

Ropivacaine

An experimental and clinical study with special reference to analgesic, circulatory and antiinflammatory effects

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Abstract. Aims of the study: 1. to compare ropivacaine and bupivacaine (\pm adrenaline) concerning dermal analgesia and local vascular effects (intra-dermal injection); 2. to design a suitable test procedure to evaluate changes in skin blood flow after intra-dermal injection of local anaesthetics; 3. to evaluate changes in skin blood flow of various concentrations of ropivacaine \pm adrenaline; 4. to investigate the influence of ropivacaine, bupivacaine, lidocaine, mepivacaine and prilocaine on the production of oxygen metabolites in human polymorphonuclear leukocytes and 5. to evaluate sensory, motor and sympathetic blockade using ropivacaine for epidural analgesia.

72 male patients (transurethral surgery), 50 male volunteers and 29 blood donors participated in this study.

Dermal analgesia and sensory blockade were evaluated by pin-prick, skin colour changes by visual inspection, skin blood flow by laser Doppler flowmetry (LDF), motor blockade by a modified Bromage scale, sympathetic blockade by assessments of skin resistance level and response, skin temperature and skin blood flow. Production of oxygen metabolites was measured by luminol-enhanced chemiluminescence.

Ropivacaine produced significantly longer duration of dermal analgesia compared with bupivacaine (comparable concentrations). Addition of adrenaline increased the duration of both local anaesthetics. Local blanching was more frequent for plain ropivacaine.

The effect of drugs on local circulation may well be studied by intra-dermal injection (0.1 ml, 30-G needle) and recording of changes in skin blood flow (LDF). Not only a further increase, but also a decrease in flow could be seen, if the effect of an intra-dermal saline injection, causing a very reproducible flow increase, is considered in the evaluation of the net circulatory effect of the tested drug. Lidocaine 1% and bupivacaine 0.75% produced an increase in flow, ropivacaine 1% a flow similar to saline. A gradual decrease was seen for ropivacaine 0.75%–0.063%, where 0.063% produced a flow similar to adrenaline-injection (5 μ g/ml). Ropivacaine 1%, 0.5% and 0.25%+adrenaline did not accentuate, but instead decreased the vasoconstrictive effect of adrenaline.

By and large, a decrease in chemiluminescence was seen

with the higher concentrations of the various local anaesthetics. Ropivacaine (1000 μ g/ml) showed a depression of both intra- and extracellular responses that was similar to lidocaine (1000 μ g/ml). A marked increase for prilocaine (1000 μ g/ml) in intracellular response accompanied by a reduction in extracellular response was noted.

Ropivacaine (20 ml 0.5% or 0.75% \pm adrenaline) epidurally provided good sensory blockade and motor blockade satisfactory for transurethral surgery. Maximum sensory level of analgesia was Th 2–3 (median). The majority of patients had a marked or complete sympathetic blockade in the lower limbs. Besides mild or moderate hypotension, which responded well to treatment with ephedrine, no other serious adverse reactions were seen. Addition of adrenaline did not provide any significant prolongation of the epidural blockade, and did not alter the influence upon the sympathetic blockade nor the haemodynamic changes during onset.

This thesis is based on the following studies:

- I. Cederholm I, Åkerman B, Evers H. Local analgesic and vascular effects of intra-dermal ropivacaine and bupivacaine in various concentrations with and without addition of adrenaline in man. *Acta Anaesthesiol Scand* 1994; **38**: 322–327.
- II. Cederholm I, Evers H, Löfström J B. Effect of intra-dermal injection of saline or a local anaesthetic agent on skin blood flow – a methodological study in man. *Acta Anaesthesiol Scand* 1991; **35**: 208–215.
- III. Cederholm I, Evers H, Löfström J B. Skin blood flow after intra-dermal injection of ropivacaine in various concentrations with and without epinephrine evaluated by laser Doppler flowmetry. *Reg Anesth* 1992; **17**: 322–328.
- IV. Cederholm I, Briheim G, Rutberg H, Dahlgren C. Effects of five amino-amide local anaesthetic agents on human polymorphonuclear leukocytes measured by chemiluminescence. *Acta Anaesthesiol Scand* 1994; **38**: 704–710.
- V. Cederholm I, Anskär S, Bengtsson M. Sensory, motor and sympathetic blockade during epidural analgesia with 0.5% and 0.75% ropivacaine with and without epinephrine. *Reg Anesth* 1994; **19**: 18–33.