Original Article

The Effect of Nitrous Oxide on Postoperative Pain Third Molar Surgery

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Abstract

Introduction: The postoperative pain is one of the most important factors influencing fear and anxiety. The use of inhalation sedation makes a patient relax and pain-free during surgery. This study aimed to assess the effects of 50% nitrous oxide on postoperative pain after third molar teeth surgery. **Materials and Method:** Forty-three adult patients were involved in this prospective randomized controlled clinical trial. All patients were of ASA1 status. The subjects were divided randomly into two groups receiving 100% oxygen or 50% nitrous oxide/50% oxygen. The degree of the postoperative pain was assessed at different periods: 6 hours after the surgery, 12 hours after surgery, and 24 hours after surgery by VAS. The number of oral analgesic (Ibuprofen 400mg) taken during the first 24 hours was also assessed in the two groups. Data were analyzed with Chi-Square and Independent Sample T-test. **Results:** The pain score and the amount of total analgesic consumption in the nitrous oxide groups were significantly less than the oxygen group (P <0.005 respectively). The mean number of oral analgesics taken by the patients in the nitrous oxide and oxygen groups was 5.27 and 7.9 respectively. **Conclusion:** The admiration of nitrous oxide/oxygen mixture during third molar surgery can decrease postoperative pain.

Keywords: Dentistry, Nitrous Oxide, Pain, Third Molar

Introduction

Worldwide the number of surgical operations to remove wisdom teeth is immense, in England alone, approximately 63,000 are removed in National Health Service (NHS) hospitals each year. Many patients need time off work and their quality of life is significantly affected. However, despite these consequences, people are often most concerned about pain following the operation, which can be severe. It was suggested that the most intense pain is felt three to five hours after surgery. The pain experienced after oral surgery is widely used as a model to measure the effectiveness of painkillers in general [1].

Oral surgery procedures are often associated with fear and anxiety [2-4]. Postoperative pain is one of the most important factors influence dental fear. Pain and anxiety control during oral surgery can decrease postoperative pain [5]. Age, gender, smoking, duration of surgery, type and amount of local anesthesia and severity of tissue damage during the surgery are responsible for the postoperative pain. Many pharmacological and non-pharmacological methods are applied for postoperative pain control. The non-steroid anti-inflammatory drugs (NSAIDs) are the most common medications prescribed [5, 6]. NSAIDs are highly effective and have not sedative effect. The adverse effects of NSAIDs are gastric ulceration, renal impairment, and coagulopathy. Nitrous oxide (N2O) is widely used as an anesthetic gas and as an inhalational sedation agent for day-stay minor surgical procedures in the various medical disciplines. It has good analgesic properties. The analgesic effect of 50% N2O is equal to 10 milligrams of intramuscular morphine [7]. Inhalation sedation with N2O/O2 is one of the main techniques used for relief of pain and anxiety during minor dental procedures [5, 8-10]. It has a rapid onset, short, and provides for excellent control of the pain, anxiety, and

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awareness during the uncomfortable dental procedures [11-13]. The main disadvantage of inhalation sedation with N2O/O2 is that many patients are not adequately sedated by it. In an animal study, Goto [14] showed that 30% and 75% N2O administered before a noxious stimulation produced a preemptive analgesic effect (decrease postoperative pain). Also, Ong [15] showed that 50% N2O administration before dental surgery has no effect on postoperative pain in humans. Venchard [16] showed that sedation for dental surgery was improved by combining nitrous oxide and intravenous midazolam and found this technique to be safe and reliable, requiring reduced doses of midazolam and it made improvement in patient recovery and cooperation.

This study aimed to evaluate the effect of 50% N2O administration on postoperative pain and the need for analgesic in third molar teeth surgery.

Materials and Methods

After the approval of research in the research deputy of Isfahan Dental school, (No: 386002). In this prospective randomized controlled clinical trial, Forty-three patients from patients who referred to the department of oral and maxillofacial surgery of Isfahan University of Medical Sciences for removing their impacted third molar teeth. The Inclusion criteria were age between 20 to 40 years, no history of cardiovascular and pulmonary disease, and have not a contraindication of N2O administration. After taking a complete medical and dental history and informed consent, the patients were randomly divided into two groups, based on a random digit table: the control group who received 100% O_2 and the study group who received 50% N_2o / 50% O_2 through a nasal mask during procedure.

All patients were of ASA1 status. Exclusion criteria for the study were personality or psychiatric disorders, nasal abnormalities (septal deviations, inferior conchal hypertrophy) chronic obstructive pulmonary disease, and ASA 2 through 5 statuses. The same surgeon performed all the surgical procedures while an anesthesiologist controlled the sedation. Heart rate, respiratory rates, and oxygen saturation were monitored for both groups during surgery. After five minutes of N_2O gas administration, the local anesthetic (lidocaine 2% + epinephrine 1/100,000) was injected into the operative site. After surgery, the patient point VAS for intraoperative pain, the postoperative pain intensity was assessed by using the visual analog scale (VAS) system at different periods: 6 hours after the surgery, 12 hours after surgery, and 24 hours after surgery. The patient indicated pain intensity on a line of 10 cm long (0 no pain to 10 worst pain. The amount of the analgesic (Ibuprofen 400 mg) consumed during the first 24 hours was also recorded.

Results

The Forty- three patients who were involved in the study were divided into two groups: 100% oxygen and 50% N_2O/ 50% O_2.

