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Case report

Ketamine infusion was effective for severe pain of Non-Hodgkin lymphoma

Tomoki Nishiyama

Department of Anesthesiology, Kamakura Hospital, 3-1-8, Hase, Kamakura, Kanagawa 248-0016, Japan

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ABSTRACT

A 52 years old man with a Non-Hodgkin lymphoma had severe pain at right buttock and lower leg. Sustained-release tablet of morphine 90 mg/day, intravenous morphine 40 mg/day, granisetron 9 mg/day, metoclopramide 30 mg/day, domperidone suppository 60 mg/day, intravenous hydroxyzine 25 mg/day, and haloperidol 20 mg/day did not decrease pain and side effects. Intravenous ketamine 10 mg in 15 min was quite effective for analgesia. Then infusion of ketamine started with 7 mg/h and increased to 10 mg/h with morphine 20 mg/day, which could control pain well with no side effects until his death.

1. Introduction

For cancer pain, opioids are usually used, but in many cases, tolerance to opioids leads to increases in the dose of opioids, which induce severe side effects. Then opioids become ineffective. Many reports showed that adding ketamine to opioids had good analgesia and decreased dose of opioids in cancer pain [13]. We also report a case whose cancer pain and side effects of opioids decreased with ketamine.

2. Case report

A 52 years old man with 169 cm in height and 68.8 kg in body weight was diagnosed as having Non-Hodgkin lymphoma. He had a history of fracture of left radius treated conservatively 7 years ago. He had hypertension without any treatment and allergy to mackerel. He had a smoking habit for 32 years with 25 cigarettes per day.

He developed Non-Hodgkin lymphoma, but remitted by chemotherapy 3 years ago. Ten months ago, he felt pain on right buttocks and lower leg, and 8 months ago his serum lactate dehydrogenase increased. Computed tomography 7 months ago showed tumor in the brain and T11 to L2 spinal cord, osteolysis of sacroiliac joint and swelling of adjacent soft tissue, and lymph node swelling in the upper mediastinum.

When he was admitted to the hospital, consciousness was clear, blood pressure was 158/88 mmHg, and heart rate was 74 beats/min. He had arthralgia in multiple joints, severe pain on right buttocks and lower leg (L2-S1 dominant region), and light numbness on the upper and lower limbs on both side. Laboratory data showed pancytopenia (WBC 4510/L, RBC 234 æ 10^4/L, Platelet 4.8 æ 10^4/L), liver damage (AST 246 IU/L, ALT 331 IU/L, LDH 6660 IU/L), electrolyte imbalance (Na 127 mEq/L, K 5.6 mEq/L, Cl 82 mEq/L), increases in C-reactive protein (84 mg/L), fibirin/fibrinogen product (29.6 g/L) and D-dimer (24.8 g/L).

He was treated with irradiation; 30 Gy to the brain and 30 Gy to the right buttock and lower leg, and chemotherapy for lymphoma in the department of internal medicine. His right buttock and lower leg pain was rated as 6 to 7 (visual analogue scale (VAS) shown between 0 and 10 cm), arthralgia was 5, and numbness of upper and lower limbs were 4. Loxoprofen 180 mg/day p.o., diclofenac suppository 150 mg/day, and intravenous pentazocine 30 mg/day were administered. His pain did not change, then sustainedrelease tablet of morphine was started with 20 mg/day on the next day and increased to 30, 60, and 90 mg/day on the 3rd day of his admission. On the 4th day, intravenous morphine was added with 20 mg/day, increased to 30 mg/day on the 5th day and 40 mg/day on the 6th day. For nausea, intravenous granisetron 9 mg/day was started on the 2nd day, intravenous metoclopramide 30 mg/day was added on the 3rd day, and domperidone suppository 60 mg/day on the 4th day. For sleep disturbance, intravenous hydroxyzine 25 mg/day was started on the 2nd day, and intravenous haloperidol 5 mg/day was added on the 3rd day and it was increased to 20 mg/day on the 4th day.

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E-mail address: nishit-tky@umin.ac.jp

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Once his pain and numbness decreased to 45 (VAS) on the 3rd day, but increased to 89 on the 6th day again, then he was consulted to our department for pain relief.

We administered intravenous ketamine 10 mg in 15 min, then his pain decreased to 12 (VAS) and numbness decreased to 23. We started ketamine infusion at 7 mg/hour and increased to 10 mg/hour on the 1st day. Morphine infusion was decreased to 20 mg/day. Pain became 1 (VAS) on the 1st day and disappeared on the 3rd day and numbness had been 2 (VAS). Nausea and sleep disturbance disappeared. We continued intravenous ketamine 10 mg/day and morphine 20 mg/day. He died on the 10th day without any pain and side effects.

3. Discussion

As our present case, many reports showed that ketamine had analgesic effects on opioid tolerant cancer pain. Fine reported [1] a case with neuroectodermal tumor for whom single intravenous ketamine 0.2 mg/kg decreased opioid infusion to 50%. A case reported by Clark and Kalan [2] had a severe cancer pain tolerant to morphine, which was controlled with morphine 1000 mg/h, ketamine 200 mg/h and midazolam 12 mg/h until his death. Subcutaneous ketamine 150 mg/day provided good analgesia and could decrease oral morphine 5 g to 200 mg/day for neuropathic cancer pain [3]. Ketamine infusion at 320 mg/h [4] or subcutaneous ketamine at 2.515 mg/h [5] was effective for severe cancer pain. Ketamine was reported to be started with small doses such as 5 10 mg bolus or infusion at 0.10.2 mg/kg/h [2]. Therefore, we first administered ketamine 10 mg bolus, then started infusion of 7 mg/h.

This patient had hypertension, but no treatment was necessary. Ketamine usually increases blood pressure. However, the dose of ketamine administered was quite small, therefore, his blood pressure did not increase.

Ketamine is a non-competitive NMDA receptor antagonist and enhances opioid-induced antinociception [6], reduces hyperalgesia and prevents the induction of opioid tolerance [7]. Ketamine might be an antagonist at receptor and an agonist at receptor. Therefore, ketamine antagonizes morphine tolerance. Analgesic effects of ketamine involve descending inhibitory monoaminergic pathways [8], and an interaction with cholinergic, adrenergic and serotonin receptors [9]. Ketamine also has a direct action on the dorsal horn of the spinal cord [10]. Ketamine prevents action potential conduction through sodium and potassium channels in nerve membranes and it has local anesthetic effects [8]. These wide varieties of mechanisms of analgesia for ketamine enable it to provide strong analgesia for cancer pain.

Our case had severe side effects with morphine, therefore, we could not increase the dose of morphine and added ketamine although dose of morphine was still quite smaller than other reports [2,3].

Ketamine induces side effects such as sedation, somnolence, dissociative feelings, blurred vision, delirium, and abdominal pain. Benzodiazepines or neuroleptics decrease psychotomimetic side effects of ketamine [11]. We did not use any benzodiazepines or neuroleptics. However, the infusion dose of 7 mg/h was less than the safety starting dose of ketamine reported as 0.5 mg/kg/h [12], therefore, side effects were not observed.

In conclusion, ketamine 710 mg/h could decrease severe pain of Non-Hodgkin lymphoma and could decrease the dose of morphine without any side effects.

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