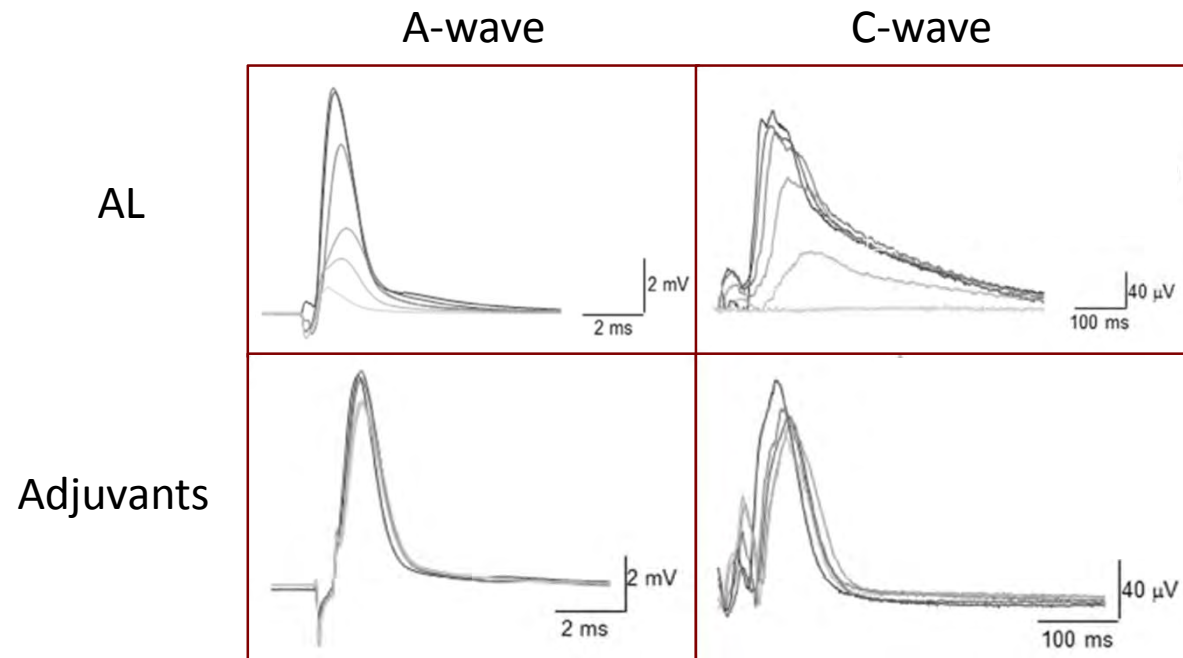


Dexaméthasone et bloc nerveux périphérique : Méta analyse d'essais randomisés

- Méta analyse d'essais randomisés contrôlés, en double aveugle
- 10 essais randomisés (734 patients, 376 avec de la dexaméthasone)
- Lidocaïne, mépivacaïne, bupivacaïne et/ou de la ropivacaïne
- Dose la plus employée de dexaméthasone: 8 mg
- La durée de l'analgésie postopératoire prolongée par la dexaméthasone (WMD= 367 min, [IC95% : 285-449], $p < 0,00001$).

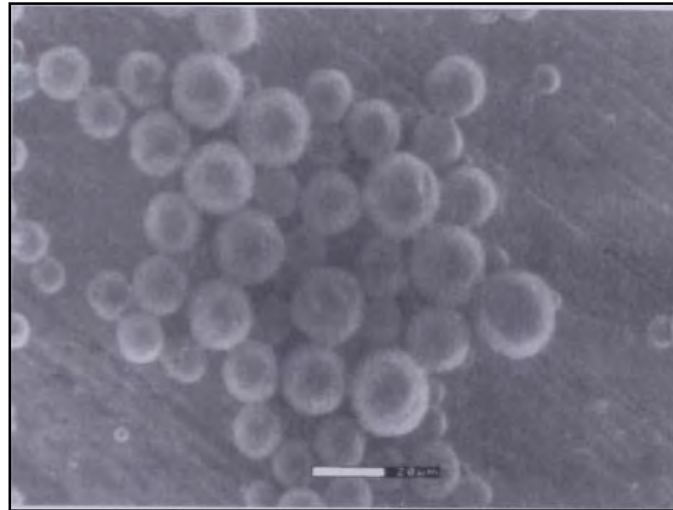
Mécanismes d'action ?

Effect of adjuvants on the action of local anesthetics in isolated rat sciatic nerves

