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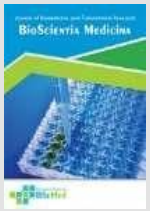

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Free Opioid Anesthesia in Cancer Patient Undergoing Total Thyroidectomy and Functional Neck Dissection Dextra: A Case Report

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A B S T R A C T

Background: The use of large doses of opioids perioperatively has been found to be associated with early recurrence in patients undergoing surgery for primary cancer. This study aimed to describe the use of opioid free anesthesia in cancer patients. **Case presentation:** A 72-year-old man with a diagnosis of papillary adenocarcinoma thyroid underwent total thyroidectomy and dextra functional neck dissection. The results of the preoperative assessment stated that the patient had ASA III physical status and would undergo general anesthesia (GA-OTT) and regional anesthesia peripheral nerve block (RA-PNB BPSS). **Conclusion:** Nonopioid regimens are recommended for pain control in the perioperative and postoperative periods in some cases. The application of free opioids can reduce opioid dependence in patients who routinely receive opioid prescriptions after discharge.

1. Introduction

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells. The innate and adaptive immune systems provide important protection against pathogenic organisms and cancer. Cancer immunosurveillance involves natural killer (NK) cells which have the inherent capacity to recognize and kill tumors via cell surface molecules. Secretion of immunoregulatory cytokines and actions of a subset of white blood cells (lymphocytes), which control and regulate anti-tumor immunity or recognize and kill transformed cells ('cytotoxic' T cells or CD8þ T cells).[1,2]

The intraoperative period is the most critical time during which surgical stress, anesthesia, and many other perioperative factors influence cancer prognosis by stimulation of the hypothalamic-pituitary axis and sympathetic nervous system and release of mediators that lead to immunosuppression. These mediators promote the proliferation of liberated remnants of tumor cells and thus can give rise to metastasis and lead to recurrence. The use of large doses of opioids perioperatively has been found to be associated with early recurrence in patients undergoing surgery for primary cancer.[3,4]

Opioids can inhibit cellular and humoral immunity, enhance angiogenesis, and stimulate tumor cell proliferation in vitro.[5,6] Opioids suppress natural killer cells, cytokine and antibody production, and phagocytic activity. Perioperative natural killer activity plays an important role in determining the outcome after cancer surgery because they are the main

defense against cancer cells. Opioid-induced suppression of NK cell numbers in humans was found to be prolonged in the postoperative period. The beneficial effects of free opioids have been widely reported in colorectal and breast cancer surgery. This study aimed to describe the use of opioid-free anesthesia in cancer patients.

2. Case Presentation

A 72-year-old man with a diagnosis of papillary adenocarcinoma thyroid underwent total thyroidectomy and dextra functional neck dissection. The results of the preoperative assessment stated that the patient had ASA III physical status and would undergo general anesthesia (GA-OTT) and regional anesthesia peripheral nerve block (RA-PNB BPSS). In this patient, several examinations were carried out, namely a complete blood count, coagulation profile, clinical chemistry, electrolytes, thyroid function examination, chest X-ray, CT scan, and electrocardiogram (ECG). In a complete blood examination, what is important to pay attention to is the number of hemoglobin levels, which is found to be within normal limits.

Considerations for the selection of anesthetic techniques in these patients are based on the type of surgery performed. The analysis of surgery or surgery in this patient is (1) the location of the operation, in this patient, the operation will be carried out in the area of the head, neck, and upper abdomen; (2) surgical manipulation, which in this case requires optimal operating field relaxation, deep anesthesia, and well-controlled pain. Intraoperative management of this patient starts from the reception room. The patient was premedicated with dexamethasone, ketamine, midazolam, and ketorolac. Administration of ketorolac, dexamethasone, and sub-dose ketamine provides the benefit of preemptive analgesia in patients.[7] Midazolam acts as an anxiolytic agent that can provide a sense of calm to the patient.

In preparation for surgery in the operating room, the patient is positioned supine. Then, do the installation of intraoperative monitoring such as blood pressure, oxygen saturation, ETC O_2, EKG, and Q-con. As a first step, start the induction process with dexmedetomidine, propofol, $MgSO_4$, and lidocaine. In the first patient, the dose was reduced because the patient is a geriatrician. Dexmedetomidine is an ideal agent for OFA because of its beneficial pharmacological features, including sedation, hypnosis, anxiolysis, sympatholysis, and analgesia. The patient was then intubated. During intubation, there is an increase in heart rate that does not exceed 20% and an increase in MAP that does not exceed 10%. The patient was then carried out intraoperative maintenance with ketofol with a mix ratio of 1:1, namely 1 mg of propofol mixed with 1 mg of ketamine and run via a syringe pump at a speed of 50-100 mcg/kgbb/hour, atracurium 0.1 mg/kgbb intermittently every 30-45 minutes and dexmedetomidine 0.5-0.7 mcg/kg/hour.

