

Original article

Safety Study about Continuous Intravenous Morphine Pumping for the Patients with Severe Cancer Pain and Cachexia

Jianyong Qin¹, Shusen Wang², Zhiqiang Du³, Guihong Liu³, Xiaofang Deng⁴, Changchun Xie⁵

1 Department of Oncology, The Liwan Hospital of Guangzhou Medical College,

2 Department of Medical Oncology, State Key Laboratory of Oncology in South China, Sun Yat-sen University Cancer Center,

3 Department of Oncology, The Second Affiliated Hospital of Guangzhou Medical College,

4 Department of ICU (Dr Deng), Tumor Hospital of Guangzhou Medical College, Guangzhou, PR China

5 Department of Anesthesiology, The Liwan Hospital of Guangzhou Medical College

Abstract

Objective: To evaluate the safety and effectiveness of continuous intravenous morphine pumping for the patients with severe cancer pain and cachexia. **Methods:** Forty-nine patients with severe cancer pain and cachexia were studied, who failed to the oral and transdermal opiates treatment. Before the study, we evaluate the NRS score and QOL score of the patients. Morphine was continuously infused intravenously via Volumetric Infusion Pump (syringe pump), and boluses of morphine were given until the initial signs of significant analgesia were detected. **Results:** In this study, little patients have severe adverse effect, no patient died from morphine related complications. All pains were relieved completely and QOL were improved significantly. **Conclusions:** Continuous intravenous morphine via Volumetric Infusion Pump is a safe and effective method to relieve severe cancer pain for the patients with advanced cancer and cachexia.

KeyWords: Cachexia; Severe Cancer Pain; Morphine; Safety; Pump

Cachexia is extremely common in the patients with advanced cancer, about 70% of the patients suffer from various pains. Because the patients with cachexia are in extreme exhaustion and associated with various medical complications, so they are often in critical condition. However the treatment of intravenous morphine is thought lead to be unsafe in these patients. The literatures showed that the needs of analgesic treatment for these patients didn't decrease. In clinical practice, we found that most of these patients have digestive dysfunction or skin disorders, the traditional analgesic treatments by oral or skin are poor effective in some patients. For this reason, we choose the patients with cachexia who are diagnosed as severe cancer pain to receive the continuous intravenous injection of morphine. In this study, we gained better clinical result, which is reported as follows.

Materials and Methods

Clinical data

Forty-nine patients with cancer were used in this study, who were inpatients in November 2004-October 2008 from Liwan Hos-

pital of Guangzhou Medical College. All were diagnosed by pathology and other clinical data is consistent with the pathological diagnosis. According to their weight loss, nutritional status, PS score and the expected survival of less than 1 month, they were diagnosed as end-stage and cachexia. These patients contain 27 male and 22 female, aged from 41 to 90 years old, average age is 73.4 years. Among the patients, 17 cases with non-small cell lung cancer, 7 cases with liver cancer, 14 cases with gastric cancer, 11 cases with colorectal cancer. All cases were in IV of TNM stage, PS score (ECOG standard) were 4; VAS score before treatment, 20 cases of 7 points, 13 cases of 8 points, 12 cases of 9 points, 4 cases of 10 points; including 35 cases with visceral pain, 11 cases with bone pain, 3 cases with other pain, so all patients have severe pain. After the detailed assessment we informed family members of patients that the advanced cancer patients need to be treated with the analgesic. The current treatment measures may result in unexpected change, so we asked the family members to sign the consent document of narcotic drug usage. In the study, other analgesic treatment is not used in all patients.

Drug and instrument

Morphine hydrochloride injections were provided by the Shenyang First Pharmaceutical Factory, Specifications: 10mg/1ml, 50mg/5ml, the drug is used without other analgesics

SP-500 syringe pump was provided by Japan JMS Co. Ltd, which largest volume is 60ml. Morphine in saline was used or replaced within 24 hours.

The diagnostic criteria for cachexia

Correspondence to: Professor Jianyong Qin, MD, oncology physician,
Department of Oncology, The Liwan Hospital of Guangzhou Medical College,
E-mail: chinese1man@foxmail.com.
Tel: +8620-81346533

Cancer cachexia is a common syndrome in patients with advanced cancer. According to weight loss, fatigue, loss of appetite, varying degrees of damage to organs, the patients were diagnosed as cachexia. All patients loss their weight more than 20% after disease, their blood albumin level were 11~22g/l, an average of 15.47g/l.

Pain assessment tools

Pain intensity was evaluated by Numerical Rating Scale (NRS), which requires patients to rate their pain on a scale of 0 (no pain) to 10 (worst pain).

0: no pain; 1 to 3: mild pain; 4 to 6: moderate pain; 7 to 10: severe pain.

The pain intensity was evaluated before treatment and in the third day after treatment.

Adverse effects

Observe all the possible side effects: respiratory depression, drowsiness, constipation, urinary retention, nausea and vomiting.

Adverse classification: mild: the rapid complete remission after treatment; severe: adverse effects may lead to death; the others as moderate.

Quality of life (QOL)

According to the guideline made in China in 1990, which refer to QOL of WHO, three main criteria were chosen as study index:

Appetite: ① almost can not eat; ② appetite <1/2 normal; ③ food intake about 1/2 normal; ④ food intake slightly less; ⑤ normal food intake.