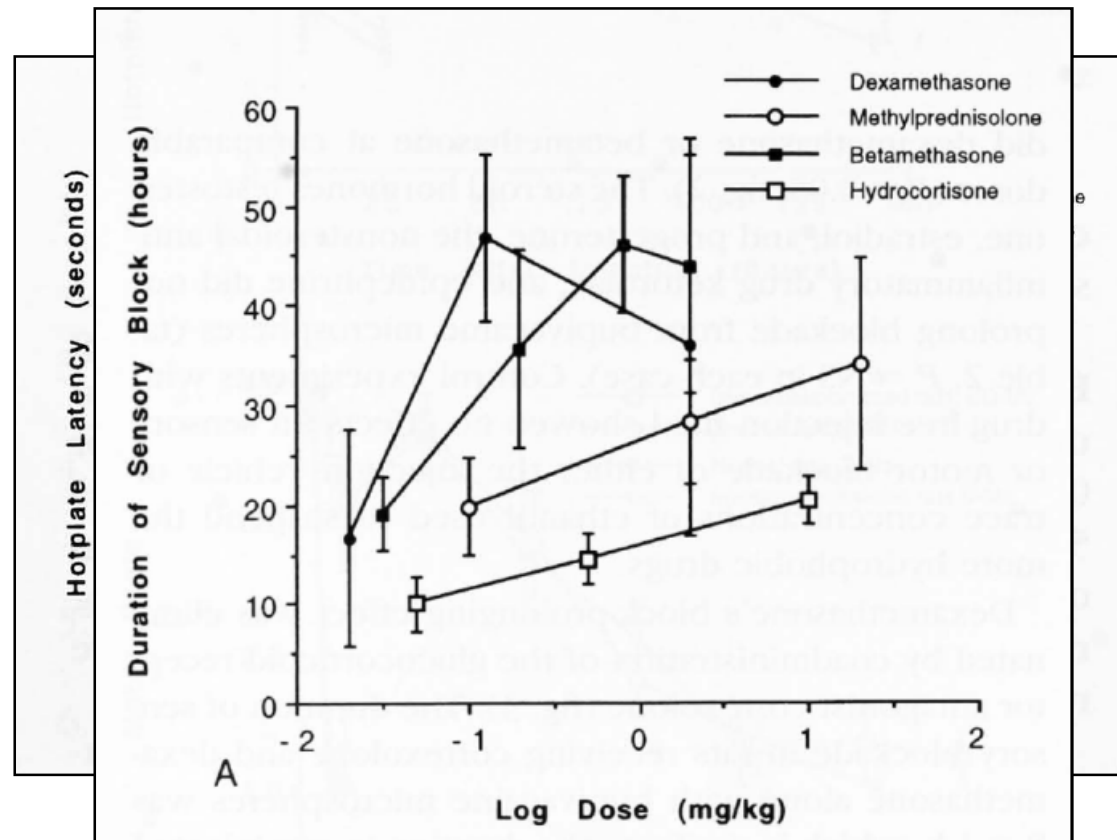


Effet DXM indirect

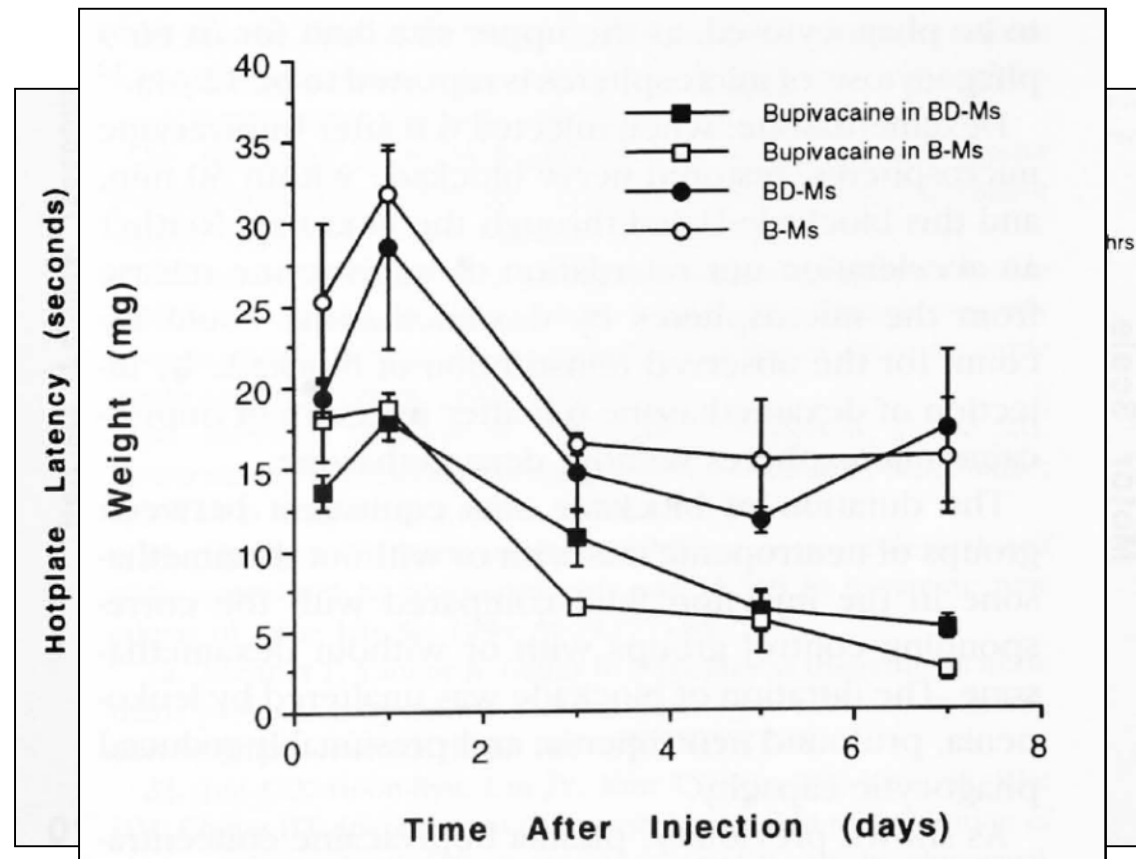
Glucocorticoids Prolong Rat Sciatic Nerve Blockade In Vivo from Bupivacaine Microspheres



MS (polymères d'acide polylactic-co-glycolic) $\equiv$ LP



MS (bupi): 7h / MS (bupi) + DXM: 47h / MS (bupi + DXM): 134h
 Durée bloc corrélée puissance antiinflammatoire glucocorticoïdes



Injection secondaire DXM (H6) rétablit bloc sensitivo-moteur
 MS résiduelles (bupi) = MS résiduelles (bupi + DXM)

Glucocorticoids Prolong Rat Sciatic Nerve Blockade In Vivo from Bupivacaine Microspheres



