

# Effect of intravenous vitamin C on postoperative pain in uvulopalatopharyngoplasty with tonsillectomy

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Accepted for publication 12 May 2016

Clin. Otolaryngol. 2017, 42, 139–143

**Background:** Postoperative pain is a common problem in hospitals. Adults undergoing uvulopalatopharyngoplasty (UPPP) with tonsillectomy experience an unacceptable level of intense postoperative pain, especially during the first 24 h after surgery. This study investigated the analgesic effects of vitamin C in patients undergoing UPPP and tonsillectomy.

**Method:** This study was done on forty patients that were evaluated in a randomised double-blinded clinical trial. Patients included in the study were within the age range of 25–50 years with BMI < 35, physical status I, II according to the American Society of Anesthesia (ASA) and who underwent uvulopalatopharyngoplasty and tonsillectomy. Patients with epilepsy, BMI > 35, any neuropsychiatric disorders, a history of chronic pain, liver and/or renal disease, drug allergy, and drug abuse were excluded from the study. All patients underwent the same method of anaesthesia and surgical procedure. During the first 30 min after the beginning of the surgery, group C (vitamin C) received infusion of 3 g vitamin C in 500 mL of Ringer and group P received 6 mL normal saline in 500 mL of Ringer. Measurements of systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and heart rate were recorded before and during anaesthesia and at intervals of

0, 15, 30 and 60 min after extubation. Pain severity was recorded according to VAS score at intervals of 0 (recovery room), 6, 12 and 24 h after the procedure, request for analgesic drugs (iv paracetamol or pethidine) according to total number of times of analgesic request and time of the first dose of analgesic use and dose of pethidine were also recorded by questionnaire.

**Results:** There was a significant difference in evaluations for mean pain severity between the two groups at recovery room, 6, 12 and 24 h after surgery ( $P$ -value = 0.001). There was a significant difference in mean times that patient requested an analgesic, time of first dose of analgesic and pethidine dose between the two groups ( $P$ -value < 0.05). There was no significant differences in measurements of systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and heart rate in different times between the two groups ( $P$ -value > 0.05). Blood loss was similar in the two groups ( $P$ -value > 0.05).

**Conclusion:** According to this study, administration of vitamin C 3 g IV intraoperative reduced postoperative pain without increased side-effects in patients undergoing UPPP and tonsillectomy.

## Introduction

A common sleep disorder is obstructive sleep apnoea syndrome, which is caused by partial or complete upper respiratory tract obstruction. This syndrome occurs in >20% of 30–70 years. Uvulopalatopharyngoplasty (UPPP) with tonsillectomy is a common method for the treatment of

moderate-to-severe obstructive sleep apnoea syndrome.<sup>1–3</sup> Postoperative pain is a common problem.<sup>1–6</sup> Adult patients undergoing UPPP with tonsillectomy experience an unacceptable level of intense postoperative pain, especially during the first 24 h after surgery.<sup>2,3</sup> Treatment of postoperative pain after UPPP and tonsillectomy always presents a challenge.<sup>3–7</sup> Different drugs and techniques are applied to reduce post UPPP pain.<sup>1–10</sup> In some procedures, postoperative pain is preventable with adequate analgesic before surgery (preventive analgesia).<sup>1,8,9</sup> Most non-steroidal anti-inflammatory drugs are considered useful for pain control,<sup>7,9,10</sup> but few researchers believe that these drugs can

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increase postoperative bleeding, that is very unpleasant, particularly with this type of surgery.<sup>11</sup>

Opioid-based analgesic protocols are usually used for postoperative analgesia, but because opioids can easily lead to respiratory depression, such treatment can be life threatening in patients with a history of obstructive sleep apnoea and airway obstruction.<sup>12</sup> It is therefore necessary to find a safe method of analgesic relief for these patients.

Vitamin C or L-ascorbic acid is a water-soluble vitamin and an antioxidant that is needed for growth, formation and development of collagen and tissue repair in all parts of the body.<sup>13,14</sup> In various studies, the benefits of vitamin C in the treatment of chronic pain and postoperative pain have been studied and proven.<sup>13–21</sup> It has been suggested that vitamin C may be a useful postoperative analgesia for patients undergoing UPPP because it provides effective analgesia but does not induce respiratory depression such as that induced by opioids and does not cause postoperative bleeding rarely seen after non-steroidal anti-inflammatory drugs. This study investigated the analgesic effects of vitamin C in patients undergoing UPPP and tonsillectomy.

## Method

The study was approved by the Ethical Committee and participants provided written informed consent. Forty patients were evaluated in the study according to a randomised double-blinded clinical trial. Patients were in the age range of 25–50 years with BMI < 35 and American Society of Anesthesia (ASA) physical status I or II. They were all undergoing UPPP and tonsillectomy procedure. Patients with any neuropsychiatric disorders, epilepsy, BMI > 35, history of chronic pain, liver and/or renal disease, or history of drug abuse were excluded from the study. Each patient was assigned to one of the two groups according to a random number table.

