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SCIENTIFIC ARTICLE

Effect of nitrous oxide on fentanyl consumption in burned patients undergoing dressing change



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KEYWORDS

Pain;
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Abstract

Background and objectives: Thermal injuries and injured areas management are important causes of pain in burned patients, requiring that these patients are constantly undergoing general anesthesia for dressing change. Nitrous oxide (N₂O) has analgesic and sedative properties; it is easy to use and widely available. Thus, the aim of this study was to evaluate the analgesic effect of N₂O combined with fentanyl in burned patients during dressing change.

Method: After approval by the institutional Ethics Committee, 15 adult burned patients requiring daily dressing change were evaluated. Patient analgesia was controlled with fentanyl 0.0005% administered by intravenous pump infusion on-demand. Randomly, in one of the days a mixture of 65% N₂O in oxygen (O₂) was associated via mask, with a flow of 10 L/min (N₂O group) and on the other day only O₂ under the same flow (control group).

Results: No significant pain reduction was seen in N₂O group compared to control group. VAS score before dressing change was 4.07 and 3.4, respectively, in N₂O and control groups. Regarding pain at the end of the dressing, patients in N₂O group reported pain severity of 2.8; while the control group reported 2.87. There was no significant difference in fentanyl consumption in both groups.

Conclusions: The association of N₂O was not effective in reducing opioid consumption during dressing changes.

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PALAVRAS-CHAVE

Dor;
 Óxido nitroso;
 Burns;
 Desbridamento

Efeito do óxido nitroso sobre o consumo de fentanil em pacientes queimados submetidos à troca de curativo

Resumo

Justificativa e objetivos: Os ferimentos térmicos e a manipulação das áreas lesadas são causas importantes de dor em pacientes vítimas de queimaduras, necessitando que estes pacientes sejam constantemente submetidos a anestésias gerais para a troca do curativo. O óxido nitroso (N₂O) tem propriedades analgésicas e sedativas, sendo capaz de fácil utilização e de ampla disponibilidade. Com isto, objetivou-se avaliar o efeito analgésico da administração de N₂O associado ao fentanil em pacientes queimados, durante a troca de curativo.

Método: Após aprovação pela comissão de ética institucional, foram avaliados 15 pacientes adultos, vítimas de queimaduras com necessidade de troca diária de curativo. A analgesia do paciente foi controlada pelo uso de fentanil 0,0005% administrado por bomba de infusão sob demanda, intravenosa. De maneira aleatória, em um dos dias foi associada mistura de N₂O a 65% em oxigênio (O₂) sob máscara com fluxo de 10 L/min (grupo N₂O) e no outro dia apenas O₂ sob o mesmo fluxo (grupo controle).

Resultados: Não se observou diminuição significativa da dor no grupo N₂O em relação ao grupo controle. A dor na EAV antes da troca do curativo foi de 4,07 e 3,4; respectivamente nos grupos N₂O e controle. Quanto à dor ao término da troca de curativo, os pacientes do grupo N₂O referiram dor intensidade 2,8; enquanto no grupo controle foi de 2,87. Não houve diferença significativa de consumo de fentanil em ambos os grupos.

Conclusões: A associação de N₂O não foi eficaz na redução no consumo de opióides durante a troca de curativos.

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Introduction

One of the biggest problems faced in caring for burn patients is the need for frequent dressings, as the burning is a major cause of pain even without its manipulation. Therefore, these patients undergo general anesthesia every other day, or even daily, with long post-anesthetic recovery and prolonged fasting.^{1,2} The consequences of this process may be malnutrition and delayed healing. Furthermore, the drugs used in general anesthesia often cause nausea and vomiting in sensitive patients. Development of dependence and tolerance to anesthetic drugs may also occur.³

Thus, there is interest in studying analgesia and sedation methods for dressing changes in burn patients, allowing rapid induction and recovery of the patients, with low incidence of side effects, at a reduced cost, which could be easy, efficient, and known by medical professionals, enabling better pain control at the most critical moment.⁴

Nitrous oxide (N₂O) has analgesic and sedative properties known for over 150 years and it is still used in general anesthesia, potentiating other intravenous and inhaled anesthetic agents.^{5,6} Its use in small procedures outside the operating room is also widespread in the medical and dental practice, and it is satisfactory in most cases, with mild and controllable side effects with the agent discontinuation.⁷⁻¹¹

The objective of this study was to evaluate the analgesic effect of 65% nitrous oxide associated with fentanyl in burn patients during dressing changes.