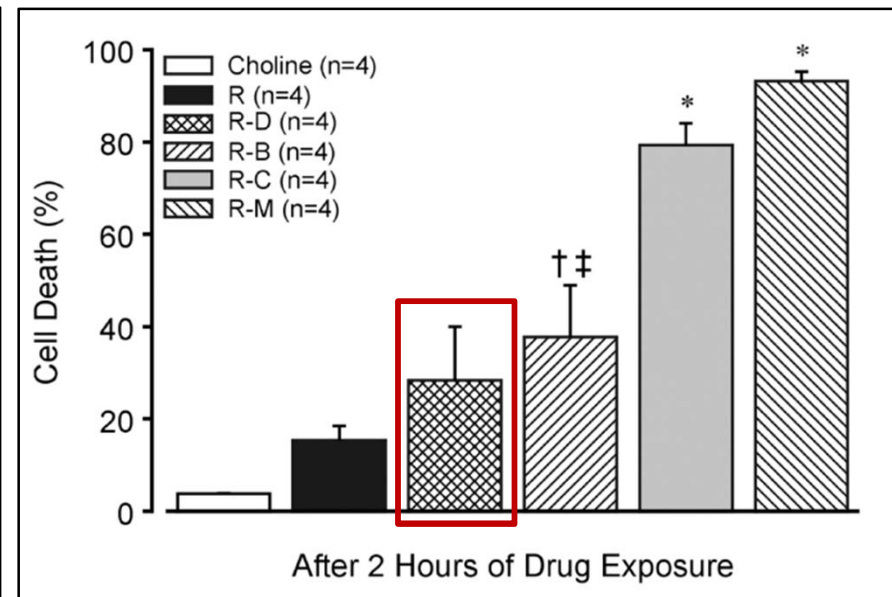
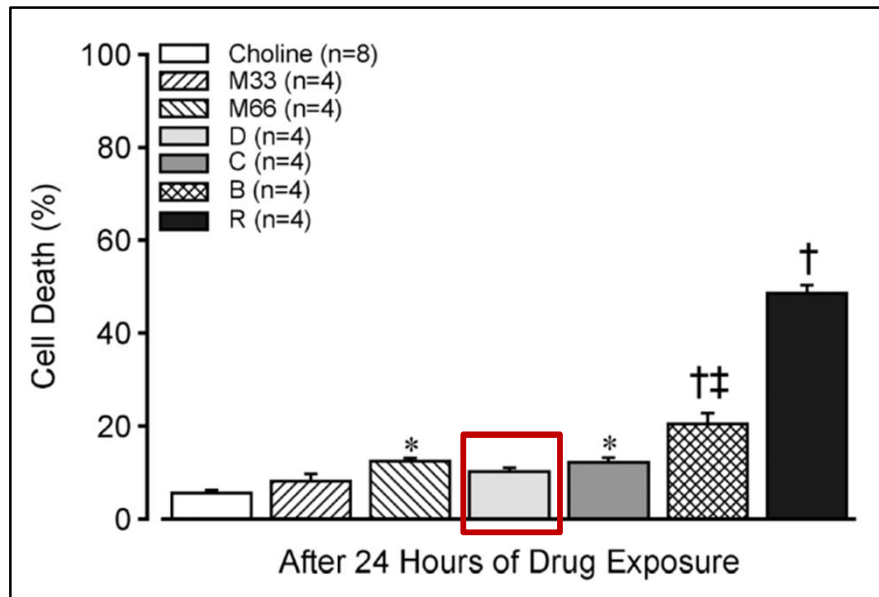
Effet DXM:

- Local
- Pharmacodynamique
- R glucocorticoïdes
- Antiinflammatoire

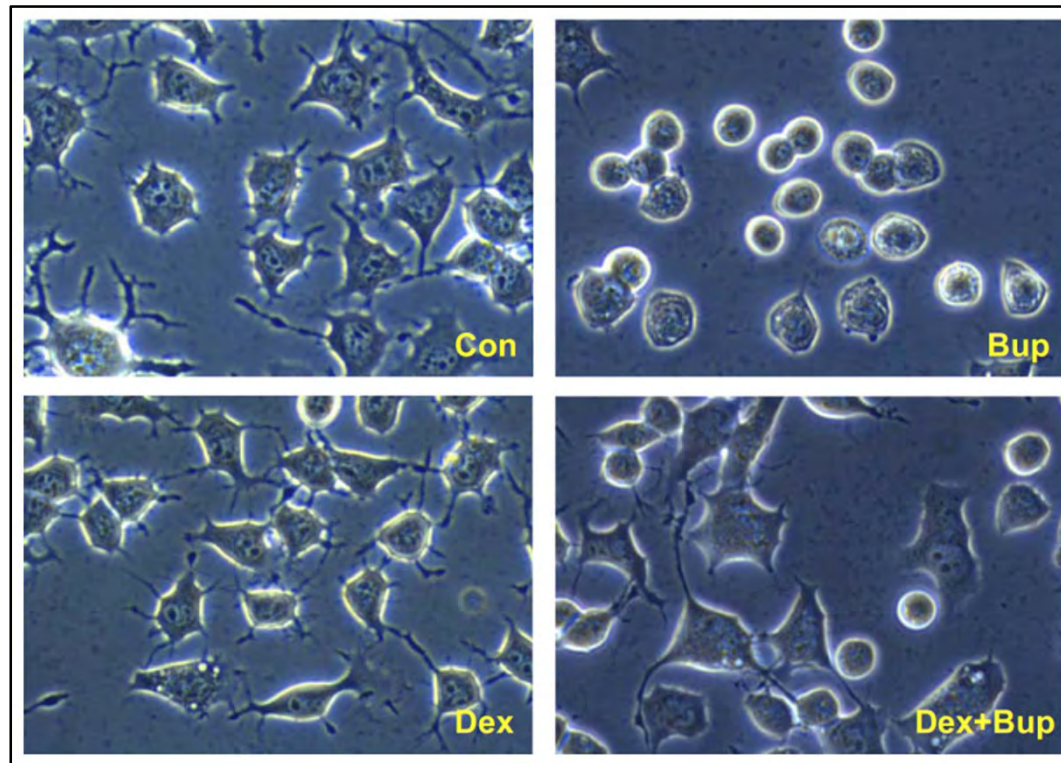
Toxicité ?

Neurotoxicity of Adjuvants used in Perineural Anesthesia and Analgesia in Comparison with Ropivacaine

- *In vitro*
- Ganglions racines dorsales rats isolés
- Mort cellulaire par test d'exclusion au bleu trypan
- Ropivacaine 0,25%
- Exposition 2h ou 24h