When monitoring patients with Q-Con 40-45, obtained an average blood pressure with MAP of 65 mmHg and a stable heart rate at 60-65 beats/minute. During the intraoperative, paracetamol 1 gram IV was added. Postoperatively, the patient received analgesia in the form of a combination of lidocaine and ketamine, paracetamol, diclofenac sodium, and ibuprofen. The NRS of the patient during the 2 days of treatment was 0 out of 10.

3. Discussion

Opioid-free anesthesia (OFA) was developed with the aim of avoiding the negative effects of opioids intraoperatively, postoperatively, and also on the physiology involved during surgery.[8] Hemodynamic stability with opioid analgesia is achieved by blocking the neurotransmitter enkephalin. Several other neurotransmitters, such as glutamate, noradrenaline, gamma-aminobutyric acid, and serotonin, are also involved in the regulation of heart rate and blood pressure, which may suggest other pharmacological agents acting on pain pathways.[9]

Intraoperative and adjuvant nonopioid analgesics such as lidocaine, α2 agonists, beta-blockers, magnesium sulfate ($MgSO_4$), ketamine,

dexamethasone, gabapentinoids, nonsteroidal anti-inflammatory agents, and paracetamol (acetaminophen) were found to suppress increases in heart rate and blood pressure. Sympathetic attenuation can be achieved by direct action of α2-agonists or beta-blockers and indirectly by $MgSO_4$ or lidocaine. Multimodal approaches that target multiple points of the pain pathway with 2 or more non-opioid adjuvants should provide additive or synergistic effects, allowing the reduction of side effects from each while maintaining hemodynamic stability.[8-10]

A meta-analysis showed that perioperative use of systemic α2 agonists resulted in reduced postoperative pain intensity and opioid consumption without prolonging recovery time.[10] administration of dexmedetomidine has a good effect, especially if the patient has comorbid obesity. Magnesium is an N-methyl-D-aspartate (NMDA) receptor antagonist in addition to its effect on calcium influx. Its anti-inflammatory and opioid-sparing effects make it a popular component of OFA. It is widely used for perioperative analgesia at a dose of 30-50 mg/kg intravascular bolus followed by an infusion of 10-15 mg/kg/hour. In this patient, we did not use magnesium continuously to avoid side effects. The analgesic effect of lidocaine is dose-dependent. A dose of 5 mg/kg of lidocaine over 30 minutes will provide a consistent analgetic response. Administration of low-dose intravenous lidocaine (with plasma concentrations below 5 μg/mL) can reduce the incidence of pain due to tissue damage without disturbing normal nerve conduction, and the incidence of side effects is low.[11,12] By administering these drugs, the patient's Q-con is obtained at 40-45. A value of 40-45 is a value indicating that the anesthesia was adequate.

Acetaminophen (paracetamol) is a known non-opioid analgesic whose mechanism of action is not fully understood. In general, acetaminophen is accepted as a centrally acting agent. The level and amount of active drug in the CNS determines the analgesic effect of this drug. It is a cyclooxygenase inhibitor, and its effect interacts with the serotonergic system. The effect of acetaminophen on hemostatic function is minimal and is always preferred as a non-opioid analgesic for patients with contraindications to NSAIDs.[13-14] Peripheral nerve block (PNB) is a local anesthetic technique that has been proven effective in the management of intra and postoperative pain. This technique has also been shown to be effective in reducing the use of opioids and the length of stay postoperatively.

Hemodynamic monitoring in these patients showed stability in which there was no sudden increase or decrease. Proper intravascular volume management is essential to avoid over and under-fluid administration. Because of increased afterload, decreased inotropic or chronotropic response, and impaired vasoconstrictive response, the elderly patient is highly dependent on adequate preload.[14] This patient was given fluids in the form of Ringer's lactate according to the patient's needs.

Management of acute postoperative pain is especially important in surgical patients, where postoperative pain can produce harmful effects. If pain control is not carried out, where pain itself can stimulate the sympathetic nerves, which will have an impact on increasing heart rate, then this will aggravate the heart's performance. This can increase morbidity and mortality, especially in elderly patients with one of the comorbid diseases, such as ischemic heart disease.

Postoperative pain affects recovery time and patient quality. The ERAS protocol is designed for rapid recovery after major surgery, supports organ function, and reduces the stress response caused by surgical trauma in cancer patients.[9] One of the main components of the ERAS protocol is postoperative pain control, and multimodal analgesia may be the optimal modality for this purpose. The rationale for multimodal or balanced analgesia strategies is the achievement of excellent analgesia because of the additive or synergistic effects of different non-opioid analgesics.

4. Conclusion

Postoperative monitoring showed that the patient was pain-free, and continuous administration of ketamine also gave satisfactory results without nightmares or hypersalivation in this patient. Non-opioid regimens are recommended for pain control in the perioperative and postoperative periods in some cases. The application of free opioids can reduce opioid dependence in patients who routinely receive opioid prescriptions after discharge.

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