For all patients, 1 mg midazolam and 2 mic/kg fentanyl was administered and general anaesthesia was induced with propofol 2 mg/kg and 0.5 mg/kg atracurium. Each patient

received 0.1 mg/kg morphine IV at the start of their surgery. Anaesthesia maintenance was with propofol 120–170 mic/kg/min and N<sub>2</sub>O-O<sub>2</sub> 50%–50%. During the first 30 min after the beginning of the surgery, group C (vitamin C) received infusion of 3 g of vitamin C in 500 mL of Ringer and group P (placebo) received 6 mL normal saline in 500 mL of Ringer. The same surgical procedure (cold steel dissection) was used for patients in both groups and all were performed by an ear, nose and throat (ENT) resident. After surgery, each patient received 8 mg dexamethasone, intravenously. Systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and heart rate were recorded before and during anaesthesia and at intervals of 0, 15, 30 and 60 min after extubation. Pain severity was recorded according to VAS score recorded in 0 (PACU), 6, 12 and 24 h intervals after the procedure. Records were made of patient requests for analgesic drug (infusion of 1 g paracetamol at pain score < 5 or bolus of 0.5 mg/kg pethidine at pain score ≥ 5 intravenously), total number of times of analgesic request and time of first dose of analgesic administration and total pethidine dose; records were taken by questionnaire.

Vitamin C side-effects (diarrhoea, dizziness, faintness, flushing or redness of skin, headache, increase in urination, stomach cramps) were recorded. All data were analysed using SPSS software version 15 and statistical tests. A *P*-value < 0.05 was considered significant.

## Results

In this randomised double-blinded clinical trial, a study was done on 40 patients aged 25–50 years with American Society of Anesthesia (ASA) physical status I, II who underwent UPPV and tonsillectomy. Evaluation of mean of age, duration of surgery, duration of anaesthesia, duration of recovery, amount of blood loss and gender distribution were similar in the two groups (Table 1). The mean duration of the operation was a little long for these reasons: Our hospital is a teaching hospital, and we used cold steel dissection for

**Table 1.** Demographic and surgery characteristics of all patients

Variable	Vitamin C	Placebo	Test	<i>P</i> value
Sex (Male/Female)	17/3	16/4	Chi-square	1.000
Age (mean ± SD, years)	32.65 ± 2.31	32.80 ± 1.89	<i>t</i> -test	0.96
Duration of surgery (mean ± SD, min)	111.75 ± 20.82	113.65 ± 20.90	<i>t</i> -test	0.775
Duration of anaesthesia (mean ± SD, min)	122.15 ± 20.31	124.50 ± 22.17	<i>t</i> -test	0.729
Duration of recovery (mean ± SD, min)	13.65 ± 2.66	14.40 ± 2.01	<i>t</i> -test	0.321
Blood loss (mean ± SD, mL)	146.98 ± 52	157.09 ± 40	<i>t</i> -test	0.49

SD, standard deviation.

tonsillectomy and at the end took advantage of suture ligation with VICRYL 4-0 for homeostasis. Our surgeon (resident of ENT) was trained to control and check any bleeding very meticulously and reduce the risk of technical complication. There were no significant differences between the two groups for measurements of mean arterial pressure and heart rate taken at various time intervals. There was a significant difference in mean pain severity according VAS score between the two groups in 0 (recovery room), 6, 12 and 24 h intervals after surgery (Table 2). No side-effects were observed in the vitamin C group. There was no case of severe bleeding among patients.

There was a significant difference between the two groups in terms of total number of times of analgesic request, time of first dose of analgesic use and total pethidine dose (Table 3).

## Discussion

Patients undergoing UPPP and tonsillectomy experience unacceptable intense postoperative pain, especially during the first 24 h after surgery.<sup>1-6</sup> So the treatment of postoperative pain after UPPP and tonsillectomy presents a challenge.<sup>7</sup> The major goal in postoperative pain management is to minimise the dose of medications to lessen the side-effects and provide adequate analgesia. The side-effects of commonly used pain medications are known to be the reasons that could lead to inadequate postoperative pain treatment. Opioids are regarded as the best analgesics but they increase the risk of respiratory depression that, especially in patients with obstructive sleep apnoea is more

dangerous.<sup>12</sup> Non-steroidal anti-inflammatory drugs are good analgesics but few researchers believe that these drugs increase the risk of bleeding after UPPV and tonsillectomy.<sup>11</sup>

Studies have been done on the effect of different drugs and methods such as ketorolac, ketoprofen, dexmedetomidine, sucralfate, parecoxibe and opioids, nerve block and local anaesthetic infiltration on postoperative pain after UPPP and tonsillectomy.<sup>1-10</sup> There has been no study to date that presents an exact evaluation of the effect of vitamin C on postoperative pain in patients undergoing UPPP and tonsillectomy.

One agent that can exert antinociceptive and pain-reducing effects is vitamin C.<sup>13-21</sup> The present study investigated the analgesic effects of infusion of 3 g vitamin C in patients undergoing UPPP with tonsillectomy.