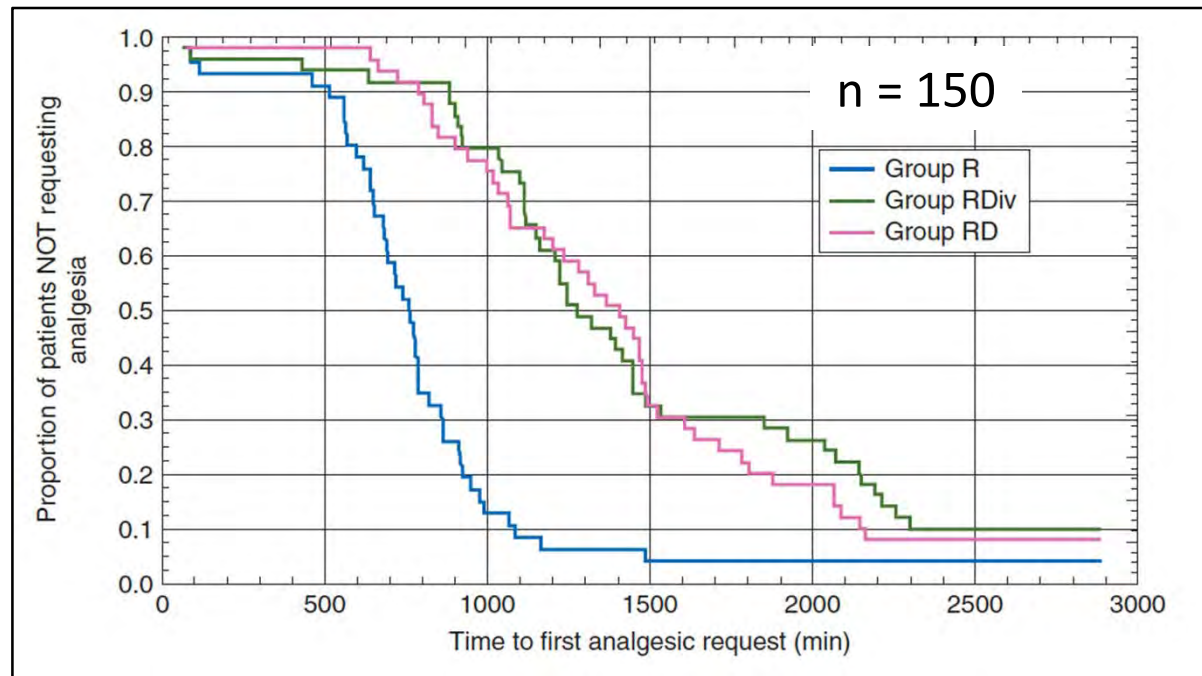


DEXAMETHASONE ATTENUATED BUPIVACAINE-INDUCED NEURON INJURY *IN VITRO* THROUGH A THREONINE–SERINE PROTEIN KINASE B-DEPENDENT MECHANISM



Voie d'administration ?

I.V. and perineural dexamethasone are equivalent in increasing the analgesic duration of a single-shot interscalene block with ropivacaine for shoulder surgery: a prospective, randomized, placebo-controlled study



La durée du bloc (délai 1^{ère} prise antalgique):

- R: 757 minutes
- RDiv (1275 min) et RD (1405 min) vs R ($p < 0,0001$)
- RDiv vs RD ($p = NS$)

Perioperative Single Dose Systemic Dexamethasone for Postoperative Pain

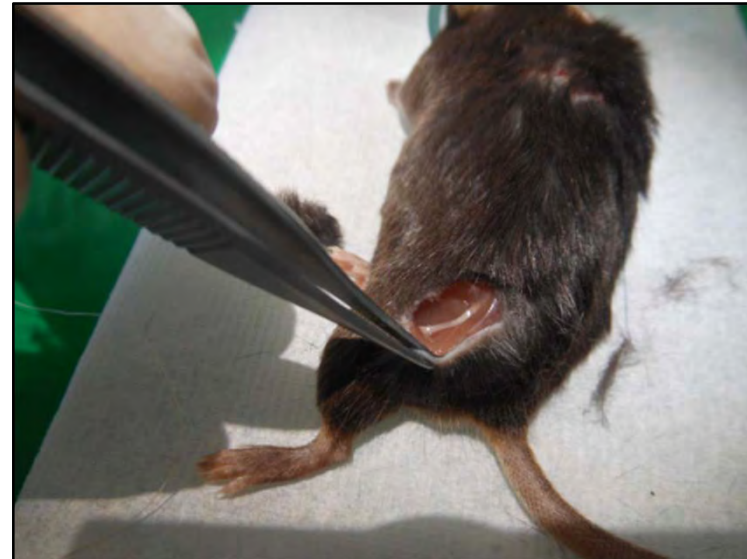
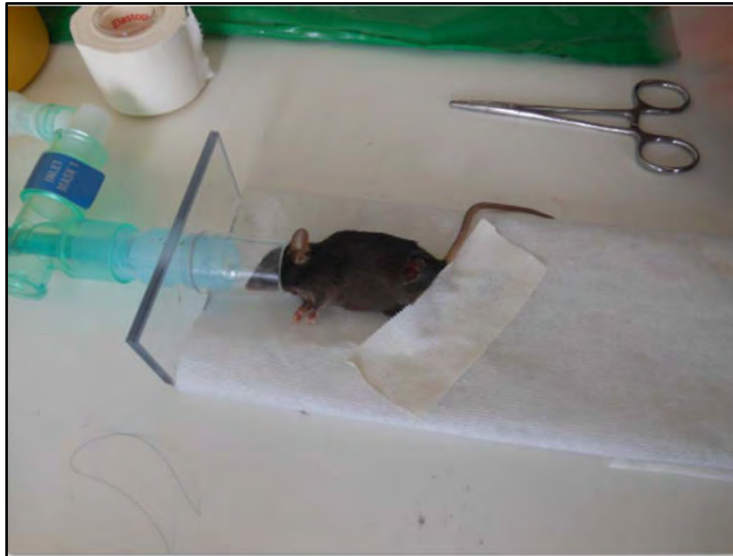
A Meta-analysis of Randomized Controlled Trials

GS De Oliveira, Anesthesiology 2011

Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis

NH Waldron, Br J Anaesth 2013

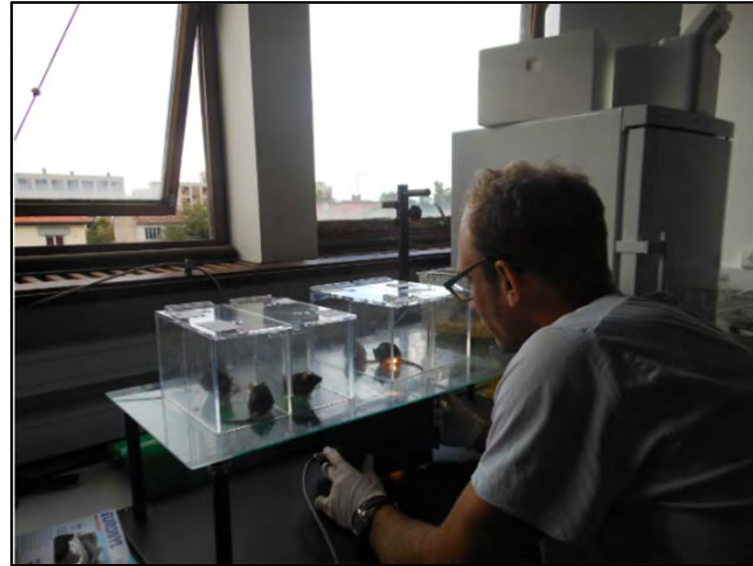
From Bedside to Bench: Adjuvant Dexamethasone for Ropivacaine Sciatic Block in Mice



