

Chronic pain relief after the exposure of nitrous oxide during dental treatment: longitudinal retrospective study

Alívio da dor crônica após exposição ao óxido nitroso durante tratamento odontológico: estudo retrospectivo longitudinal

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ABSTRACT

The objective was to investigate the effect of nitrous/oxygen in chronic pain. Seventy-seven chronic pain patients referred to dental treatment with conscious sedation with nitrous oxide/oxygen had their records included in this research. Data were collected regarding the location and intensity of pain by the visual analogue scale before and after the treatment. Statistical analysis was performed comparing pre- and post-treatment findings. It was observed a remarkable decrease in the prevalence of pain in this sample (only 18 patients still had chronic pain, $p < 0.001$) and in its intensity ($p < 0.001$). Patients that needed fewer sessions received higher proportions of nitrous oxide/oxygen. Nitrous oxide may be a tool to be used in the treatment of chronic pain, and future prospective studies are necessary to understand the underlying mechanisms and the effect of nitrous oxide/oxygen in patients according to the pain diagnosis and other characteristics.

Keywords: chronic pain, nitrous oxide, dental treatment, pain relief.

RESUMO

O objetivo deste estudo foi investigar o efeito do óxido nitroso na dor crônica. Os prontuários de 77 pacientes com dor crônica submetidos a tratamento odontológico com sedação consciente (óxido nitroso/oxigênio) foram incluídos. Os dados sobre localização e intensidade de dor pela escala visual analógica foram considerados, e foi realizada comparação e análise estatística entre os momentos pré- e pós-tratamento. Foi observada redução marcante na prevalência de dor nesta amostra (apenas 18 doentes ainda tinham dor, $p < 0,001$) e na intensidade de dor ($p < 0,001$). Os doentes que precisaram de menor quantidade de sessões receberam maiores proporções de óxido nitroso/oxigênio. Em conclusão, pode-se considerar o óxido nitroso como uma ferramenta a ser investigada no tratamento da dor crônica em estudos futuros prospectivos, que poderão identificar os mecanismos associados de acordo com o diagnóstico de dor e outras características.

Palavras-chave: dor crônica, óxido nitroso, tratamento odontológico, alívio da dor.

Conscious sedation with nitrous oxide is a well-known method used for more than 100 years for dental treatment. Since 1976, it started to be used associated with oxygen and became more secure¹. It helps in the control of anxiety and fear which play a role in acute pain perception, which wide application at the dental practice^{2,3}.

Some of the observed effects of this type of sedation is the reduced need of analgesic drugs in the postoperative period^{4,5,6,7,8,9}. Initially, nitrous oxide was considered an anesthetic drug, however these findings brought an evidence of an analgesic effect^{7,8,9}. This effect meant reduced doses of analgesic

drugs after several types of surgeries⁸, and it was considered a prevention for acute and chronic postsurgical pains^{9,10,11}.

The antalgic efficacy of nitrous oxide in acute pain models have been investigated since that^{12,13,14,15}. On the other side, chronic pain is described as 'pain for more than 6 months' by the International Association for the Study of Pain¹⁶. Only recently, a review showed that nitrous oxide can be a tool in the prevention of chronic pain development, but little is known about its effect in preexistent chronic pain conditions¹⁷.

A study from 5 years ago showed persistent pain alleviation in a neuropathic pain model by a single exposure

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to nitrous oxide/oxygen in rats¹⁸. This finding and the clinical observations are promising, and the effect and mechanisms of pain alleviation by nitrous oxide need further investigation.

Thus, the objective of this study was to investigate the effect of nitrous/oxygen in chronic pain of patients that were under dental treatment.

METHOD

Subjects

The dental profiles of 77 patients were included in this longitudinal retrospective research. They had been treated at the dental office under conscious sedation with nitrous oxide/oxygen March 2003 and April 2010. These patients were included because they presented in their anamnesis complaint of chronic pain in some part of their body for more than 6 months, which was part of their medical history. They had complete profiles including the location and intensity of pain by the visual analogue scale, which had been applied immediately before and immediately after the complete dental treatment. The patients that needed more than one session of sedation had their pain measured before the first session and after the last one. The duration of pain relief was not assessed.

The patients were 43 (44.8%) women and the mean age was 58.1 ± 10.6 (20-83) years old. This study was approved by the Ethics Committee of our institution.

