

Case Report

Combination of Tramadol-Paracetamol in Palliative Care Pain Management: A Case Report

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ABSTRACT

One of the basic goals of palliative care is to reduce the suffering of the patient, which includes relieving the pain. Some facts show that sometimes a doctor is afraid to give opioid analgesic monotherapy to his patients because she is worried on one hand about the effect of addiction. In addition, in some cases, NSAID analgesics mono-therapy can also cause a series of side effects or even the patient may be contraindicated against the use of NSAID or paracetamol class drugs. Actually, this can be prevented by giving a combination of opioids and non-opioids analgesic. By providing this combination of therapy, it is hoped that this can accelerate the onset of work, extend the working period which can reduce the dose of drugs consumed, and more importantly minimize the side effects of each drug. The fixed dose combination of Tramadol-Paracetamol (Tramadol 37.5 mg–Paracetamol 325 mg) is an example of a drug combination preparation that has been shown to be effective in the treatment of pain. In this case report, a patient who is currently undergoing palliative therapy for cancer is described. On the way, the patient felt spinal pain as a result of the spread of the disease. The combination of Tramadol-paracetamol was administered twice a day with a dose that adjusted to the VAS Score observations before and after drug administration. And in this case, there was a decrease in the VAS score after being given Tramadol-Paracetamol combination.

Keywords: *analgesic combination, palliative care, Paracetamol, Tramadol*

Introduction

The management of palliative care in patients emphasizes on psychological, emotional, spiritual and social factors. Inadequate handling of pain suffered due to an advanced stage illness can certainly cause new problems for patients. The illness the patients suffer from will feel more severe because of the stress resulting from the pain that may be unbearable. This will certainly worsen the patient's quality of life.

Inappropriate handling of pain can make a patient's illness worsen and difficult to treat. This certainly affects the patient's quality of life. To overcome this, in addition to proper diagnosis and treatment of the underlying disease, providing analgesics to treat pain is needed. It aims to improve the patient's quality of life.

Pain management can be done by reducing various factors that cause pain, both peripherally and centrally. There are three classes of drugs used to inhibit the action of nociceptive afferent fibers, the first is the non-opioid type of analgesic (NSAIDs and paracetamol), the second is the opioid analgesic type (codeine and tramadol), and the last is the analgesic group that uses a local anesthetic (lidocaine).^{1,2,3}

Most types of analgesics have a limited dosage range to avoid unwanted side effects, such as liver damage due to paracetamol, gastrointestinal irritation, myocardial infarction due to non-steroidal anti-inflammatory drugs (NSAIDs), and also side effects in the form of constipation due to opioids.^{4,3} On the other hand, pain can be felt due to various underlying factors making it very difficult to get rid of pain optimally through mono-therapy / single administration of analgesics. Various studies have shown that analgesic combination can achieve better results because it is expected to reduce addiction, accelerate the onset of work, reduce side effects, and get a synergistic effect.³

Paracetamol and tramadol are a type of analgesic combination that is widely used to treat pain in various conditions, for example postoperative pain, osteoarthritis, low back pain, fibromyalgia, and other diseases.

Therefore, this case report will describe how the mechanism of action, therapeutic effects, benefits, and side effects of paracetamol and tramadol combination in optimal pain management.^{5,6}

Material and Methods

Mrs. SS, 52 years old who lived in Cipondoh Tangerang, Banten, was a patient suffering from Non Hodgkin's Lymphoma. She was one of the patients at the Dharmais Cancer Hospital referred from the Tangerang District General Hospital. She had undergone a supporting examination, in this case the Biopsy examination. From the results of these examinations, Mrs. SS was declared to be suffering from Diffuse Large Lymphoma type Non Hodgkin's lymphoma which was thought to have originated from the spread of the right tonsil. Apart from that, Mrs. SS was also examined for histopathological support. On histopathological examination, it was found that there was a long process of specification. From the results of the biopsy, the doctor concluded that metastases had occurred and spread to the spine.

Previously, Mrs. SS had undergone radiation therapy twenty-one times and chemotherapy eight times. During the course of her illness, Mrs. SS had several disorders she felt, such as skin disorders in the form of pressure sores, coughing, shortness of breath, impaired mobilization, eating disorders, lack of appetite, urinary incontinence, incontinence alvii, and paraplegia. Apart from these complaints, Mrs. SS also felt pain in her spine for several times.

The doctor then assessed the pain score felt by Mrs. SS using the VAS

(Visual Analog Scale) assessment. After the assessment, it was found that the pain felt by Mrs.SS was in VAS 5 (moderate pain). To reduce the pain felt by Mrs.SS, doctors who treat Mrs.SS have given analgesic therapy combination of Tramadol-Paracetamol (Tramadol 37.5 mg - Paracetamol 325 mg). Before giving the Tramadol-Paracetamol combination, the patient was examined first. Several types of examinations and assessments performed on patients include: examination of vital signs, and monitoring of changes in the pain score felt by the patient (VAS score).

The combination of Tramadol-Paracetamol (Tramadol 37.5 mg - Paracetamol 325 mg) was given twice a day (first at 09 am, and then at 09 pm). The drug effect was observed, whether or not there was a decrease in the VAS score, or it was persistent. If there was a decrease in the pain scale, then the next action was to reduce the dose of the Tramadol-Paracetamol combination. On the other hand, if the VAS score was judged to be persistent (no reduction in pain), the next step was to think about increasing the number of drug doses or changing the pain medication regimen.

