THE EFFICACY OF VITAMIN C INFUSION IN REDUCING POST-INTUBATION SORE THROAT

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ABSTRACT

Objective. Vitamin C may be a beneficial adjunct for decreasing sore throat following tracheal intubation. Therefore, the aim of this study was to evaluate the effect of vitamin C infusion on post-intubation sore throat reduction.

Methods. This double-blind randomized study was conducted on 70 patients undergoing elective laparoscopic surgery in Shahid Sadoughi Hospital. The patients were allocated into two groups (experimental and control). All patients received 2 mg midazolam and 100 microgram fentanyl citrate premedication. Thirty minutes after induction of anesthesia, 5 mg morphine was given to all patients. In the next step, the experimental group received vitamin C (2 g) mixed with normal saline for the total injection volume of 500 mL during 30 min and those in control group received normal saline without vitamin C.

Results. In current study, no remarkable difference was observed between the experimental and control groups, considering age, sex and BMI (p>0.05). Significant difference was observed between the experimental and control groups in terms of postoperative sore throat at specified time including 1, 6 and 24 hours. A significant difference was noticed between experimental and control groups with respect to postoperative pain score at specified time (p<0.05). However, no difference was seen between the experimental and control groups regarding postoperative nausea, vomiting and itchy throat (p>0.05).

Conclusion. According to the results of this study, the use of vitamin C reduced the incidence of sore throat and pain score in patients undergoing laparoscopic surgery. It seems that vitamin C can decrease morphine indicated for postoperative pain.

Key words: intubation, intratracheal; pharyngitis; ascorbic acid

EFIKASNOST INFUZIJE VITAMINA C U SMANJIVANJU UPALE GRLA POSLE INTUBACIJE

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SAŽETAK

Cilj. Vitamin C može biti korisno sredstvo za smanjenje upale grla posle endotrahealne intubacije. Zbog toga je cilj ove studije bio da se proceni efekat infuzije vitamina C na smanjivanje upale grla posle intubacije.

Metode. Ova dvostruko-slepa randomizovana studija sprovedena je na 70 pacijenata koji su bili podvrgnuti ekstremnoj laparoskopskoj operaciji u bolnici Šahid Sadugi. Pacijenti su raspoređeni u dve grupe (eksperimentalna i kontrolna). Svi pacijenti su primili medikaciju u vidu midazolama od 2 mg i 100 mikrograma fentanil citrata. Trideset minuta nakon indukcije anestezije, svim pacijentima je ordinirano 5 mg morfijuma. U sledećem koraku, pacijenti u eksperimentalnoj grupi su primili 2 g vitamina C, pomešanog sa normalnim fiziološkim rastvorom ukupne zapremine 500 ml tokom 30 minuta, a pacijenti u kontrolnoj grupi su dobili normalan fiziološki rastvor bez vitamina C.

Rezultati. U našoj studiji nije primetna značajna razlika između ekperimentalne i kontrolne grupe, imajući u vidu starost, pol i BMI (p>0.05). Značajna razlika je primetna između ove dve grupe u pogledu postoperativne upale grla u određenom vremenu, uključujući 1, 6 i 24 sata. Značajna razlika primetna je između grupa u odnosu na postoperativni bol izmeren skalom i to u određenom vremenu (p<0.05). Međutim, nije primetna razlika između ekperimentalne i kontrolne grupe u pogledu postoperativne mučnine, povraćanja i svrba u grlu (p>0.05).

Zaključak. Rezultati ove studije ukazuju da je upotreba vitamina C smanjila učestalost upale grla i bola koji je meren skalom, kod pacijenata koji su bili podvrgnuti laparoskopskoj operaciji. ćini se da vitamin C može smanjiti upotrebu morfijuma kod postoperativnog bola.