Materials and methods

After obtaining the institutional Ethics Committee approval and written informed consent of all participants, 15 burn patients, aged between 18 and 60 years, ASA I and II, admitted to the specialized unit for burn treatment at the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP), requiring daily dressing change were evaluated.

Exclusion criteria were patients with burns in the airways, face or cervical region compromising the proper management and air mask coupling; history of significant side effects (e.g., significant agitation or prolonged nausea and vomiting) with N₂O inhalation, those with severe or uncontrollable side effects, confused or poorly collaborative, with psychiatric disorders that prevent participation in the study, SpO₂ < 90%, and pregnant.

Patients underwent sedation with 0.0005% fentanyl solution administered intravenously by patient-controlled analgesia (PCA) in loading dose (1 mcg kg⁻¹) and, if with more severe pain, bolus of 30 mcg on-demand at 5 min intervals during dressing change carried out in the bed by the nursing staff on two occasions. The use of PCA pump was previously explained to the patient, with the demand bolus triggered by the patient or investigator physician. In one of the days, a mixture of 65% N₂O and oxygen (O₂) under mask with flow rate of 10 L min⁻¹ (N₂O group) was associated, and the next day only O₂ under the same flow (control group), provided by a portable Takaoka dental anesthesia device.

The study participants were monitored with pulse oximetry, non-invasive pressure, and cardioscope during the procedure and for at least 45 subsequent minutes, following possible adverse reactions and their severity. Patients were discharged from the post-anesthetic care unit after reaching an Aldrette–Kroulik index >8.

The following results were recorded for analysis: side effects during follow-up; modality of analgesic drugs used for analgesic control during hospitalization; dose of intravenous morphine in the last 24 h and the time since the last administration; severity of pain using a visual analog scale (VAS) from 0 to 10 before, during, and at the end of the procedure; intravenous fentanyl required (number of bolus and total dose received) recorded in micrograms (mcg) during dressing; patient satisfaction with the technique used: very satisfied (VS), satisfied (S), unsatisfied (U), very unsatisfied (VU), indicating which of the modalities was more effective for pain control: anesthesia used in the first day of the study, anesthesia used in the second day of the study or any technique used in the previous dressing changes; duration of the procedure; time of 100% O₂ administration after the end of the procedure; and the interval between the end of the procedure and obtaining the recovery criteria described above.

Data analysis was performed using the Student's paired *t*-test for comparing total fentanyl consumption between the control and N₂O groups. VAS comparison between procedures and time points was performed with analysis of variance for repeated measures and post-test with Bonferroni multiple comparisons, considering a *p*-value < 0.05 significant.

Results

Data were collected between June 2010 and March 2012. We evaluated 15 patients, 12 men and 3 women. The average age and weight were 36.27 years and 66.57 kg. Of the analyzed patients, 13 were ASA I and two were ASA II by systemic arterial hypertension (SAH) and epilepsy, and SAH and Chagas disease.

Regarding burn characteristics, the mean body surface area burned (BSAB) was 15.1%, with 20% of participants also presenting with third-degree burns. The time elapsed between the burn and the first treatment used in the study ranged from three to 61 days, averaging 15 days. Regarding the types of burns, there were alcohol, petrol or gas burnings (40%); contact with fire or abrasion (20%); electrical (27%) and scald (13%) (Table 1).

Table 1 Demographic data.

Characteristics	Mean
Age (years)	36.27
Weight (kg)	66.57
ASA I:II	13:02
BSAB (%)	15.10%
Burn Time (days)	15

ASA, physical status according to the American Society of Anesthesiologists classification; BSAB, body surface area burned.