Results showed that pain scores (according to VAS score) were lower in the recovery room, 6, 12 and 24 h after surgery in the vitamin C group compared with the placebo. Also, total number of times of analgesic request was lower in the vitamin C group, time of first dose of analgesic administration was longer and total pethidine dose was lower in the vitamin C group compared with the placebo group. Unfortunately, many of the patients were from other cities and their evaluation (VAS and other parameters) for longer times after discharge from the hospital was difficult, so do not. The analgesic effect of vitamin C was considerable in this study, and that result is similar to results reported in other studies. Kanazi GE *et al.*<sup>15</sup> assessed the role of a single prophylactic dose of vitamin C (2 g) in reducing postoperative consumption of morphine in patients undergoing laparoscopic cholecystectomy. Similar to the results of this study, tests showed that supplementation with vitamin C (2 g) decreased opioid consumption in the postoperative period in patients undergoing laparoscopic cholecystectomy. That study also reported no significant difference in side-effects between vitamin C and placebo groups. Zollinger *et al.* assessed the effectiveness of 500 mg vitamin C daily for 50 days, and Besse *et al.* assessed the effectiveness of 1 g vitamin C daily in the prevention of complex regional pain syndrome after orthopaedic surgery. They revealed that

**Table 2.** Mean VAS score  $\pm$  SD between the two groups at different times (Mann–Whitney *U*-Test)

	Vitamin C	Placebo	<i>P</i> value
0 (Recovery room)	3.1 $\pm$ 0.912	4.6 $\pm$ 1.465	0.001
6 h	4.1 $\pm$ 1.021	5.6 $\pm$ 1.188	0.001
12 h	3.45 $\pm$ 3.139	5.85 $\pm$ 1.182	0.001
24 h	2.5 $\pm$ 0.899	3.85 $\pm$ 0.745	0.001

**Table 3.** Total number of times of analgesic request, time of first dose of analgesic use and pethidine dose (Mann–Whitney *U*-Test)

Variables	Analgesics	Vitamin C	Placebo	<i>P</i> value
Total number of times of analgesic request (mean $\pm$ SD, number)	Paracetamol	0.75 $\pm$ 0.716	1.45 $\pm$ 0.887	0.012
	Pethidine	0.15 $\pm$ 0.366	1.30 $\pm$ 0.733	0.001
Time of first dose of analgesic use (mean $\pm$ SD, h)	Paracetamol	6.00 $\pm$ 0.0	8.12 $\pm$ 2.95	0.023
	Pethidine	12.0 $\pm$ 0.0	2.76 $\pm$ 2.46	0.003
Dose of analgesic (mean $\pm$ SD, mg)	Pethidine	5.5 $\pm$ 0.65	45.5 $\pm$ 0.5	0.0001

vitamin C significantly reduced the prevalence of complex regional pain syndrome.<sup>16,17</sup> Byun *et al.*<sup>18</sup> showed that in a case of post-herpetic neuralgia, which did not respond to a conventional therapy such as analgesics and nerve block, an intravenous infusion of vitamin C reduced pain immediately. This patient was treated with 2.5 g ascorbate intravenously, daily on days 1, 3 and 5. Chen *et al.*<sup>19</sup> reported that vitamin C infusion was also effective in zoster-associated neuralgia treatment. Ruirui Lu *et al.*<sup>20</sup> investigated the antinociceptive efficacy of the antioxidants vitamin C and vitamin E in mouse models on inflammatory and neuropathic pain. The research showed that systemic administration of a combination of vitamins C and E inhibited neuropathic pain behaviour after peripheral nerve injury.

Fukushima R and Yamazaki R assessed requirements and optimal dose of vitamin C supplementation in surgical patients. They showed that in uncomplicated surgical patients, a dose of more than 500 mg/day of vitamin C may be required, with much higher doses for patients in surgical intensive care units. In uncomplicated gastrointestinal surgery, continuous parenteral administration of 500 mg/day of vitamin C reduced postoperative oxidative stress as manifested by reduced urinary excretion of isoprostane. Postoperative atrial fibrillation was prevented after cardiac surgery by perioperative vitamin C supplementation. Research has reported that in critically ill patients, parenteral supplementation of high doses of vitamin C, vitamin E and trace elements was needed.<sup>21</sup> Vitamin C side-effects (diarrhoea, dizziness, faintness, flushing or redness of skin, headache, increase in urination, stomach cramps) are rare and can be seen in the long-term use. In this study, like other studies, vitamin C administration caused no side-effects.

According to this study, infusion of vitamin C 3 g during surgery reduced postoperative pain without any side-effects in cases of UPPP and tonsillectomy. So vitamin C can be introduced for administration in UPPP and tonsillectomy, where the use of opioids should be limited because of potential for respiratory depression in patients with obstructive sleep apnoea.

### Acknowledgement

This study was financially supported by the Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran, as part of Mrs. Shima Dehghanpoor Farashah dissertation to be graduated in General Medicine.

### Conflict of interest

None.

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