

Morphine versus morphine-ketamine association in the management of post operative pain in thoracic surgery

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Abstract : The aim of this study was to assess the quality of postoperative analgesia obtained with morphine-ketamine association administered in self-pain controlled analgesia, as well as the amount of morphine that has been spared. Patients who had to undergo thoracic surgery were selected. They were divided into two groups : G1 was made up of patients receiving 0.5 mg/ml of morphine associated with a placebo, with boluses of 2 ml and refractory periods of 5 minutes ; and G2 made up of patients receiving 0.5 mg/ml of ketamine associated with 0.5 mg/ml of morphine with same boluses and refractory periods. The assessment of pain at rest and on stimulation was carried out with the visual analogue scale. The response to pain and the amount of morphine spared were evaluated.

Fifty patients with an average age of 34 years were selected. The assessment showed that the response to pain at rest was the same in the two groups as from the twelfth hour. On stimulation, the analgesic response was better in G2 as well as the amount of morphine spared. This study shows that the administration of ketamine in association with morphine in the post operative period procures a favourable efficiency-tolerance relationship and provides a good means of sparing morphine.

Key words : Postoperative analgesia ; ketamine ; morphine.

INTRODUCTION

Ketamine is a narcotic agent with antagonistic properties to the N-methyl-aspartate (NMDA) receptors and it is used for induction and maintenance of general anaesthesia. It is a mixture of isomers of a racemic dextrogyre and levogyre compounds in equal parts. Its interaction with morphinomimetics explains one aspect of its actions on the NDMA receptors on the central nervous system. As concerns the mode of action, some authors evoke an additive analgesic effect with morphine while others suggest that it is a synergic effect (1-3). Another mechanism that has been evoked is the effect of ketamine on the NMDA central receptors and an interaction with morphinic receptors. Its combination with morphine spares the amount of morphine

and also improves analgesia when it is used in a patient controlled analgesia (PCA) (4). To the best of our knowledge, no study has been done on PCA in general and the association of ketamine and morphine in particular in the sub-saharan Africa. This explains the choice of this study. Its aim was to assess the quality of analgesia obtained with the association of morphine and ketamine used in PCA mode as well as the amount of morphine that has been spared.

METHODOLOGY

The study was carried out in the anaesthetic and intensive care service of the Yaounde General Hospital between the 1st of January and 31st of December 2005. All the patients undergoing thoracic surgery were recruited. These patients were seen during pre anaesthetic consultation where contraindications to morphine and ketamine were excluded. Patients consent and ethics committee approval were obtained. Patients were divided into two groups : G1 was made up of patients receiving 0.5 mg/ml of morphine with a placebo used in PCA with boluses of 2 ml and refractory periods of 5 minutes ; G2 made up of patients receiving 0.5 mg/ml of morphine associated to 0.5 mg/ml of ketamine with the same boluses and refractory periods. The post operative analgesia was completed with 1g of paracetamol every six hours for all the patients. These protocols were carried out at complete recovery from anaesthesia and was were used for postoperative analgesia within the first 48 hours. Within this period, postoperative pain was assessed

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with the visual analogue scale (VAS) every 4 hours, as well as the quantity of morphine used. The following parameters were evaluated : haemodynamic parameters (arterial pressure, pulse), respiratory parameters (respiratory frequency, arterial blood oxygen saturation) and side effects (nausea, vomiting, pruritus, somnolence). Values were compared using the Student's t-test. For this analysis, the level of significance used was 95% ($P < 0.05$).