Table 2 Morphine consumption the day before the dressing change.

Technique	Morphine use (patients)	Mean dose (mg)
N ₂ O	9	4.55
Control	7	3.42

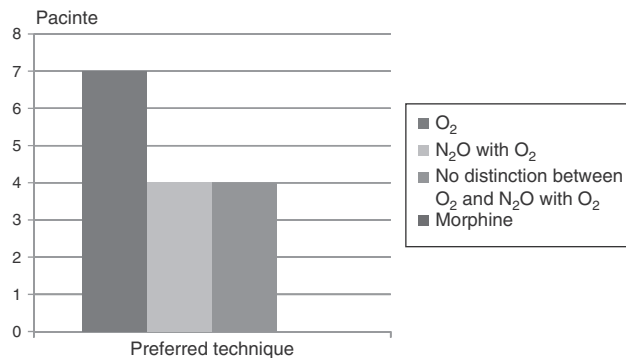


Figure 1 Preference of patients for the two techniques used.

The mean duration of dressing change was 38.8 min in N₂O group and 43.33 min in control group. Four patients in N₂O group had side effects (3: dizziness; 1: nausea). Only one case was reported in control group (dizziness). None of the patients required additional measures to control the symptoms, with spontaneous resolution.

The standard treatment of pain used in the burn ward consisted of intravenous bolus administration of morphine, minutes before manipulation of patients and in case of severe pain. Seven patients (46.7%) in control group received morphine (mean dose of 3.42 mg) the day before the dressing change; while nine patients (60%) in N₂O group received a mean dose of 4.55 mg per person (Table 2).

There was no significant decrease in pain in N₂O group compared to control group. VAS pain score before dressing change was 4.07 (*p*=0.808) and 3.4 (*p*=0.838), respectively. The most severe pain during the procedure was 6.33 (*p*=0.532) and 6.73 (*p*=0.547). Regarding pain at the end of dressing change, patients in N₂O group reported pain severity of 2.8 (*p*=0.663) and control group of 2.87 (*p*=0.786) (Table 3).

Fentanyl consumption in N₂O group was 147.43 mcg, while in control group it was 157.77 mcg. There was no significant difference in consumption (*p*=0.46) (Table 4).

Regarding the assessment of techniques used and patient satisfaction, seven patients preferred the use of O₂ alone (46.6%), four patients preferred the mixture of N₂O and O₂ (26.7%), and four patients preferred the two techniques without distinction (26.7%). None of the patients chose the previous use of morphine as a favorite. Among patients who preferred one of the techniques, only one chose the first day technique, while 10 chose as favorite the second day technique (Fig. 1).

The analysis of patient satisfaction with the techniques used in the study showed that in N₂O group four patients declared themselves very satisfied (VS), while 11 patients said they were satisfied (S). In control group, the proportion

Table 3 Dressing change and pain variation.

Procedure	Time	Mean	SD	Median	Minimum	Maximum	<i>p</i>
Control	Before	3.40	3.25	2	0	10	0.838
	During	6.73	2.12	7	3	10	0.547
	End	2.87	3.04	2	0	10	0.786
N ₂ O	Before	4.07	3.13	4	0	10	0.808
	During	6.33	2.06	6	3	10	0.532
	End	2.80	2.57	2	0	8	0.663

Table 4 Fentanyl consumption during procedure.

Variable	Group	Mean	SD	Median	Minimum	Maximum	<i>p</i>
Total fentanyl (mcg)	Control	157.77	74.25	152	60	335	0.460 ^a
	N ₂ O	147.43	49.93	145	55	230	

^a Result of paired Student *t*-test.

Table 5 Patient's satisfaction according to group.

Technique	VS	S	U	VU
N ₂ O	4	11	0	0
Control	6	9	0	0

VS, very satisfied; S, satisfied; U, unsatisfied; VU, very unsatisfied.

was six (VS) and nine (S). There was no report of dissatisfaction (Table 5).