Sleep: ① very difficult to sleep; ② difficult to sleep; ③ poor sleep; ④ sleep a little worse; ⑤ very satisfied.

Spirit: ① very poor; ② poor; ③ neither poor nor good; ④ good; ⑤ very good.

Results

The use of morphine

Initial dose is 50mg-200mg/d, an average of 98.76mg/d, initial rapid titration dose is 3mg-10mg, an average of 5.78mg, maintenance dose is 50mg-250mg/d, an average of 124.36mg/d. In most cases, we increased or reduced the dosage of morphine according to pain intensity. Total treatment time is from 3 to 28 days, an average of 12.19 days. There were 4 patients who reduced or stop the dosage of morphine before death.

Adverse effects

Respiratory depression happened to 1 of 49 patients, which is life-threatening and lead to apnea, finally the patient was rescued successfully. Later analysis reveals that respiratory depression was associated with the usage of sedatives and the patients suffered from chronic obstructive pulmonary emphysema too. Subsequently we reduced the dose of morphine and take intensive care, there was no accident of apnea in two weeks before death. Other adverse reactions includ drowsiness in 3 cases, constipation in 12 cases, and none of urinary retention, nausea and vomiting. All patients were in end-stage, whose ultimate death cause was not related to morphine drug.

Analgesia

Pain relief time in first treatment All pains were within 15 minutes after morphine bolus (rapid titration of morphine), NRS score fell below three points or less. Pains were relieved in 10 minutes by rapid titration of morphine in 48 patients (97.95%).

Effect of pain control All patients diagnosed as severe pain were 7 or more of the NRS score before treatment. The NRS score down to 3 points or less after treatment, of which 1 score or less were 42 (85.71%). The total treatment period of all patients were 672 days, in which there were 7 times of outbreak pain. But before treatment, the outbreak pains in all patient were more than 3 times a day each.

Evaluation of quality of Life After treatment, QOL of the patients had been significantly improved, as below:

Appetite score: 1.21 before treatment, 1.58 after treatment.

Sleep score: 1.39 before treatment, 4.78 after treatment.

Spirit score: 1.07 before treatment, 2.52 after treatment.

Discussion

The patients with advanced cancer often suffer from not only severe pain but also cachexia, they sometimes need the therapy of intravenous morphine. General infusion and speed-controlled infusion are difficult to control accurately the infusion rate, which lead often to various adverse reactions from overdose morphine, such as respiratory depression, apnea even death, we have to give up those kinds of treatment. Syringe pump, as a speed-controlled device, is used for intravenous injection of morphine, we use the rapid injection function of syringe pump to relieve the outbreak pain quickly. We believe that continuous intravenous morphine by syringe pump can be safely used in the advanced cancer patients with severe pain and cachexia.

The safety of continuous intravenous morphine treatment by syringe pump to the patients with cachexia

Respiratory depression is the main serious adverse events of morphine, which is sometimes life-threatening. In this study, a

life-threatening apnea happened to one patient who suffered from lung cancer, the patient was rescued to restore normal breathing finally, so no morphine-related death happened. The physiological function of the end-stage patient with cachexia is highly unstable, especially the patient with various organ dysfunction, so there is the danger of morphine poisoning in the continuous intravenous morphine treatment [1], especially when the blood gas analysis showed that lung function decompensation, or some sedatives were simultaneously used .

The detail talk with the patients family members is necessary before the treatment. The patient family should know that the morphine treatment can relieve severe pain, but may lead to various adverse effects. Doctor should understand the attitude from their relatives, and the family members should be invited to the signing of the consent of Narcotic Drugs Use.

Morphine also has some other adverse effects such as constipation, urinary retention and nausea and vomiting, which are more common and easier to be treated. Generally we made a preventive treatment, so a lower incidence in this study. Large doses of morphine can cause orthostatic hypotension and bradycardia, relatively rare, which did not happen in this study.

Effectiveness of continuous intravenous morphine treatment by syringe pump

Intravenous morphine is infused directly into the blood, of which about 1/100 can enter the central nervous system. Morphine produces the effect of analgesia, by the action to the third ventricle around, the neural structure from the end of the third ventricle to the tip of the fourth ventricle and so on. Continuous intravenous morphine via Volumetric Infusion Pump may maintain stable plasma concentration, and relieve outbreak pain rapidly by real-time dose at any time [2]. The disadvantage of continuous intravenous morphine is that it is invasive therapy [3], restrictions to walk. But the patients with cachexia often has been bed-ridden, the majority

of who were with a catheter in their deep vein. Therefore, continuous intravenous morphine is an efficient second-line analgesic method.

In this study, all patients gained complete pain relief within 15 minutes, and all have achieved a good therapeutic effect.

This study suggests that continuous intravenous morphine via Volumetric Infusion Pump may be safely used in the patients with advanced cancer and cachexia. To ensure the safety of the treatment, we need a detailed assessment before treatment, which contains the necessity and contraindications of intravenous morphine [4], and the function assessment of major organs. The end-stage patients often enter failure quickly, the assessment of NRS and adverse effects at least one time a day was need. If necessary, timely reduction, withdrawal or antagonist treatment should be carried out. Morphine, belonged to the controlled drugs in most countries, doctor should have the consent of the family before use. We should talk about its possible adverse reactions and please the family members to sign the consent of Narcotic Drugs Use. Pain treatment in end-stage is still in the scope of palliative care, is hospice care, not euthanasia.

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