- ***In vivo***
- 4 groupes (10/groupe):
 - Sham
 - Ropi 0,5%
 - Ropi 0,5% + DXM périnerveux (4 μ g)
 - Ropi 0,5% + DXM intrapéritonéal (8 μ g)

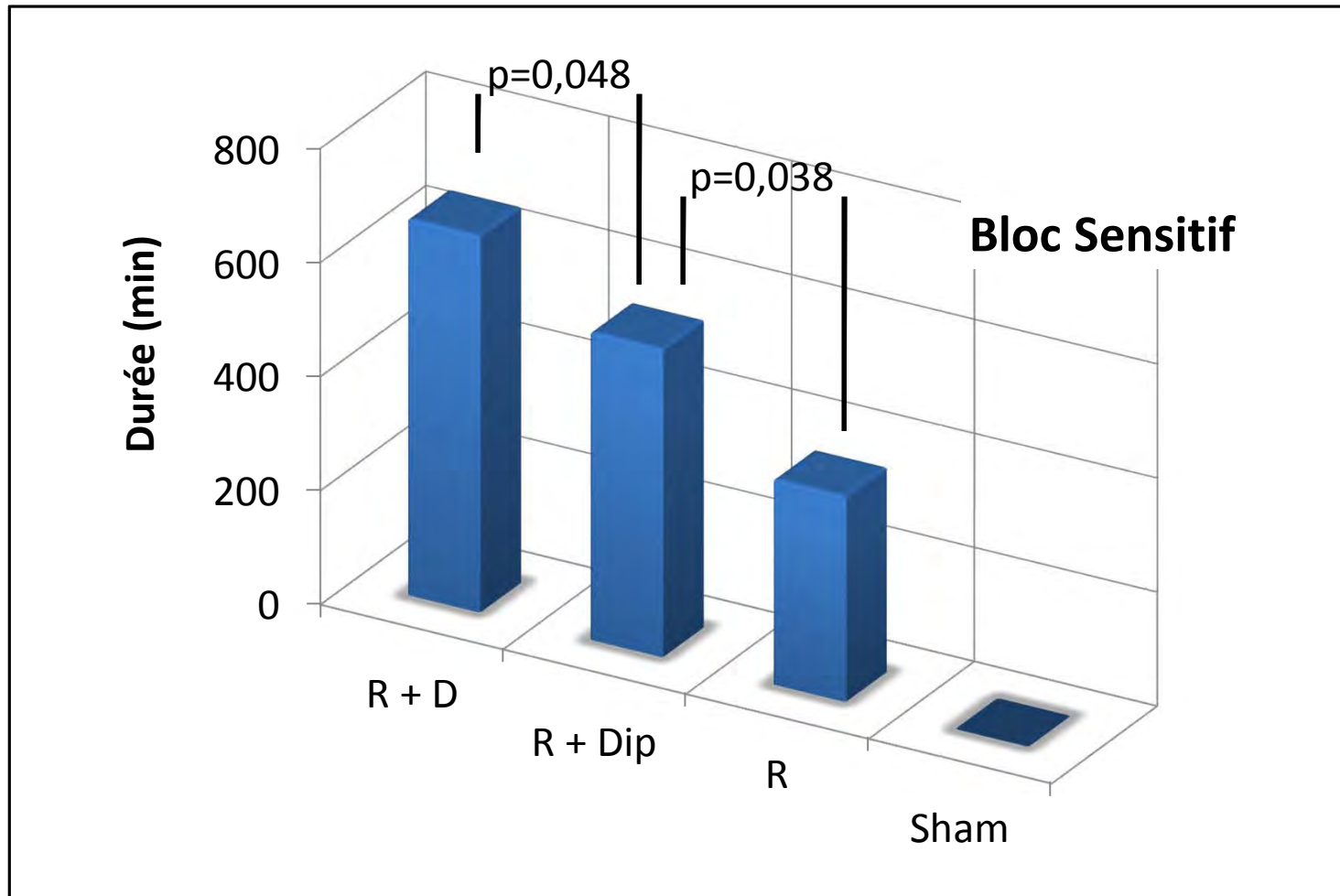
P Marty et al
Données personnelles

From Bedside to Bench: Adjuvant Dexamethasone for Ropivacaine Sciatic Block in Mice



- Evaluation BNP toutes les 30 minutes
 - Sensitif: temps de latence de retrait patte (source de lumière chauffante)
 - Moteur: échelle de 0 (normal) à 3 (pas dorsiflexion)
- Evaluation histologique J14: inflammation (œdème/infiltrat) et lésion (axone/myéline)