Discussion

The main finding of this study was that the N₂O association was not effective in reducing the opioid consumption during dressing changes.

The primary effects of N₂O are exerted in the central nervous system, with analgesic action on supraspinal GABA inhibition and spinal GABA activation. N₂O promotes the release of endogenous opioids with subsequent release of norepinephrine in the spinal cord and inhibits pain transmission.¹² The use of N₂O for pain relief in procedures outside the operating room in the burned pediatric population is an issue widely discussed in the literature,^{8,9,13} in contrast to the paucity of data on the adult population. In a survey of more than 7000 cases, Zier et al.¹⁴ noted that higher concentrations of N₂O, up to 70%, were safe in several small procedures performed in children, with higher incidence of side effects when used for more than 30 min. A systematic review involving 26 articles also reported the efficacy of using nitrous oxide for procedures in children.¹³ In contrast, in this study, the use of N₂O 65% offered no additional benefit in pain control, with no statistical difference when compared with the control group. A point to be considered is that many of the studies in the literature use N₂O as a technique for pain relief of procedures whose pain stimulus is reduced, such as peripheral venous access, lumbar puncture, and intramuscular injections.¹³ When

pain stimulus is more severe, as in the present study, N₂O showed no statistical difference of when it is not used.

However, the study patients preferred the techniques used (PCA with or without N₂O), with 100% satisfaction, rather than the use of morphine before dressing change, as was the service routine. The use of PCA infusion pump is easy, allowing the proper use after a simplified explanation. It allows the patient to self-administer a predetermined dose of fentanyl to the infusion limits set by the physician.¹⁵ When there is a request, fentanyl reaches equilibrium at the effector site with an average of 6.4 min.¹⁴ The preference for the technique used on the second day by most patients, independent of the use of the N₂O and O₂ mixture (N₂O group) or O₂ alone (control group), can be explained by the better use of PCA, due to the experience gained from use on the previous day.

Our results show that PCA with target controlled infusion pump with fentanyl may be used as an alternative in sedation of patients undergoing burn dressing changes. The loading dose of fentanyl (1 mcg kg⁻¹) used in the study with bolus of 30 mcg was insufficient to alleviate the pain satisfactorily during dressing change, compared to studies involving the use of other opioids.^{16–18} Prakash et al.¹⁶ compared four different administration schemes of bolus fentanyl on-demand (10, 20, 30, 40 mcg) after loading dose of 1 mcg kg⁻¹ and reported better pain control in the groups receiving 30 or 40 mcg of fentanyl (4.7 ± 0.83 and 3.9 ± 0.63) in VAS, compared to receiving 10 and 20 mcg (7.73 ± 1.33 and 7.20 ± 1.21). Despite the similarity between the doses used, the worst pain control in the present study may be explained by the dressing change intrinsic characteristics such as time and technique used by the practitioners, in addition to pain intensity fluctuations throughout the day and its subjective interpretation by burn patients.

However, this study had several limitations that should be considered. The sample size was limited, which was the study main limiting factor. Although patients were blind to the drugs used, the blind nature of the study was not complete because the investigator knew to which group the patient was allocated. Moreover, bedside sedation control without additional resources, such as the BIS, is difficult and

subjective. The interaction with patients, either with verbal or tactile stimulation, performed by doctors or nurses during the procedure is the conduct advocated by most studies to assess the level of consciousness.¹⁹ The technique safety was observed with a sedation in which the patient remained conscious, collaborative, using the PCA on his own, and remained with his vital signs stable.

The study results show that patient-controlled analgesia at bedside associated with the use of N₂O during dressing change in burn patients does not benefit pain control or decreases fentanyl consumption, although this technique is safe, affordable, resource-sparing, and associated with greater patient satisfaction, regarding the use of morphine alone. However, more studies are needed to assess the most appropriate dose of medications used in a larger population simple to assess the validity and the statistical significance of the findings.

Conflicts of interest

The authors declare no conflicts of interest.

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