Ključne reči: intubacija, endotrakealna; faringitis; askorbinska kiselina
INTRODUCTION

In spite of development of anaesthetic techniques, sore throat following endotracheal intubation is the most frequent adverse side effect of anaesthesia (1-19). Sore throat is associated with stress, unpleasant feelings, dissatisfaction and morbidity (20). The sore throat incidence varies from 14.4% to 50% after tracheal intubation and 5.8% to 34% after laryngeal mask insertion (21). The etiology of disease is related to factors including sex, age, smoking, intubation factors such as duration (21), intra-operative tube movement (2,23), tube size (2, 24), intracuff pressure (2,24), cuff design (23) and suctioning. In addition, the type of surgery and study population are other important causative factors (20). The sore throat complication includes mucosal erosion caused by the cuff of the tracheal tube, mucosal dehydration and trauma from tracheal intubation (25). Several studies in developed and Western populations have been done to prevent postoperative sore throat (26). On the other hand, pharmacological and non-pharmacological procedures are used for the elimination of sore throat (27). Therefore, decreasing and minimizing postoperative sore throat is the main goal (28).

It has been obviously demonstrated that using a smaller tracheal tube decreases sore throat incidence likely due to reduced pressure at the tube–mucosal interface (Mc). Modern and new anaesthesia practices and improved airway tools have decreased these complications (25). Opioids as the most widely used class of analgesics have been used in management of postoperative pain, but they may increase the risk of nausea and vomiting and postpone postsurgical recovery of gastrointestinal mobility (28). New, non-opioid analgesic alternatives have been recommended for decreasing pain and restricting opioid-related side effects (29). However, these non-steroidal drugs have side effects of their own (30). Vitamin C is a medication with virtually no side effects and complications (30). It as a water-soluble vitamin with neuropsotective, and neuromodulating properties (31,32). Vitamin C also demonstrates anti-inflammatory characteristics and decreases inflammation including pro-inflammatory cytokines, C-reactive protein, interleukins and tumor necrosis factor-alpha. It is also considered as a necessary micronutrient that acts as a cofactor in several chemical and enzymatic pathways (33). The accurate mechanism of analgesic effect of vitamin C is not well understood. It acts an antioxidant and inhibits reactive oxygen species (ROS) formation. Vitamin C deficiency is rare in population of developed countries, with prevalence in United States of about 6% (34,35). Diseases such as surgery and trauma lead to depletion of vitamin C in body (36). Infection, sepsis (37), cancer and colon surgery (28) are other diseases which are associated with vitamin C deficiency. Recent studies have shown that vitamin C may be effective in reducing post-operative pain especially in chronic and acute pain following orthopedic surgeries (30). Jeon et al., also confirmed a previous study and reported that vitamin C might be a beneficial adjunct for management of pain without main side effects (28). Carr et al., also demonstrated the effect of vitamin C on the incidence of complex regional pain syndrome in ankle and wrist surgery (34). Since the role of vitamin C in reducing sore throat after intubation is not specified, the aim of this study was to evaluate the efficacy of vitamin C infusion in reducing sore throat after intubation.

PATIENTS AND METHODS

This double-blind randomized study was conducted on 70 patients (age range: 20-60 years old) undergoing elective laparoscopic surgery in Shahid Sadoughi Hospital, Yazd, Iran during the period from June 2016 to September 2017. Written consents were taken from the patients and the study was approved by the ethic committee of Shahid Sadoughi University of Medical Sciences. Demographic data including age, body mass index (BMI), sex and clinical data were extracted from medical records.

Patients undergoing elective laparoscopic surgery with ASA1 and ASA2 from 2016 to September 2017 were entered into the study. However, the patients with a history of sore throat, voice violation, throat and laryngeal disease, cardiovascular disease, addiction and sensitization were excluded from the study. Moreover, if the duration of the patient's intubation was more than 2 hours, or if the intubation was done more than once, there was traumatic throat and Larynx injury during intubation, these patients were excluded from the study.