P Marty et al
Données personnelles



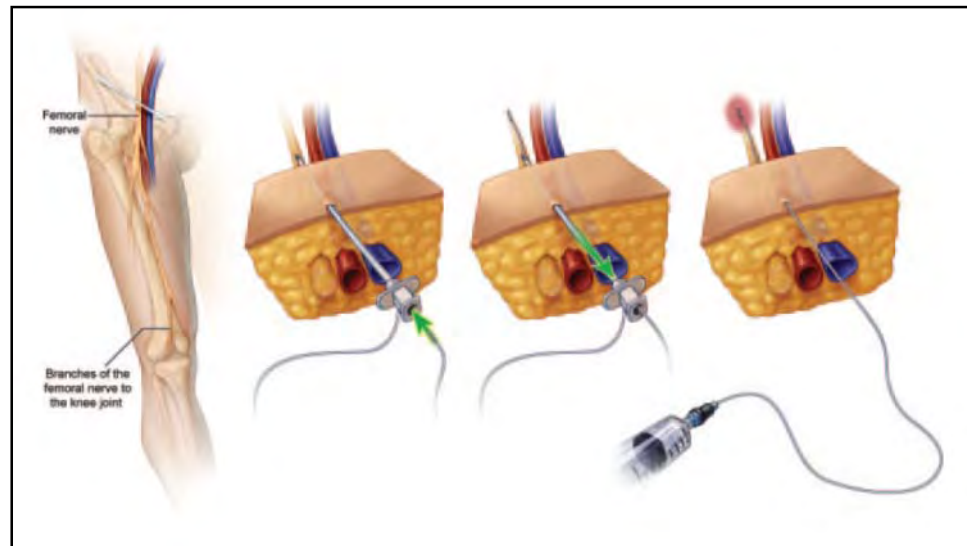
1. Augmenter concentration/dose des AL

2. Adjuvants

- *Durée du bloc*
- *Mécanismes d'action*
- *Toxicité*
- *Voie d'administration*

3. Cathéters périnerveux

Continuous Peripheral Nerve Blocks: A Review of the Published Evidence



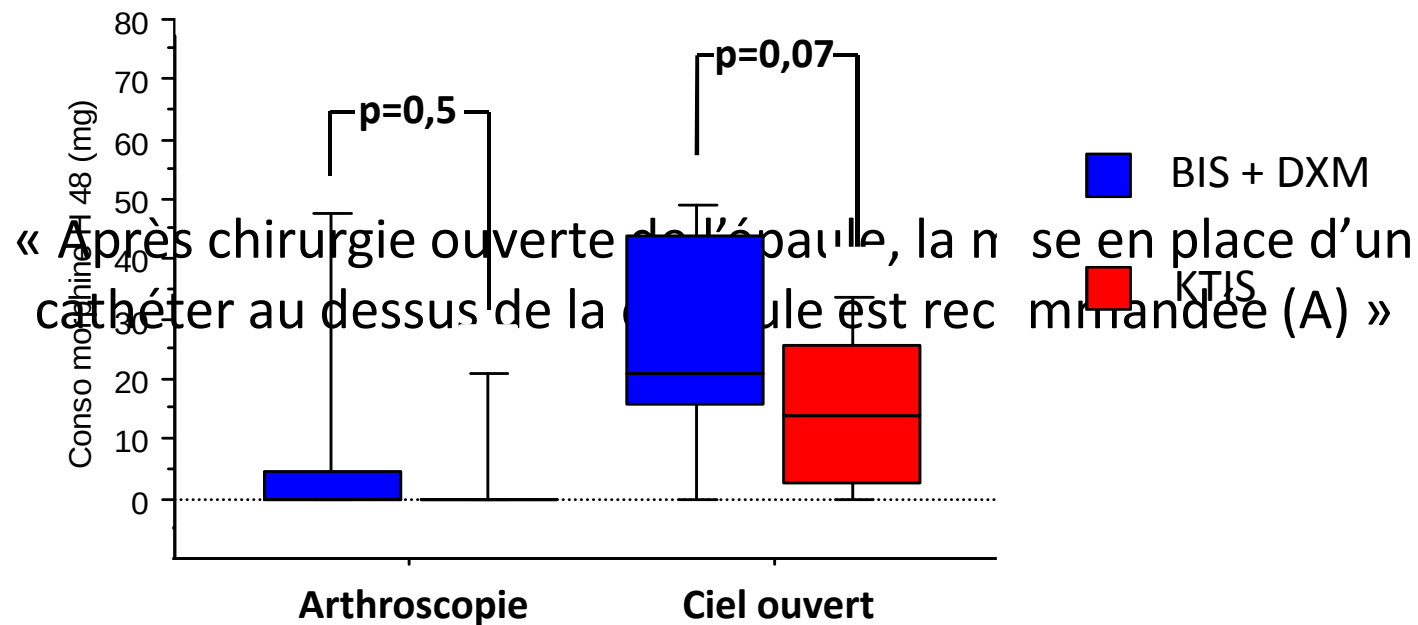
Review Article

The Role of Continuous Peripheral Nerve Blocks



Single-Injection Interscalene Block with Dexamethasone added to Ropivacaine compared with Continuous Interscalene Block for Shoulder Surgery

Single-Injection Interscalene Block with Dexamethasone added to Ropivacaine compared with Continuous Interscalene Block for Shoulder Surgery



CONCLUSION

1. **Pas d'augmentation concentration/dose ALs !!**
2. **DXM**
 - *Prolonge durée bloc sensitivomoteur*
 - *Effet pharmacodynamique, local, indirect*
 - *Innocuité/toxicité non démontrée*
 - *Administration IV ou périmébrale*
3. **Cathéters pour chirurgies (très) douloureuses > 24h**