After the first administration of the Tramadol-Paracetamol (Tramadol 37.5 mg - Paracetamol 325 mg) drug combination (at 09.00 am), observation for 2 hours. After 2 hours, at 11.00 am, a reassessment (by checking vital signs and determining the VAS score) showed significant results in reducing the pain felt by Mrs.SS. In this case, VAS score decreased to a score 2 (mild pain) at 2 hours after administering the Tramadol-Paracetamol combination (Tramadol 37.5 mg - Paracetamol 325 mg).

Mrs.SS then ran her homecare. Further evaluation on the physical and vital signs examination, showed the following results: Blood pressure 140/90 mmHg, respiratory rate 100 times / minute, chest circumference 72 cm, pelvic circumference 73 cm, and composmental

awareness. Two days later, at the next visit, the team of palliative doctors placed a catheter on Mrs.SS, so that the urine was not stored for a long time, which could lead to a long wound healing process. In addition, a reassessment of the VAS score was carried out, the VAS score was at VAS 2 and the patient admitted that the bone pain felt better and under control.

Results

Palliative care is a comprehensive integrated health care with an integrated multidisciplinary approach. The goal of palliative care is to reduce the suffering felt by the patient, extend his life, improve the patient's quality of life, and also provide support to his family. From this definition, it is found that one of the basic goals of palliative care is to reduce the suffering of the patient, which includes relieving the pain.

From the results of Mrs. SS case, the use of Tramadol-Paracetamol combination therapy (Tramadol 37.5 mg - Paracetamol 325 mg) can significantly reduce pain. The degree of pain was monitored using VAS score. In this case, there was a decrease in the severity of pain from VAS = 5 (moderate pain) to VAS = 2 (mild pain). This was as expected, where the reduction of pain felt by the patient can improve the quality of life in palliative care.

Discussion

One of the absolute principles in palliative care is to relieve pain and other disturbing complaints so that patients can avoid stress from the pain they suffer and improve the patient's quality of life. For this reason, pain management in palliative care is something that must be considered together.^{3,5}

Some doctors at this time still rarely use analgesics from the opioid class because of the dangers of addiction. This may result in a not optimal pain management. Many patients still feel pain

even though they have been given analgesic drugs from NSAID class or Paracetamol. Of course, in this case, the correct dose of opioid analgesic will help to relieve pain.⁴ This is also applied to patients who become intolerant of the use of paracetamol and NSAID analgesics due to the side effects of these various drugs.

In medicine, it is common to use opioid analgesics in combination with paracetamol, aspirin, or ibuprofen. The aim of combining analgesics with different mechanisms of action is none other than to reduce the dose of each drug component and to increase the analgesic effect without increasing side effects. Low doses of opioids that are less effective in mono-therapy when combined with non-opioid analgesics will produce an effective and relatively safe drug benefit.⁴

It has been shown that the combination of analgesics with rapid onset of action and duration of action for mild pain (paracetamol) and analgesics with long onset of action and duration of action for moderate pain (tramadol) do not have dangerous addictive effects and do not increase side effects.^{4,7,8}

Tramadol-Paracetamol is a rational combination because the pharmacodynamic (mechanism of action) and pharmacokinetic profiles (onset of action and duration of action) of these two drugs are different and also mutually beneficial.³ Paracetamol inhibits pain centrally by blocking the NMDA or substance P present in the dorsal horn of the medulla so that pain signals cannot be transmitted to the thalamus and cerebral cortex. Meanwhile, Tramadol works by occupying the μ receptors in the brain and inhibiting the uptake of norepinephrine and serotonin so that pain can be inhibited more strongly.

Paracetamol acts rapidly with an onset of action for about 20 minutes and its analgesic effect is achieved quickly but decreases rapidly.² In contrast, tramadol has a longer onset of action than paracetamol, which is 50 minutes, but its

analgesic effect lasts longer and decreases slowly. Thus, the combination of these two drugs has a fast starting action (17 minutes) and a long duration of action (5.03 hours).^{1,2,9}

The combination of Tramadol-Paracetamol (Tramadol 37.5 mg - Paracetamol 325 mg) does not cause harm to organs such as the digestive organs, kidneys and heart, so that it can be used as an alternative of analgesic drugs that act on selective cyclooxygenation-2 (COX-2) or non-selective NSAIDs. In addition, this combination of drugs can also reduce the dose of paracetamol so that the harm to the liver can be reduced.⁵ This drug also has no effect on platelets, does not suppress body immunity, safe for the elderly, and for long-term use.^{2,3} Although the combined price of the two drugs is more expensive than mono-therapy drugs, this combination of drugs will reduce the number of drugs that must be taken so that it creates comfort for patients (geriatric patients) who take various types of drugs every day.^{5,8,10}

Conclusion

The combination of Tramadol and Paracetamol (Tramadol 37.5 mg - Paracetamol 325 mg) in palliative care which works synergistically is proven to have a fast onset of action, a long working life, and minimal side effects. This combination is then suggested as an alternative analgesic therapy for patients with NSAID contraindications in dealing with moderate to severe pain.

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