RESULTS

Fifty patients were selected among whom were 32 males and 18 females. The average age was 34 years \pm 4 years, with extremes of 54 and 19 years. Twenty-six patients were ASA I and 24 were ASA II. The patients were operated for : intra thoracic tumours (n = 21), pleural decortications (n = 22) and thoracic trauma associated with multiple rib fractures or sternal fractures needing osteosynthesis (n = 7). The patients were divided into two groups : G1 :25 patients and G2 : 25 patients. The average duration of surgery was 212 minutes \pm 12 minutes. The assessment of pain at rest revealed the following values at the VAS : G1 : VAS = 2, G2 : VAS = 2 at the twelfth hour. At the twenty fourth hour, this value was zero in both groups. On exertion provoked by coughing, the assessment gave : G1 : VAS = 5 and G2 : VAS = 3 at the twelfth hour ($P < 0.05$). These values were respectively 4 and 1 at the twenty fourth hour ($P < 0.05$) (Table 1). Concerning the consumption of morphine, the amounts were as follows : G1 : 52 \pm 12 mg and G2 : 31.5 \pm 16mg ($P < 0.05$). The side effects were : G1 : nausea and vomiting (n = 6), pruritus (n = 5) ; G2 : pruritus (n = 4). It was noticed that dysleptic effects were absent in the two groups.

DISCUSSION

The effects of ketamine are very important in the postoperative period. Ketamine, used alone at

low dosage is only a weak analgesic. Many studies show that it is an interesting adjuvant in association with morphinomimetic drugs, local anaesthetics and other non-morphinic drugs (5-9). Its importance is seen in painful procedures such as thoracic surgery. This explains the choice of our sample. Other authors have used the same technique in other types of surgeries such as abdominal surgery (3). The VAS was used to evaluate pain, with the patient attributing a value that corresponded to the level of his pain. The main inconvenience of this method is that the patient should be conscious and cooperative. Other authors have however used this method, especially MORTERO and JAVERY (4, 5). With the latter, high values were obtained at the VAS at the twenty fourth hour : the average value for the group receiving ketamine and morphine was 2.3 while for the group receiving only morphine this value was 4.5 (5). The absence of pain at rest in the two groups in the twenty fourth hour as noted in our study can be explained by cultural factors. In sub-Saharan Africa, feeling pain following surgery is almost considered as normal. At times, expressing the pain is considered as a sign of weakness ; and as such, the patient only complains when the pain becomes very severe. The side effects noted in our study have also been mentioned in literature (3). Neurological side effects were looked for, through a meticulous clinical examination, but were absent. However, some studies have shown the occurrence of such side effects, although they were rare (1). This observation can also be explained by cultural factors. Concerning the routes of administration of ketamine, the intravenous route was used in this study. Other routes can be used notably the epidural route. The oral route is still under study and could be interesting. For the spinal route, the uncertainty of the medullar toxicity imposes limitations to its usage only in clinical research protocols couple with the fact that this route does not seem to offer analgesia of much more superior quality (10). Transcutaneous route has also been tested in post-operative period (11). The administration can be directly associated in a PCA syringe. The technique

Table 1
VAS at rest and on stimulation in G1 and G2

	VAS at rest	VAS on stimulation	P
G1 : Twelfth hour	2	2	$P > 0.05$
Twenty fourth hour	0	0	$P > 0.05$
Forty eighth hour	0	0	$P > 0.05$
G2 : Twelfth hour	5	3	$P < 0.05$
Twenty fourth hour	4	1	$P < 0.05$
Forty eighth hour	0	0	$P > 0.05$

saves up to 50% of morphine and reduces the incidence of its side effects. Apart from these types of administration, ketamine can be used in continuous infusion in the postoperative period. Dosages of 1-2 micrograms/kg within the first two days lead to a reduction in the intensity of post operative pain and pericardiac hypersensitivity within the first seven post operative days (12). This technique however presents the risk of accumulation. The side effects of ketamine, when it is used as an analgesic drug are very few. Haemodynamic, respiratory and sedative effects are moderate and inferior to those obtained with morphine.

CONCLUSION

The relationship, efficiency-tolerance of ketamine associated to morphine in the management of post operative pain in thoracic surgery is very interesting. Ketamine usage at low dosage in this association seems optimal with a significant impact on pain and on morphine requirements.

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