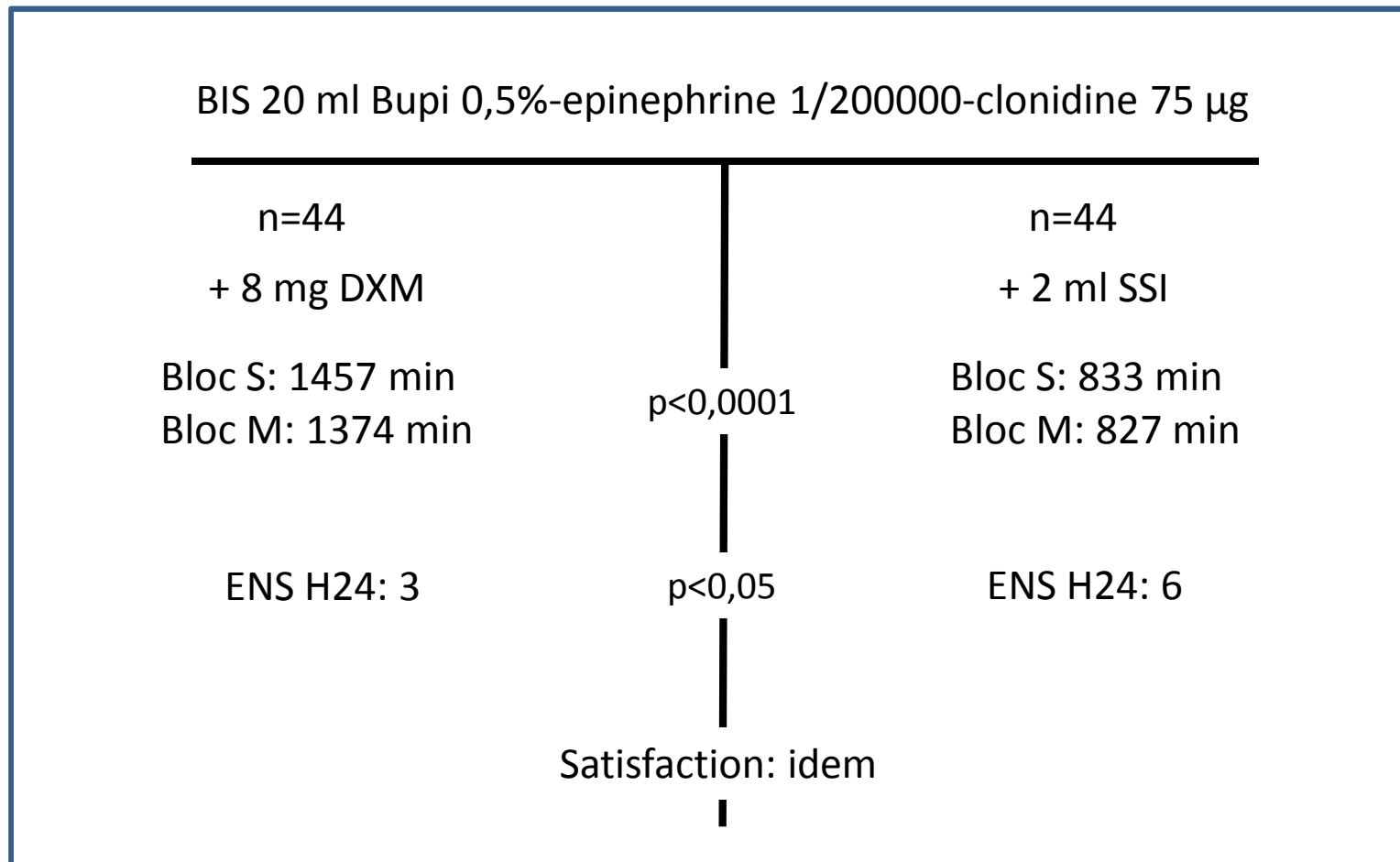
Duration of exposure 10mM (hours):	100mM	500mM	1000mM
4			
24		R, B	R, B
48	B	C, L, M, R, B	C, L, M, R, B
72	R, B	C, L, M, R, B	C, L, M, R, B

Toxicité corrélée à la concentration et à la durée d'exposition ALs

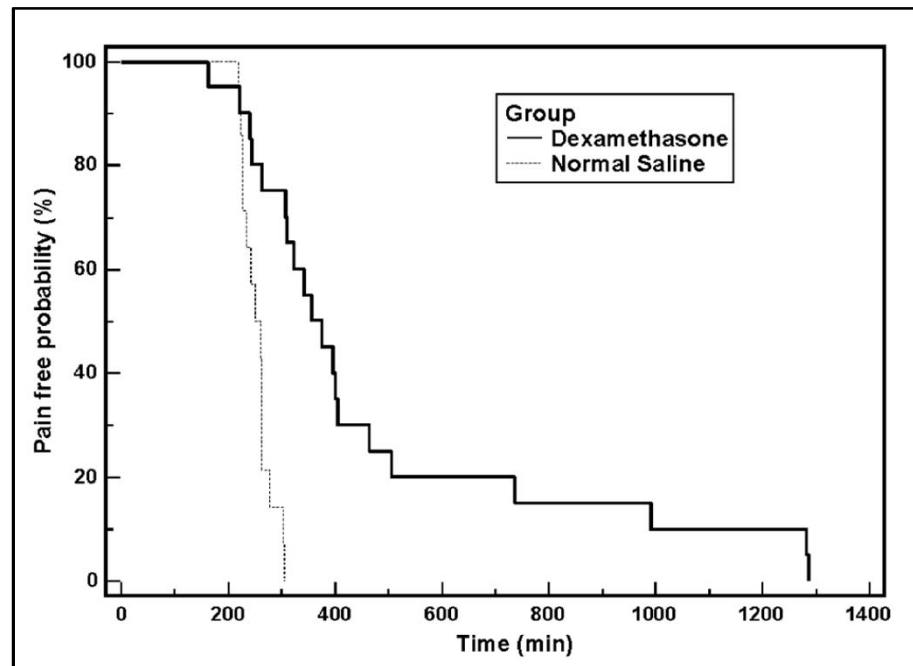
Dexamethasone Added to Lidocaine Prolongs Axillary Brachial Plexus Blockade

A Movafegh, Anesth Analg 2006

Dexamethasone with bupivacaine increases duration of analgesia in ultrasound-guided interscalene brachial plexus blockade



Dexamethasone Added to Mepivacaine Prolongs the Duration of Analgesia After Supraclavicular Brachial Plexus Blockade



- CJP: délai 1^{ère} manifestation douloureuse site chirurgical
- DXM n=24 / SSI n=21
- 332 min (225-448) vs 228 min (207-263); $p = 0,008$

***Dexamethasone Prolongs Local Analgesia after
Subcutaneous Infiltration of Bupivacaine Microcapsules in
Human Volunteers***

K Holte, Anesthesiology 2002

**The Dose Response and Effects of Dexamethasone on
Bupivacaine Microcapsules for Intercostal Blockade
(T9 to T11) in Healthy Volunteers**

