Notat

Til: Alle brukere ved
Avdeling for Komparativ medisin (KPM)

Kopi:

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Saksbeh.:

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Sak: Use of multimodal analgesia in surgical animal models

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Use of multimodal analgesia in surgical animal models will be expected from KPM and Mattilsynet in future FOTS applications

Multimodal analgesia is the combination of different analgesic agents, typically opioids, local analgesia and NSAIDs. Combination of analgesic agents provides additive and complimentary effects, improving overall efficacy, time of action and time to onset. This is in many ways comparable to the beneficial additive effects obtained during balanced anaesthesia versus single agent anaesthesia.

Being the optimal method of analgesia, **multimodal analgesia will be the expected default in future FOTS applications involving surgical interventions at KPM**. This default expectation does not mean that multimodal analgesia is relevant or compatible with all animal models. **The applicant must hence relate to these expectations, and if relevant describe valid scientific reasons in their FOTS applications why one or more components of multimodal analgesia cannot be used in their animal model.**

KPM is quite aware that the use of NSAIDs very often is incompatible with the study objectives of many animal models. If that is the case with your model, make sure to clearly describe this incompatibility in the Methods section of your FOTS id. A single sentence is needed in obvious cases, while better arguments and perhaps scientific documentation may be required in less obvious cases.

KPM is aware of very few experimental objectives that precludes the use of local analgesia and subcutaneous infiltration in surgical animal models. Local analgesia is very effective, easy to apply, does not affect wound healing and is very cheap. The preemptive combination of opioids and local analgesia is hence the expected default minimum multimodal analgesia in FOTS applications involving major surgical interventions at KPM. In case you are doing little invasive and superficial surgery (e.g. subcutaneous implantation of tumor material through a minimal skin opening), subcutaneous infiltration with a long acting local analgesia is considered adequate analgesia.

Buprenorphine (Temgesic) and bupivacaine (Marcain) are the recommended opioids and local analgesia to be used in rodents. Both are available at KPM. Marcain has a long duration and is generally described as having a slow onset of action. Based on the enclosed reference (Ribotsky

BM, *et al*, *J of the American Podiatric Med Assoc*, 1996, 86(10);487-491), a period of 3 minutes from subcutaneous administration of Marcain to start of surgery is the minimum time required. The reference also document that Lidocain and mixtures of Marcain and Lidocain is inferior to Marcain with respect to both time to onset and duration. The toxic dose of bubivacaine is 2 mg/kg in man and most mammals. As toxicity is the limiting factor with local analgesia, the recommended dose focus on the maximum dose (which is often in excess of what is needed), rather than an absolute dose in mg/kg. The considerations above assume lege artis procedures, including application of aseptic techniques.
For more information on analgesia and dose recommendations in general, see Guidelines for the Assessment and Management of Pain in Rodents and Rabbits. *JAALAS* 2007, 46(2); 97-108

Practical use of Marcain in rodents
Marcain 2.5 mg/ml (Marcain) is the recommended local analgesia due to its longer time of action. A 1:9 mixture of Marcain:sterile saline at a maximum dose of 0.07 ml/10 g body weight of diluted Marcain is recommended in rodents. Diluted Marcain is infiltrated subcutaneously on either side of the incision line **at least 3 min before start of surgery**. Use 25-27 G needles in rats-mice, tunnel along both sides of the incision line and dose gradually as the needle is retracted. Discard unused dilute Marcain at the end of the day.

Marcain is available at KPM at the following conditions:
0,1 ml Marcain in 1 ml syringes is provided to users at no cost, provided that the user adds 0.9 ml sterile saline to create the 1:9 dilution and that no more than 3 syringes of 0.1 ml is requested at the same time.
If users request ready to use diluted Marcain, the cost will be 50 kr/ml diluted Marcain.
KPM does not provide whole vials of Marcain to the users. Users that require whole vials of Marcain for animal use can request a prescription from KPM and must settle the payment directly with the pharmacy.

Vedlegg:
Guidelines for the Assessment and Management of Pain in Rodents and Rabbits. *JAALAS* 2007, 46(2); 97-108
Ribotsky BM, *et al*, *J of the American Podiatric Med Assoc*, 1996, 86(10);487-491