Improvement of postoperative pain by ropivacaine: a radiotelemetric study of freely-moving rats following calibrated laparotomy

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Pain is defined by the I.A.S.P (International Association for Study of Pain) as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Today, most of the "pain reaction" measured in the animal is based on the analysis of threshold values to produce motor reflexes after noxious or non-noxious stimuli. If useful, these tests require animal handling, produce a variable degree of stress and do not allow to obtain information on spontaneous pain expression [1].

To avoid or limit stress in animal, we have used radiotelemetry to measure some key physiological parameters in freely-moving animals recovering from surgery [2] Transmitters used in the present study (volume: 7cc; weight: 3g) allowed to record changes in the heart rate, respiratory frequency, abdominal temperature and locomotor activity in real time and for the whole duration of the experiments. A surgery is required to implant this type of miniaturized electronic biocaptors in the peritoneal space of the animal and we defined strict conditions of animal surgery time and anaesthesia. To evaluate postoperative pain, we characterized the mechanical sensitivity around the abdominal scar using calibrated von Frey filaments. We first show that, immediately after surgery, the animal exhibited a strong mechanical allodynia, *i.e.* animals show a pain symptom although mechanical stimulation is non noxious. This mechanical allodynia in the periphery of the abdominal scar persists significantly for up to 10 days. Interestingly, pain hypersensitivity is timely associated with a significant locomotor impairment, hyperthermia and tachycardia.

To confirm which of these symptoms are correlated with pain expression, we characterized the effect of ropivacain, a long-lasting local anesthetic [3] on the postoperative recovery. If ropivacain is administered subcutaneously around the scar either before the beginning of surgery or just before the awakening of the animal [4], no more signs of mechanical allodynia could be detected during the following days after surgery. Locomotor activity and heart rate values, measured in ropivacaine-treated animals, were similar to those of animals having fully recovered (*i.e.* more than 15 days after implantation). Interestingly, only hyperthermia persisted 7-10 days and was unaffected by the ropivacaine treatment, letting us thinking than that is induced by scaring process, and do not reflect pain. This was not the case if the single infiltration of ropivacaine was performed 3 days after the surgery. Indeed, we observed a transient and short-lasting analgesic effect but we did not see any changes in the locomotor impairment, tachycardia or hyperthermia.

In summary, we have been able to monitor simultaneously the pain hypersensitivity resulting from abdominal surgery and some physiological/autonomic parameters. This study was conducted in freely-moving and non-handled animals which limit possible bias due to stress. We have characterized the time-course of mechanical allodynia and the impairment of locomotor and heart rate values during the recovery period of the surgery. Strongly supporting than control of side-effects is crucial for successful surgery and fast-track rehabilitation [5] we show than modifying slightly the surgery protocol by using subcutaneous ropivacaine injections in a short time window (*i.e.* before or just before awakening of the animal) appears to prevent the immediate and long-lasting allodynia as well as locomotor impairment and tachycardia. The mechanism involved in this phenomenon is currently under investigation.

References

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