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The Effectivity of Ondansetron and Dexamethasone Combination as Post-Operative Nausea and Vomiting (PONV) Prophylaxis after Total Abdominal Hysterectomy and Bilateral Salpingo-Oophorectomy (TAH-BSO) Procedure at Mangusada General Hospital, Bali, Indonesia

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Abstract: ***Introduction: Post-operative nausea and vomiting (PONV) can be a devastating and traumatizing condition following a surgery. Risk stratification and proper prophylactic management are required to prevent PONV, particularly in high-risk patients. Case Report: A 46-year-old female with ASA II and simplified Apfel score of 3 underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO) under spinal anesthesia.4 mg of ondansetron and 5 mg of dexamethasone were administered at induction. After the procedure, the patient went stable and moved to be treated at the ward for 3 days. No nausea and vomiting were observed until the patient was discharged. Conclusion: In this case report, the combination of ondansetron and dexamethasone were sufficient to prevent PONV after TAH-BSO procedure.***

Keywords: PONV, dexamethasone, ondansetron, TAH-BSO

1. Introduction

Post-operative nausea and vomiting (PONV) is defined as nausea and/or vomiting which occurs during the first 24-48 hours after surgery. Along with post-discharge nausea and vomiting (PDNV), they make up one of the most common side effects of surgery and anesthesia. It is estimated that the incidence of PONV is found in up to 30% of general surgical population, and even higher, up to 80% for high-risk population. [1–3]Approximately 14 to 21 million cases of PONV are recorded annually in the United States. The incidence of PONV in Indonesia is not well recorded, but it is projected that PONV can be seen in 20-30% of surgeries performed in Indonesia. [4]Although PONV alone usually do not cause mortality, but it can trigger a morbidity cascade of longer post-anesthesia care unit (PACU) length of stay, electrolyte imbalance, unplanned admissions, delay of return to the normal activities of daily living, and increased medical costs. [1, 2]

Major gynecologic surgeries, including hysterectomy, carry high incidence of PONV. The etiology of PONV in gynecologic surgeries are not fully understood, but it is attributed to residual pneumoperitoneum after carbon dioxide insufflation and positional changes. In addition, several factors may contribute in the increased risk of PONV in gynecological surgeries, such as the use of intraoperative volatile agents, opioids, and phase of menstrual cycle. Some studies suggest that the incidence of PONV may be as high as 92% of every gynecological surgeries performed. [5, 6]

Guidelines of PONV management stratified risk factors for PONV, in which four groups of risk factors are addressed: patient-specific, anesthetic, surgical, and type of surgery risk factors. Female gender is one of the most found risk factor for PONV. In addition, specific gynecological surgeries are found to put patients more at risk for PONV. Prior to surgeries, every patients are assessed for PONV risk factors to inform and guide therapy. Apfel and Koivuranta scores are mainly used to assess patients for PONV risk factors. [3] The Apfel simplified risk score is based on four predictors: female sex, history of PONV and/or motion sickness, nonsmoking status, and use of postoperative opioids. The incidence of PONV with the presence of 0, 1, 2, 3, and 4 risk factors is approximately 10%, 20%, 40%, 60%, and 80%, respectively. Patients with 0-1 Apfel score is considered having low risk of PONV, 2 Apfel score as medium risk, and 3-4 score as high risk. [7]

According to management algorithm for PONV guideline, medium risk patients are advised to be given up to two interventions to prevent PONV. Combination therapy for PONV prophylaxis is preferable to using a single drug alone. Antiemetics working on different receptors can work synergically to prevent PONV. [7]

2. Case Report

We report one 46 years old female diagnosed with uterine myoma scheduled for total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO) laparotomic surgery in Mangusada General Hospital, Bali-Indonesia. The patient presented with excessive and prolonged menstruation accompanied with fatigue for two months. History of nausea and vomiting were denied.

Physical examination showed blood pressure of 123/70 mmHg, pulse pressure of 82 beats per minute, respiratory rate of 20 times per minute, axillary temperature of 36.0^{o}C, GCS was $E_4V_5M_6$. Anemic conjunctiva, icteric sclera, dry

oral mucosa, distended abdomen, and cold extremities were not found. Laboratory examination five days prior to surgery showed hemoglobin of 10.6 g/dL, hematocrit 36%, white blood cells 20.01 x 10^3/uL, platelets 250 x 10^3/uL. Liver and renal function test appeared to be normal. Random blood glucose was 79 mg/dL. Bleeding time was 1.5 minute, clotting time was 11 minutes. ECG showed normal sinus rhythm. Chest X-ray suggested bronchitis and cardiomegaly.

Patient was assessed with ASA II physical status, proceeding with spinal anesthesia (subarachnoid block). The patient was given 4 mg of ondansetron, 2 mg of midazolam, 5 mg of dexamethasone, and 5 mg of diphenhydramine intravenously. Subarachnoid block was planned to be done using midline approach. The patient was positioned right lateral decubitus with log-roll technique, followed by bupivacaine 0.5% 10 ml. Pain prick and anamnesis technique were used to assess hyperesthesia on sensorics block area. After the anesthesia was administered, the operating personnel proceed with the procedure.