The patients were allocated into two groups (n=35). All patients received 2 mg midazolam and 100 microgram fentanyl citrate premedication. The induction of anesthesia was taken with 2 mg/kg propofol and 0.5 mg/kg atracurium. After 3 minutes, the patients underwent mechanical ventilation. In order to maintain anesthesia, propofol infusion (100-200 μg/kg/min) was used. Thirty minutes after the induction of anesthesia, 5 mg morphine was given to all patients. Then the experimental group received vitamin C (2 g) mixed with normal saline for a total injection volume of 500 mL during 30 minutes and those in the control group received normal saline 500 mL without vitamin C. Patients were extubated following the end of surgery.

Parameters including severity of sore throat, pain, nausea, vomiting, itchy throat, sore throat and severity of sore throat were measured at 1, 6, and 24 hours after entering the recovery and recorded in a questionnaire. The visual analog scale (VAS) measured acute and chronic pain.
After completion of the study, data were entered into SPSS version 21. Tests such as Mann-Whitney test, Chi-square test and independent t-test were used for analysis of data. P-value<0.05 was considered statistically significant.

RESULTS

In the current study, 45.7% and 51.4% of patients in experimental and control group were men, respectively. Demographic properties of patients showed no remarkable difference between the experimental and control groups. The mean age (± standard deviation) in the control and the experimental group was 39.91±12.78 and 41.4±12.2 years, respectively (t-test, p=0.618). The mean body mass index (BMI) in the control and the experimental group was 22.43±3.1 and 22.26±2.55 kg/m² (t-test, p=0.800).

The frequency of complications in patients undergoing elective laparoscopic surgery is shown in Table 1. There are a significant difference was observed between experimental and control groups in terms of postoperative sore throat at specified time including 1, 6 and 24 hours (p<0.01). However, no significant difference was seen between experimental and control groups in terms of postoperative nausea, vomiting and itchy throat (p>0.05).

There are significant differences between the experimental and the control groups considering postoperative pain scores. The mean scores (± standard deviations) at 1 hour were 2.09±2.44 and 3.54±2.44 (p=0.011), at 6 hours 1.66±1.84 and 3.34±2.04 (p=0.001) and at 24 hours 1.11±0.57 and 1.61±1.6 (p=0.001), for the experimental and the control groups, respectively.

DISCUSSION

Administration of vitamin C infusion in patients undergoing laparoscopic surgery showed that sore throat and score pain decreased compared to the control group. Vitamin C has a neuromodulating action (38), particularly dopamine and glutamate mediated neurotransmission (28). Laparoscopic colectomy leads to oxidative stress and ROS formation which contributes to abdominal inflation/deflation. Increased ROS and decreased pre and postoperative level of vitamin C can be compensated by supplementation such as vitamin C.

Jeon et al., evaluated the effect of Vitamin C on postoperative pain after Laparoscopic Colectomy. This study was conducted on 100 patients undergoing laparoscopic colectomy (28). One group of these patients received 50 mg/kg vitamin C and the other group received placebo. The findings showed that the patients who received vitamin C had higher level of this vitamin in plasma than the control group and needed less morphine, however no significant difference was seen between these two groups in terms of side effects, fatigue score, or pain score during cough. Therefore, according to these findings, high dose of vitamin C infusion reduced postoperative pain during the first 24 hours which is consistent with our study. Moreover, Jeon et al., reported that vitamin C decreases consumption of morphine in the early periods of postoperative period. It seems that higher dose of vitamin C with longer time of infusion may be essential to retain enough vitamin concentration and hold analgesic effects (28). Kanazi et al. evaluated the effect of vitamin C on using of morphine after laparoscopic cholecystectomy. They selected 80 patients and allocated

