Department of Anaesthesia and Intensive Care
The Chinese University of Hong Kong

INFORMATION SHEET FOR PATIENTS

Title of study
Intravenous methadone in perioperative acute and chronic pain management in Chinese adult cardiac surgical patients: a pilot feasibility trial

Principle Investigator:
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Background information
Chronic postsurgical pain (CPSP) after median sternotomy is not uncommon after cardiac surgery. The reported incidence ranges from 28% to 56% up to 2 years after surgery. Poorly controlled acute pain in the perioperative period can trigger central sensitization, which can lead to hyperalgesia and chronic pain. Good perioperative acute pain control not only provides postoperative pain relief, but also prevents occurrence of chronic pain. Opioids such as fentanyl and morphine are used mainly for the management of acute pain after cardiac surgery, either by intermittent boluses or through a patient-controlled device. The primary problem with this mechanism of delivery is that significant fluctuations in serum opioid concentrations can occur, resulting in effects which ranges from inadequate analgesia to overdose and respiratory depression. These peaks and troughs of analgesia that occurs with intermittent opioids administration may explain the suboptimal pain control during the initial postoperative period. Methadone is an opioid with rapid onset and the longest half-life of all clinically used opioids. A single dose administered on anaesthesia induction should provide significant pain relief up to 1-2 days postoperatively. Methadone is also useful pharmacologically in preventing chronic pain development, which is of high risk in cardiac surgical patients

Aim of the study
The aim of the study is to determine the potential for using intravenous methadone for acute and chronic pain management in adult cardiac surgical patients

Description of the trial procedures and assignment to treatments
Overview

A total of 86 patients (43 in each group) will participate in the study, all of whom will be patients having elective cardiac surgery and will be prospectively enrolled at Prince of Wales Hospital. There are two groups (Group 1 = intervention, Group 2 = control) in this study. Group 1 will receive single injection of methadone at induction of anaesthesia and Group 2 will receive an equipotent dose of morphine at induction of anaesthesia. There will be no difference in anaesthetic management between groups otherwise. You will be assigned into one of the two groups randomly. There is a 50:50 chance of each group which is determined by the allocation

Risks and discomforts

Intravenous methadone has been widely used in cancer pain treatment. It has also been described for sternotomy pain control in cardiac surgical patients. It is safe and rarely produces any major complications. The potential complications include drowsiness, pruritis, respiratory suppression, and remote association with cardiotoxicity and prolonged QTc. Full cardiovascular monitoring will be used during anaesthesia which further enhance the safety of the drug. The patient are followed up by the study investigators and pain team for postoperative 5-7 days for the potential side effects of methadone. The pain score will be reviewed on daily basis for analgesia regimen.
We do not expect any risks, other than those that have been discussed. We will ensure that the patient receives adequate and effective analgesia during surgery. There will not be any insurance liability arrangement for this study.

Data collection

The baseline demographics, medical history and perioperative surgical and anaesthesia record will be collected for study purposes. Perioperative blood samples will be taken at 0.5, 1, 2, 4, 8, 12, 24, 48, 72 and 96 hours after dosing to measure plasma level of the study drug. We will also collect the postoperative pain score and analgesia consumption record to study the analgesia efficacy of methadone. At 3 and 6 months after surgery, we will have phone follow-up for chronic postsurgical pain using standardized questionnaires.

Ethics approval

This study have been approved by The Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee (Tel. no: 3505 3935). You may also contact The Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee for enquiries about your rights.

Other information

You will be approached by one member of the investigating team regarding participation in the study to determine your eligibility. The investigator or investigating team member will have first checked your notes to check that you are suitable. Should you be eligible, the purpose of the study

and the potential risks and benefits will be explained and you will be given time to consider your participation. If you agree to participate, you will be asked to sign the informed consent form located at the end of this document. By signing the consent form you agree to participate in the study, undergo the randomization, and provide us a permission to extract some of your clinical and radiological data from your records. Your participation in the study will last 6 months after signing of the informed consent.

Your participation in this study is voluntary. You can freely choose to participate or not to participate. There will be no charge from you for the participation. One member of the investigating team will discuss this alternative with you. You have every right to withdraw before or during the study without penalty of any kind, and the quality of care will not be affected. Your data will be kept in strict confidence and will not be shared with anyone except with you consent or as required by law. The data, with identifying information removed will be securely stored in a locked office in the Principal Investigator's office and/or on secure password-protected computers. The research data and informed consent form will be kept for 3 years and access to data will be restricted to study investigators. If the results of the trial are published, your identify will remain confidential. For the purposes of ensuring the proper monitoring of the research study, it is possible that a member of The Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee, and/or other regulatory authority(ies), will be granted access to your research data and original medical records for verification of clinical trial procedures and/or data without violating your confidentiality to the extent that permitted by applicable laws and regulations. By signing the accompanying consent form, you authorize such access. According to the Personal Data (Privacy) Ordinance, you have rights for the protection of the confidentiality of your personal data. You also have the right to get access to your personal data we collected during your participation in the study. For any query regarding personal data protection, you may consult Privacy Commissioner for Personal Data or his/her office (Tel No. 2827 2823).

Further information or any problems

If you require further information or if you have any queries concerning this study project, you can contact the Principal Investigator, Dr Henry Man Kin Wong, telephone 3505 3984. If you have any complains about any aspect of the project, the way it is being conducted or any question about your rights as a research participant, then you may contact the Patient Relations Office at 3505 2433 or 2468 5111.

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Consent Form

I have read the information provided and understand the explanation including the randomization process of this study that has been given to me.

I agree to participate in this study and I give my full consent for my clinical and radiological data to be used for the purposes of this study.

I understand that The Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee is one of the authorized parties that can access my study records for the purpose of ethics review.

I understand that I will not receive payment for my participation.

I understand that there is no insurance liability arrangement for this study.

I understand the research data and informed consent form will be kept for 3 years and access to data will be restricted to study investigators.

I understand that I am also able to make an enquiry to The Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee regarding my rights in the study at 3505 3935.

I understand that I am able to contact Principal Investigator Dr Henry Man Kin Wong at 3505 2734 if I have any further questions.

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Name of Participant Signature of Participant Date

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Name of Investigator Signature of Investigator Date