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SCIENTIFIC ARTICLE

Comparison of postoperative analgesia with methadone versus morphine in cardiac surgery☆

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KEYWORDS
Methadone;
Morphine;
Postoperative pain;
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Abstract
Background and objectives: Pain is an aggravating factor of postoperative morbidity and mortality. The aim of this study was to compare the effects of methadone versus morphine using the numerical rating scale of pain and postoperative on-demand analgesia in patients undergoing myocardial revascularization.
Method: A randomized, double-blind, parallel clinical trial was performed with patients undergoing coronary artery bypass grafting. The subjects were randomly divided into two groups: morphine group and methadone group. At the end of cardiac surgery, 0.1 mg.kg^{-1} adjusted body weight of methadone or morphine was administered intravenously. Patients were referred to the ICU, where the following was assessed: extubation time, time to first analgesic request, number of analgesic and antiemetic drug doses within 36 h, numerical pain scale at 12, 24, and 36 h postoperatively, and occurrence of adverse effects.
Results: Each group comprised 50 patients. Methadone showed 22% higher efficacy than morphine as it yielded a number-needed-to-treat score of 6 and number-needed-to-harm score of 16. The methadone group showed a mean score of 1.9 ± 2.2 according to the numerical pain scale at 24 h after surgery, whereas as the morphine group showed a mean score of 2.9 ± 2.6 ($p = 0.029$). The methadone group required less morphine (29%) than the morphine group (43%) ($p = 0.002$). However, the time to first analgesic request in the postoperative period was 145.9 ± 178.5 min in the methadone group, and 269.4 ± 252.9 in the morphine group ($p = 0.005$).

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Conclusions: Methadone was effective for analgesia in patients undergoing coronary artery bypass grafting without extracorporeal circulation.

PALAVRAS-CHAVE
Metadona;
Morfina;
Dor pós-operatória;
Cirurgia cardíaca

Comparação da analgesia pós-operatória com uso de metadona *versus* morfina em cirurgia cardíaca

Resumo
Justificativa e objetivos: A dor é fator agravante da morbidade e mortalidade pós-operatória. O objetivo foi comparar o efeito da metadona *versus* morfina quanto à dor e demanda de analgesia pós-operatória em pacientes submetidos à revascularização do miocárdio.
Método: Ensaio clínico randomizado, duplo-cego, em paralelo. Pacientes submetidos à cirurgia de revascularização do miocárdio foram randomizados por blocos em dois grupos: Grupo Morfina (Gmo) e Grupo Metadona (Gme). No fim da cirurgia cardíaca, 0,1 mg.kg^{-1} peso corrigido de metadona ou morfina foi administrado por via venosa. Os pacientes foram levados à UTI, onde foram avaliados o tempo até a extubação e a necessidade do primeiro analgésico, o número de doses necessárias de analgésicos e antieméticos em 36 horas, a escala numérica de dor em 12, 24 e 36 horas após a cirurgia e a ocorrência de efeitos adversos.
Resultados: Foram incluídos 50 pacientes em cada grupo. A metadona apresentou eficácia 22% maior do que a morfina com *Number Needed to Treat* (NNT) de 6 e *Number Needed to Harm* (NNH) de 16. Gme apresentou média de dor pela escala numérica em 24 horas após o procedimento de 1,9 ± 2,2 em comparação com o Gmo, cuja média foi de 2,9 ± 2,6 ($p = 0,029$). O Gme necessitou de menos morfina de resgate 29% do que o grupo Gmo 43% ($p = 0,002$). Entretanto, o tempo até a necessidade de analgésico no pós-operatório foi de 145,9 ± 178,5 minutos no Grupo Gme e de 269,4 ± 252,9 no Gmo ($p = 0,005$).
Conclusões: A metadona mostrou-se eficiente para a analgesia em cirurgias cardíacas de revascularização do miocárdio sem circulação extracorpórea.

Introduction

Longitudinal median sternotomy is the most commonly used incision for cardiac surgeries. Associated with the use of retractors, it is the best method for exposing the anatomical region.[1] However, the described method associated with an extended surgery time, places chest muscles under great tension and stress causing great pain to the patient in the postoperative period, which hinders deep breathing and reduces the elimination of secretions from respiratory tract that may trigger atelectasis and respiratory infections.[2]

Despite the advances in analgesic drugs, different routes of administration, and non-pharmacological techniques for pain relief, this is still considered an important postoperative problem and, to date, there is no standardized protocol in several hospitals. Among the options for postoperative management of cardiac surgeries are opioid analgesics and supportive measures.[3]

Currently, many institutions use intravenous opioids with high clearance and relatively short half-lives, such as morphine, that produce important fluctuations in serum opioid levels, ranging from inadequate analgesia to toxic values.[4] The option, in this case, would be intravenous infusion of analgesics, either on-demand or continuous infusion. Both methods, however, require high-cost apparatus.[3] Thus, an optional method that promotes continuous analgesia without the problems associated with infusion techniques would be the use of an agent with long half-life and low clearance applied intraoperatively, such as methadone. Methadone is a synthetic opioid of long duration and latency, used for several years in the treatment of drug addiction[5] and rediscovered as an analgesic for treating chronic pain,[6] cancer pain,[7] and also for postoperative analgesia, both in adults[8] and children.[9,10]

Methadone has an interindividual variation in pharmacokinetics as well as the potential to cause late toxicity due to its elimination half-life, which ranges from 8 to 59 h, making it difficult to handle that may be a problem, particularly in minor surgeries.[11] However, other studies have used methadone to control acute postoperative pain in short-duration surgical procedures, such as cholecystectomies.[12] Its multimodal profile contributes to postoperative pain management. The *R*(−) isomer of methadone has β-agonist activity, while its *S*(+) isomer is almost inactive at that receptor. However, this isomer has NMDA receptor antagonist activity. Consequently, there is synergism between the