| Parameters                        | Experimental | Control | p-value |
|----------------------------------|--------------|---------|---------|
| Sore throat 1 hour after surgery | 17 (48.6)    | 28 (80 )| 0.006   |
| Sore throat 6 hour after surgery | 18 (51.4)    | 22 (82.9)| 0.005  |
| Sore throat 24 hours after surgery| 8 (22.9 )   | 24 (68.6)| <0.001 |
| Nausea 1 hour after surgery      | 7 (20 )      | 12 (34.3)| 0.182  |
| Nausea 6 hour after surgery      | 15 (42.9)    | 13 (37.1)| 0.628  |
| Nausea 24 hours after surgery    | 6 (17.1 )    | 8 (22.9)| 0.553   |
| Vomiting 1 hour after surgery    | 3 (8.6)      | 2 (5.7 )| 0.643   |
| Vomiting 6 hour after surgery    | 2 (5.7 )     | 5 (14.3) | 0.235  |
| Vomiting 24 hours after surgery  | 1 (2.9)      | 2 (5.7 )| 0.558   |
| Itchy throat 1 hour after surgery| 1 (2.9)      | 0 (0)   | n.a.    |
| Itchy throat 6 hour after surgery| 3 (8.6)      | 4 (11.4)| 0.690   |
| Itchy throat 24 hours after surgery| 1 (2.9)   | 1 (2.9)| 1       |

numbers represent absolute values (percentage); n.a.-not applicable
them to 2 groups. One group consumed 2 g vitamin C and other group placebo before anesthesia induction. Patients were assessed at 2, 4, 6, 12 and 24 hours after surgery. The findings of this study showed that consumption of morphine was lower in the vitamin C group compared to the placebo group. Moreover, no significant difference was observed between the two groups with respect to pain score or complications. Satisfaction scores were also similar in both groups. Vitamin C (2 g) reduced consumption of morphine in the postoperative period in these patients. Chen et al., in 2016 assessed perioperative vitamin C on postoperative pain undergoing surgical procedures. They concluded that 2 g perioperative dose of vitamin C was useful for decreasing morphine consumption after surgery (39). Another study confirmed previous studies and reported that 2 g vitamin C decreases requirement of morphine, non-steroidal antiinflammatory drugs and side effects of patients under laparoscopic cholecystectomy (30). Carr et al., in 2017 reported that administration of vitamin C in patients with chronic regional pain syndrome reduced these symptoms (37).

In another study, oral dose of vitamin C (2 g) was administered to patients with randomised cholecystectomy 1 hour before anesthesia. The level of plasma vitamin C was assessed 1 h post-randomization. The findings showed that the level of this vitamin in vitamin C group and placebo group were 57 ±28 and 23 ± 17 µmol/l, respectively. Postoperative morphine consumption and pain score were recorded during 24 hours. Morphine consumption in the placebo group was higher than vitamin C group. However, no significant difference was seen between two groups in terms of pain score (37) which was not consistent with our study. Co-administration of vitamin C (1 g/kg) with morphine inhibited morphine tolerance development and physical dependence in mice (40). Intraperitoneal injection of vitamin C (400 mg/kg) in rats significantly reduced consumption of morphine and syndrome signs (41). Murata et al., have shown that consumption of opioid drugs has been decreased in patients who received 0.5-3 g/day vitamin C, while only 17% of patients who received 5-30 g/day vitamin C needed opioids in contrast to 79% in the control group (34). Vitamin C showed anti-nociceptive effects in mice. In addition, it demonstrated additive and synergistic effects in combination with the opioids morphine and tramadol (42). Therefore, administration of vitamin C seems to have potential application as an adjunctive therapy to reduce opioid need and dependence. Several mechanisms have been suggested for vitamin C analgesic properties. It participates in the biosynthesis of amidated opioid peptides as a cofactor for peptidyl-glycine α-amidatingmonooxygenase, the enzyme to convert carboxy terminal residue of neuropeptides and peptide hormones to amide (37). Vitamin C also participates for biosynthesis of norepinephrine, release of noradrenaline and acetylcholine from synaptic vesicles (43). These neurotransmitters are an important component of the inhibitory pain way (44). Carr et al., reported that vitamin C affects up regulation or down regulation of specific gene by regulating epigenetic markers and transcription factors (34).

In conclusion, the use of vitamin C reduced the incidence of sore throat and pain score in patients undergoing elective laparoscopic surgery. It seems that vitamin C can decrease morphine indicated for postoperative pain. Therefore, vitamin C is considered as effective and efficient adjunctive therapy for decreasing pain. It is proposed that vitamin C infusions administered to patients undergoing elective laparoscopic surgery.

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