The study group included 22 patients (11 male and 11 female). With a mean age of 26.6±5.5 years. The control group included 21 patients (8 male and 13 female) with a mean age of 26.5±6.1 years (Table: 1). Besides, in each group, 13 patients had a history of dental treatment and the others had not. There was no significant difference in age, gender, and history of dental treatment between two groups (Chi-Square, P = 0.85). Therefore, the influence of age, gender, and history of dental treatment had little effect on the treatment outcomes.

The mean number of local anesthetic cartilage used in the control and study groups was 2.57 and 2.05 respectively. The mean time of surgery was 33.1 for the study group and 32.3 for the control group and not different in two groups ($p>0.05$). At the end of the surgery, the patients were asked to provide an overall evaluation of the pain experience during surgery on a line of 10 cm long (0 = no pain and 10 =worst pain possible)

The intensity of pain during surgery, the intensity of pain during the first 24 hours after surgery, and amount of analgesic consumption during the first 24 hours after the surgery was significantly higher in the control group compared to the study group (Independent Sample T-test $P<0.000$, $P < 0.009$ and $P <0.005$ respectively). (Tables: 2, 3 and 4).

The sedation score during surgery was higher in the study group. (Mann Whitney, P=0.000). (Table: 5)

The patient had not any medical complications such as hypoxia, hypertension, and hypotension during treatment.

Discussion

Many animals and humans studies showed that local anesthesia could provide preemptive analgesia by preventing central sensitization. Kissin [17] stated that the preemptive analgesia block would need to be of sufficient strength and duration to be effective. Another study by Gorden [18] demonstrated that blockade of postoperative pain during the first 4 hours with bupivacaine following oral surgery resulted in less postoperative pain 1 to 2 days after surgery. Concerning nitrous oxide, there is paucity in researches that study the preemptive analgesic effect of N2O in humans. Venchard [16] found that combining nitrous oxide and Midazolam improved patient's sedation during oral surgery and reduced doses of Midazolam administered to them. Patients were initially titrated with 10% nitrous oxide, increasing by increments of 10% up to a maximum of 40% nitrous oxide and 60% oxygen. Midazolam was then titrated (initially 2 mg wait 2 min with increments of 1 mg every minute until appropriately sedated) whilst still administering

40% nitrous oxide. Goto [14] has shown that N2O produces a dose-dependent preemptive analgesic effect in rats. In his study, he showed that 20 minutes of 30% or 75% nitrous oxide administered before a noxious stimulation (formalin injection), produced a lasting effect on the pain behavior in the animal. A recent study by Ong [15]showed that 50% N_2O administered preoperatively for 20 minutes does not have any preemptive analgesic effect in patients having impacted third molar teeth extraction under local anesthesia. In our study, 50% of nitrous oxide was used to produce conscious sedation. Our results are consistent with the results of the study of Goto [14] and Venchard [16] but contradict these of Ong [15]. In Ong [15] study, nitrous oxide was given for 20 minutes before the surgical procedure. In our study, the nitrous oxide was started 5 minutes before the local anesthesia administration and continued throughout the surgical procedure. The mean time of the surgical procedures was 32.7 minutes.

The administration of N_2O for a longer time (more than 20 minutes) may have led to the difference in results between our study and the Ong [15] study. As was stated by Kissin [17], sufficient strength and duration are needed for the analgesic block to be effective. Extending the N_2O administration into the intraoperative period may have provided adequate time for blocking the development of central sensitization. The intraoperative pain and anxiety may also influence the postoperative pain. By using N_2o for patient's sedation during the surgical procedures, the patient and the surgeon are more comfortable and the patients may experience less intraoperative pain. We have also found that the patient's intraoperative pain in the study group was significantly lower than that of the control group ($P<0.005$). So, we can also conclude that N_2O sedation may have decreased the postoperative pain by improving the conditions of the surgical procedure for the patient and the surgeon. As stated before, due to the lack of adequate studies on the preemptive analgesic effect of N_2O in humans, further assessment and larger studies are necessary to confirm our findings.

Conclusion

The result of our study showed that using 50% N_2O administered five minutes before surgery for removal of impacted teeth and continued until the end of the operation, could significantly decrease postoperative pain and the number of analgesics taken by patients.

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Table 1: Characteristics of two volunteer groups (M=male, F=female)

Group	Gender M/F	Age
50% N_2O	11/11	26.6(±5.5)
100% O_2	8/13	26.5(±6.1)
P Value	0.85	0.85

Table 2: The amount of pain intensity during surgery (VAS= Visual Analog Scale).

	Control group	Study group	p value
Pain	2.88(±1.09)	4.88(±1.13)	0.000

Table 3: The amount of pain intensity in 2 groups (VAS=Visual Analog Scale ; h=hours)

	Control group	Study group	p value
Pain during first 6h	4.09(±0.89)	3.35(±0.8)	<0.009
Pain during first 12h	3(±0.75)	1.95(±0.8)	<0.009
Pain during first 24h	1.6(±0.66)	0.97(±25)	<0.009

Table 4: Amount of analgesic consumption in the first 24 hours

	Control group (number of tablets)	Study group (number of tablets)	p- Value
First 6h	2.86(±1.01)	1.77(±0.60)	<0.005
First 12h	5.21(±1.09)	3.23(±0.75)	<0.005
First 24h	7.9(±1.86)	5.27(±1.03)	<0.005

Table 5: Sedation score in tow groups

	Control group (number of patients)	Study group (number of patients)	p- Value
Fully awake	20	2	0.000
Drowsy	1	4	0.000
Eye closed responsed to verbal command	0	8	0.000
Eye closed responsed to mild physical stimulus	0	8	0.000