

CHAPTER 5

DISCUSSION

Postoperative nausea and vomiting (PONV) are among the most common adverse events related to surgery and anesthesia. Although the medical impact of PONV is minor, it can disturb the patients and sometimes causes major problems (58). In addition, from the patients' perspective, PONV is undoubtedly distressing. Surgical patients reported the fear of suffering PONV more than the fear of postoperative pain(3).

Several factors are known to provoke PONV. These include age, weight, sex, together with the individual's predisposition to motion sickness and previous experience of PONV(4). An opioid premedication has been shown to lead to increase in nausea and vomiting after operation(59). Various anesthetic agents and techniques have also related. Other factors such as the presence of hypotension, postoperative opioid use, pain and mobilization have been implicated as well(59). The above factors were comparable in each group in this study.

In this study , the incidence of PONV in placebo group was 61.1% confirming previous study, which reported about 45-75% after spinal anesthesia with intrathecal morphine in arthroplasty patients(1). We are able to demonstrate that the incidence of PONV in ginger group and placebo group were statistically significant different (p -value= 0.021). Ginger was efficacious in preventing PONV. The result was confirmed by absolute risk reduction equaled to 22% with confidence interval from 3.6% to 40.4%. Primary outcome in the present study considered the incidence of PONV in the first 24 hours after operation because we interested in the effect of ginger

on both nausea and vomiting. Both nausea and vomiting can make the patients suffer. Either nausea or vomiting was considered bad outcome. However, nausea and vomiting are biologically different phenomena and nausea is not a little vomiting(60). Nausea is the subjective sensation of a desire to vomit, while vomiting is a complex reflex from the central autonomic and motor system, which leads to a forceful expulsion of gastrointestinal contents through the mouth. Consequently, nausea and vomiting were also reported and analyzed separately. In this study, no patient vomited without nausea, so the incidence of nausea was the same as that of PONV. Thus, ginger was more efficacious than placebo in preventing nausea as well with the same absolute risk reduction, confidence interval, and p-value. In contrast, the incidence of vomiting in ginger group was less than that in placebo group (27.8% VS 44.4%) but the difference was not statistically significant different (p-value = 0.071). We concluded that ginger had more anti-nausea effect than anti-emetic effect. However, the sample size might too low to detect the difference in anti-emetic effect. Emetic episode per patient could confirm that anti-emetic effect of ginger was less pronounced. There was no statistically significant difference between both groups according to emetic episode per patient. Considering the period of symptom, the incidence of PONV , nausea , and vomiting at the different periods ; intraoperative, 0-6 hour postoperatively, 6-24 hour postoperatively were lower in ginger group, but there were not statistically significant different. Again, the sample size might too low to detect the difference. The observed incidences of PONV in both groups at intraoperative period were equal. The possible reasons were 1) the drug did not reach the peak of action at that time, 2) the incidence of PONV at this period was very low, so that the sample size might too low to detect the difference, 3) there were any other related factors such as stress , and particularly hypotension after spinal anesthesia, that ginger might not be able to prevent PONV from this mechanism.

Considering the severity of nausea, the percentage was high at score= 0 or no nausea and tended to lower in higher score in ginger group. Patients who received ginger were found to have lesser severity of nausea than those who received placebo (p-value = 0.033).

There were a few studies reported the effect of ginger in prevention of PONV. All of these studies observed in gynecological patients after general anesthesia. The present study considered PONV after intrathecal morphine. There was no study observed the effect of ginger in prevention of PONV after this kind of anesthetic technique. Bone and colleagues (24) compared the effect of ginger with placebo and metoclopramide in gynecological patients and found that ginger significantly reduced the incidence of postoperative emetic sequelae compared to placebo and had the same effect as metoclopramide. In the same way, Phillip et al (33) reported that the incidence of nausea and vomiting was similar in patients given metoclopramide and ginger and less than in those who received placebo. The present study confirmed the aboved studies. In the contrary, Arfeen and colleagues (48) reported negative study of ginger in laparoscopic gynecological surgery. Yet the incidence of nausea and vomiting was monitored 3 hour after surgery. In the current study, we found that the period that had highest incidence of PONV was 0-6 hour postoperatively. Only 3 hour observation might not be adequate. The first 3 hour might have too low incidence to detect the difference or ginger might not reach the peak action yet .

