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INTEREST OF OPIOID FREE ANALGESIA IN UROLOGICAL SURGERY

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Abstract:
Morphine saving, the principle of balanced analgesia, is a topical topic. The use of opioids occupies a prominent place in the anesthesia associated with hypnotics and curares by reducing their consumption, providing intraoperative analgesia and ensuring post-operative analgesia.

OFA opioid free analgesia has a definite interest in carcinological surgery in urology with a high risk of opioid-related side effects. Morphine saving allows multimodal management of post-operative pain and early post-operative rehabilitation.

The side effects of morphines made of nausea-vomiting, urine retention, and sedation have a direct impact in slowing down the post-operative rehabilitation resumption of a normal life and thus prolonging the length of hospitalization.

Introduction:

Opioids have demonstrated their effectiveness in relieving especially severe pain after surgery.

However, several limitations were noted when performing post-operative analgesia based on the use of morphines alone. Indeed, post-operative pain was not always accompanied by pain due to excess nociception and neuropathic pain could also compose this type of pain.

The concept of the use of analgesics with different mechanisms of action than morphines has been developed with the aim of reducing the need for opioids or even avoiding their use.

The combination of several analgesics is the basis of the concept of multimodal or balanced analgesia developed by Kehlet and Dahl in the 1990s [1]. This association also aims to strengthen analgesia by decreasing pain scores

and side effects especially those of morphines.

From a pharmacodynamic point of view, the combination of analgesics has two objectives: the first is to increase their effectiveness through a synergistic or additive combination and the second is to reduce their toxicity by reducing their doses. The combination of analgesics may be based on a different site of action such as the combination of morphine (central action) and non-steroidal anti-inflammatory (peripheral action)

The association can either lead to an analgesia lower than that of the addition of the effect of two molecules taken individually (infra-additivity or antagonist), or give an analgesic effect simply equal to the addition of the effects of the two molecules taken individually (additivity) or have a higher result (supra-additivity or synergy).

The effect of the combination of two molecules having the same effect can be studied using an isobologram. For each molecule, the dose to obtain 50% of the maximum analgesic effect is calculated (ED50). A line is then drawn between these 2 points. It represents the theoretical line of additivity. The combinations of the two molecules are then tested. If the ED50 of the combination is below the curve, the association is considered to be synergistic.

Conversely, the combination of the two analgesics can be infra-additive when the point is above the curve Fig.1a. [2]

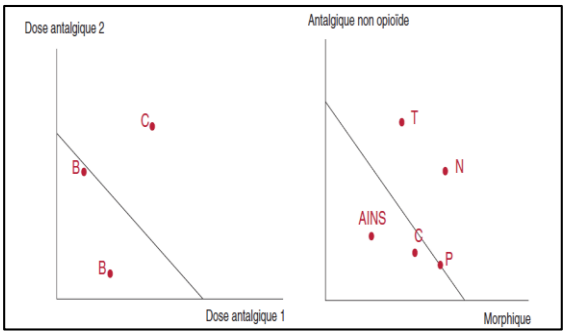

Figure 1. Isobolographic analysis of interactions of non-opioid analgesics with morphine. On the X-axis, the ED 50 value of morphine and the ED50 value of the analgesic. The figure on the left shows the different situations in the co-administration of two products. Point A represents a supra-additivity or synergy, point B represents an additivity and point C represents an infra-additivity. The figure on the right shows the results of isobolographic analyses of a morphine-non morphine analgesic association. C: clonidine. P: Paracetamol. NSAID: non-steroidal anti-inflammatory. N: Fopam. T: Tramadol.

The interaction of opioids with certain analgesics has been investigated experimentally. The associations of morphine-paracetamol, morphine-NSAIDs and morphine-clonidine were evaluated in animals (rats). Fletcher et al. showed, in a pain model with essentially an inflammatory component, that the combination of paracetamol and intravenous morphine was additive [3]

(fig. 1b). Diclofenac-morphine was synergistic in this model (fig. 1b). The intravenous injection of clonidine and morphine was additive in a model with excess nociception (fig. 1b). In humans, the association of nephpam or tramadol with morphine has been studied in patients with moderate to severe pain in post-interventional care. In this context, a combination of nephpam or tramadol with morphine is infraadditive. Finally, the association of an NMDA receptor blocker with morphine was also shown to be additive. Thus, the experimental studies allow to conclude that only the

morphine-NSAID association is synergistic while other combinations of non-morphine analgesics with morphine are at best additive.

The antagonistic association of NMDA receptors (ketamine) and morphine: The interest of antagonists of receptors associated with PCA morphine has been the subject of many publications. Several trials have used ketamine at low doses for antihyperalgesia purposes rather than analgesics. It was used in bolus at the beginning of the intervention continued in intraoperative and stopped before the end of the intervention [2].

Some studies have however found a remote benefit of ketamine administration showing that the interest in inhibiting the NMDA receptor does not so much concern the consequences in terms of morphine savings (effect on tolerance) but more on the reduction of hyperalgesia and allodynia phenomena [4].

We are presenting a retrospective, descriptive, monocentric study over a 4-month period (December 1, 2021 to March 31, 2022). An opioid-free anesthesia protocol was introduced for 22 patients who had a total cystoprostatectomy with or without bypass.

A ketamine bolus of 0.25 mg/kg at induction plus electric syringe maintenance at 0.15 mg/kg/h and stopped 20 minutes before the end of the surgical procedure. Dexamethasone in 8 mg dose after induction.

Post-operative analgesia was anticipated by Paracetamol IV. A morphine titration was proposed if EVA was greater than 30 mm The main objective was to evaluate the effectiveness and impact on post-operative analgesia by taking into account pain scores, the use of analgesics and or morphine.

Results: The average age was 77.86± 6.83 years, the duration of interventions was 273.5± 64.7 min. the protocol included dexamethasone =6.30 1.5 mg, induction ketamine at 27.5± 4.5 mg maintained at 10 ml/h. The pain assessment by the EVA on arrival and exit were respectively 23± 4.8 mm and 26.5± 13.5 mm. The extubation-1st analgesic in post-intervention care room = 61 ±18.5 min. The use of analgesics and morphine only in 6.7%. No post-operative nausea and vomiting. EVA pain score at H 24 was 1.5 ± 0.8 mm

Conclusion:

The OFA could take its full interest in this type of surgery. It would be interesting to develop it in patients in urological surgery especially carcinological with high risk of side effects related to opioids. Morphine saving allows multimodal management of post-operative pain and early post-operative rehabilitation.

Keywords: Morphine savings - benefits by literature – protocol

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