DJ Kopacz, Anesth Analg 2003

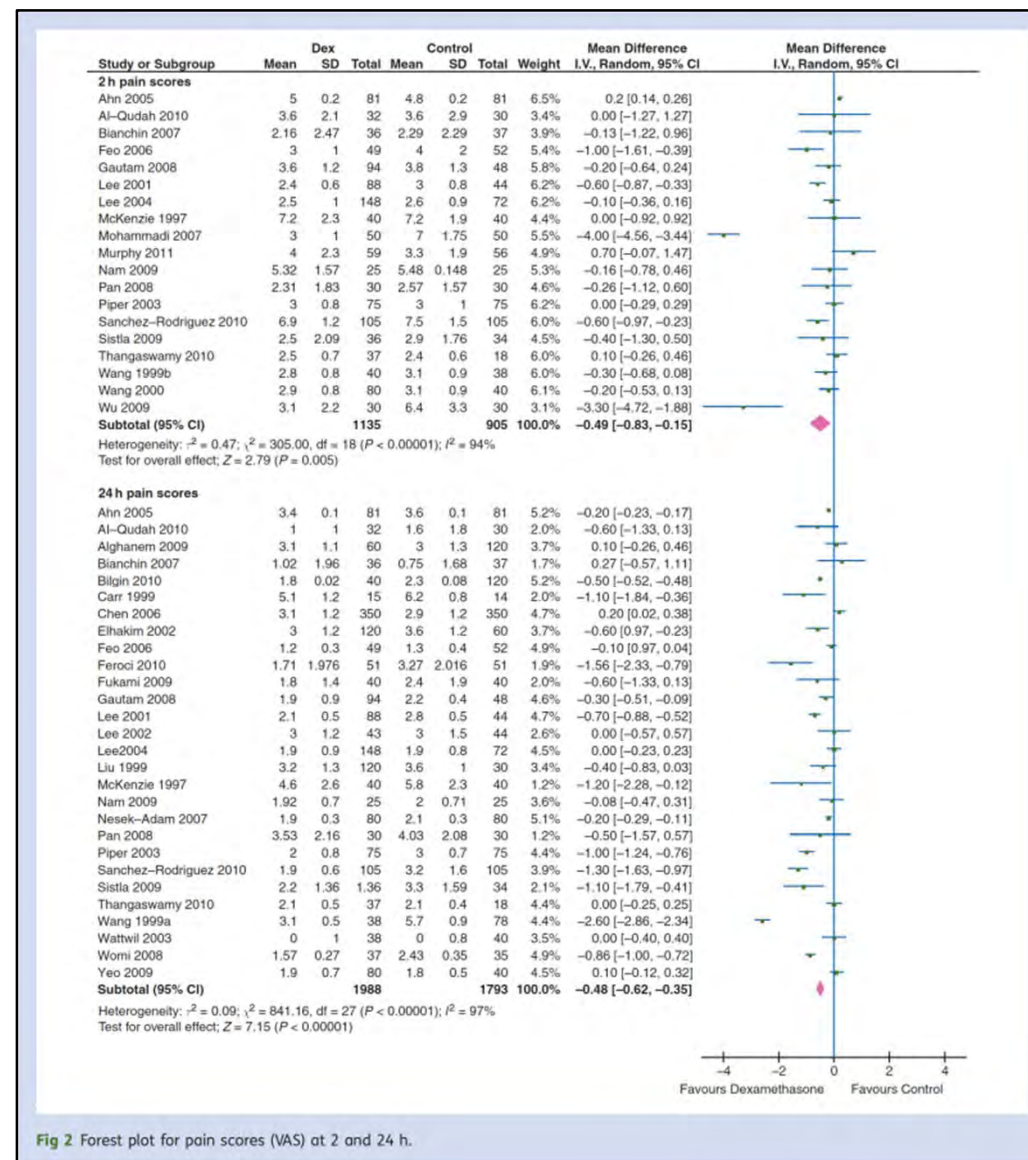


Fig 2 Forest plot for pain scores (VAS) at 2 and 24 h.

Steroids to Ameliorate Postoperative Pain

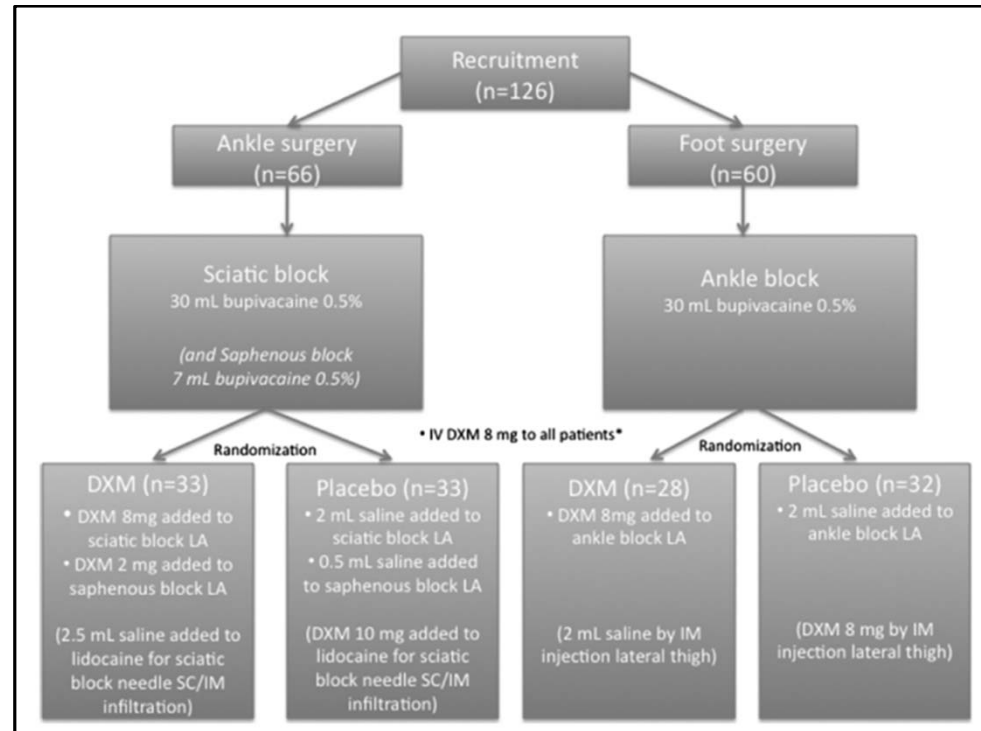


“... dexamethasone ameliorates acute postoperative pain ... [but] what remains unclear is the risk-benefit ratio.”

	BIS + DXM	KTIS	p
Durée réalisation (min)	9,3 ± 4,8	18,5 ± 5,6	<0,0001
Coût (€)	11,3	87,2	

Adjuvant Dexamethasone for Bupivacaine Sciatic and Ankle Blocks

Results From 2 Randomized Placebo-Controlled Trials



Critère de jugement principal: douleur à la 48^{ème} heure