Visual analogue pain scores were varies from minimum (score=0) to maximum (score=10) in both groups but they were normally distributed , which mean SD equaled to 3.68 ± 2.63 in ginger group and 3.61 ± 2.33 in placebo group. Most patients rated low pain except two in ginger group and one in placebo group who rated score 10. The reason that the patients scored such a high pain score may be the fact that we assessed at 24 hour after operation , which spinal morphine might wear off in some cases. However, pain could relieve by oral paracetamol. No patient needed more potent analgesia. Furthermore, the requirement rate of analgesia in both group were not

statistically significant different. Therefore, ginger was not found to have analgesic effect compared to placebo, which not supported the action of (6)- shagaol on substance P containing primary afferents of rat that had been suspected to be responsible for the analgesic effect of ginger (61).

Regarding prevention of PONV, the issues of side effect and NNT are also of great importance. There were seven patients who had urinary retention, one in ginger group and six in placebo group. Urinary retention is the side effect of spinal morphine. No patient complained either pungent smell or heart burn after ingestion. No other side effect was noted in the current study.

The pronounced effect of ginger on PONV observed in this study resulted in a NNT of 5, with 95% confidence interval from 2 to 28. This indicated that ginger prevented PONV in one of every five patients exposed to ginger. Compared to ondansetron, Tramer and the colleagues (21) reported in the systematic review that the best number needed to treat to prevent PONV with the best recommended regimens of ondansetron was between 5 to 6 . Yet ondansetron significantly increased the risk for elevated liver enzymes (number needed to harm was 31) and headache (number needed to harm was 36). Ondansetron is also very expensive. In the systematic review, Henzi and the colleagues(19) reported that the number needed to treat to prevent early nausea with droperidol in adult was 5, the number needed to harm for extrapyramidal symptoms in children was 91 and in adult was 408, and the number needed to harm for sedation and drowsiness was 7.8. Surprisingly, metoclopramide, although used in clinical practice for almost 40 years, did not show any clinically relevant anti-emetic efficacy when used for prevention in the usual dose (10 mg in adult)(20). Thus, when comparing the efficacy to the low side effect and cost, ginger is worth in prevention of PONV in this type of surgery and anesthesia.

However, this study was limited to study only in lower extremity surgery. The result might have differed in other types of surgery, particularly in intraabdominal surgery. In the other word, postoperative nausea and vomiting in the present study is

mainly the result of intrathecal morphine, whereas that in the other types of surgery and anesthetic techniques has multifactorial mechanisms.

Ginger has been shown to be effective in prevention and treatment of nausea and vomiting such as motion sickness, hyperemesis gravidarum(11), chemotherapy-induced nausea(12). Although the active ingredients have been identified, the mechanism has not clarified. In addition, the use of ginger as an antiemetic is limited at present, because no parenteral preparation is available. To be acceptable by the oral route, ginger needs to be encapsulated to prevent oral and esophageal irritation. The dosage that is commonly used required the administration of two large capsules which some patients may find difficult to swallow especially if preoperative fluid is limited. Furthermore, ginger capsule is not suitable for emergency or full stomach cases, which it can hardly absorbed. Moreover, the optimal dose of ginger has not yet been established. The dose of 1 g is arbitrary and has been used before, but no dose response studies have been performed. The other limitation of ginger use is the variation of the preparation of ginger. Since ginger is the herbal medicine, the quality control of preparing is important. The quantity of active ingredients may be varied by geographic origin and degree of maturity when harvested. To minimize this problem, the ginger was harvested at the same origin, same time of harvesting and maturity and the sampled ginger capsules was tested by the quantitative and qualitative analysis. In addition, the shelf life of ginger capsule is unknown, so its quality may reduce by time. Therefore, ginger capsules in the current study were prepared no longer than three months.