The surgery lasted for two hours. Hemodynamic of the patient was stable during the surgery, with systolic blood pressure ranging from 110-140 mmHg, diastolic blood pressure ranging from 60-90 mmHg, pulse rate ranging from 60-80 beats per minute. Bleeding of ± 300 ml was measured, urine output was ± 300 ml, 1000 ml of ringer's lactate was given intraoperatively.4 mg of ondansetron and 5 mg of dexamethasone were given intravenously for PONV prophylaxis. Analgesia of fentanyl 175 mg and ketorolac 60 mg in dextrose 5% 24-28 micro drops per minute was given.

After the procedure, the patient was transported to recovery room for observation of risk and complications following the procedure. The patient went stable and returned to the ward. The patient was hospitalized for three days after the procedure, with no PONV reported.

3. Discussions

The patient has presumably normal physical examination, except for the anemia condition due to the abnormal uterine bleeding. Before the procedure, the patient had to undergo 2 units of packed red cells transfusion. Therefore, the patient was assessed with ASA II physical status. [8]

Apfel simplified score is commonly used to identify risk factors for PONV. Apfel simplified score is based on four predictors: female sex, history of PONV and/or motion sickness, nonsmoking status, and use of postoperative opioids. The incidence of PONV with increases in every presence of risk factors: approximately 10%, 20%, 40%, 60%, and 80% with the presence of 0, 1, 2, 3, and 4 risk factors, respectively. [3] This patient had Apfel simplified score of 3, attributable to three risk factors found: being female, non-smoker, and the use of post-operative opioids (fentanyl). Therefore, this patient is categorized as "high-risk" patient. This patient possessed an approximately 60% increased risk of developing PONV.

An algorithm of PONV management was established to guide anesthesiologists to manage PONV. The algorithm consists of five steps: identifying risk factors, mitigating risks, risk stratification, initiation of prophylaxis, and preparing for rescue treatment. Referring to the algorithm, three to four agents are recommended for patients with two or more risk factors. Recent guidelines recommend the use of multimodal prophylaxis for PONV. The first line of PONV prophylaxis is 5-HT_3 receptor antagonists, corticosteroids, and anticholinergics. For adults, several 5-HT_3 receptor antagonist mediations can be used, including ondansetron, palonosetron, ramosetron, granisetron, and tropisetron. However, ondansetron remains the drug of choice for PONV prophylaxis. For corticosteroids, dexamethasone is superior to other corticosteroids. The only anticholinergic medications recommended for PONV prophylaxis is transdermal scopolamine because of its mild adverse events compared to other anticholinergic medications used for PONV prophylaxis. [3]

Due to limited resources available in Indonesia, including our center, this patient only received double therapy for PONV prophylaxis consisting of 4 mg of ondansetron and 5 mg of dexamethasone given intravenously. Transdermal scopolamine patch was not available in our center. Regardless, no PONV was observed until the patient was discharged. Although three or more medications are recommended for patients at high risk for PONV, several studies are suggesting that two medications which have different mechanism of actions is sufficient. One randomized control study reported that combination of ondansetron and dexamethasone alone was able to prevent >80% of PONV cases in high-risk patients: the ones undergoing abdominal hysterectomy. [9] Earlier guidelines report that each independent medication used for prophylaxis can reduce PONV risk by 25%, [7] therefore the use of two medications are able to reduce PONV risk by 50%, leaving high-risk patients for 10% risk of PONV after gynecological surgeries. Another studies also report that there is no significance difference in severity of nausea and vomiting for those receiving transdermal scopolamine and the control group. [5, 10] One study reported case series in which transdermal scopolamine causes numerous side effects intraoperatively, the most serious being central anticholinergic syndrome, characterized with delayed emergence from anesthesia. Removing the transdermal scopolamine resulted in resolution of all the cases. [11]

Changes in gastrointestinal tract physiology and mechanics, such as surgical techniques and procedures that are attributable to stomach manipulation can cause increased intra-abdominal pressure, leading to an increased risk of PONV. Gynecological procedures, including TAH-BSO can lead to alteration gastrointestinal physiology and mechanics. [1] Several studies report that ondansetron and dexamethasone combination therapy are able to prevent PONV from gynecological procedures. [12, 13] The exact mechanism of how ondansetron and dexamethasone synergically act to prevent PONV from gynecological procedures remains unknown.

In contrary with the results in the abovementioned studies, some studies showed significant reduction of PONV in patients receiving triple therapy of ondansetron, dexamethasone, and transdermal scopolamine. [2, 14] However, these studies involved patients undergoing craniotomy procedure: a procedure mostly done with general anesthesia

and with an increased risk in elevated intracranial pressure, both being significant bias to the etiology of PONV. Several studies are still needed to determine the efficacy of triple therapy of PONV prophylaxis to prevent PONV especially in gynecological procedures.

4. Conclusion

PONV can be a distressful event for every patient undergoing any surgical procedures, especially for high-risk patients. Multimodal prophylaxis regiments are recommended for PONV prophylaxis. However, in resources-limited settings, a combination of only two prophylactic medications were sufficient to prevent PONV. However, further studies are still needed to determine the efficacy of an additional modality to prevent PONV, particularly in gynecological procedures.

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