Dental treatments and conscious sedation

All patients had been evaluated and treated by the same trained dentist. The treatment included dental extractions, endodontic treatment, surgeries, periodontal scalling and all received information about oral hygiene. The mean number of dental sessions was 3.9 ± 2.6 (1-11). The interval between the sessions was 2-3 days. The mean nitrous oxide proportion was 2.5 ± 0.6 units and the mean oxygen proportion was 3.7 ± 0.7 units. All had their arterial blood pressure, heart rate and oxygen rate monitored during conscious sedation. The portable gases mixture was equipped with a sound system that avoided inadequate dosage of nitrous oxide (higher than oxygen).

Initially, the mask to administrate the gases was placed at the face of the patient. The proportions of nitrous

oxide/oxygen were applied considering the following safety parameters and the individual variability of sensitivity to this technique: the majority of cases are able to inhale 50% of each (3 L/min of nitrous oxide and 3 L/min oxygen), part of patients are able to inhale 33% (2 L/min nitrous oxide and 4 L/min oxygen) and few patients are able to inhale only 16.7% (1 L/min nitrous nitrous oxide and 5 L/min oxygen). All procedures started with 6L/min of oxygen and after each 3 minutes, $\frac{1}{2}$ L/min of nitrous oxide was increased. The report by the patient of peripheral tingling (hands and feet) and or the blood parameters were the factors to determine the interruption in the increase of nitrous oxide proportions, and the limit was 3 L/min nitrous oxide to 3 L/min oxygen. After the dental treatment, the proportion of nitrous oxide was gradually reduced until only oxygen was administered for 3 to 5 minutes and the patients reported no symptoms of sedation. During all the procedure, the patients remained conscious with the protective reflexes (swallowing and cough), breathing, sensation of physical stimuli and talking with the dentist.

Statistical analysis

The sample consisted of all patients from a dental clinic that had been treated with conscious sedation with nitrous oxide/oxygen. All data were tabled and the means, standard deviations, frequencies and percentages were computed. After the initial descriptive analysis, the data were tested with Shapiro-Wilk e QQ plots in order to investigate normal distribution. The tests used for associations and differences between pre and post treatment data were oneway ANOVA, Student's, chi-square and Wilcoxon. Correlations were investigated with the Pearson's coefficient. All statistical calculations were performed using SPSS 17.0 (SPSS Inc., Illinois, USA). The level of significance was $p < 0.05$.

RESULTS

There was a decrease in the number of patients with pain complaints and in the intensity, which can be observed in Tables 1 and 2. The female gender was associated with the decrease in the number of patients with pain at the head (chi-square, $p = 0.005$), abdomen (chi-square, $p = 0.002$) and inferior or superior limbs (chi-square, $p = 0.001$).

Table 1. Pain complaint and location before and after the dental treatment with sedation (number of patients with complaints) (N = 77).

	Before the dental treatment	After the dental treatment	p-value*
Pain in any body part	77 (100.0%)	18 (23.4%)	< 0.001
Head and/or neck pain	28 (36.4%)	4 (5.2%)	0.015
Pain at thorax, back and/or abdomen	43 (55.8%)	10 (13.0%)	0.002
Superior limbs pain	22 (28.6%)	8 (10.4%)	< 0.001
Inferior limbs pain	30 (39.0%)	6 (7.8%)	0.003

*Pearson's chi-square; Fisher's exact test; Wilcoxon test.

Table 2. Pain intensity according to the location before and after the dental treatment with sedation (N = 77).

	Before the dental treatment	After the dental treatment	p-value*
Mean**	7.5 ± 2.1 (0-10)	0.7 ± 0.7 (0-7)	< 0.001
Head and/or neck **	7.5 ± 2.0 (3-10)	0.2 ± 0.2 (0-2)	< 0.001
Thorax, back and/or abdomen**	7.4 ± 2.5 (0-10)	0.6 ± 0.6 (0-4)	< 0.001
Superior limbs**	7.4 ± 2.2 (2-10)	1.4 ± 1.0 (0-10)	< 0.001
Inferior limbs**	8.0 ± 1.8 (4-10)	0.8 ± 0.6 (0-7)	< 0.001

*One-way ANOVA; paired samples T-test; **Pain intensity according to the visual analogue scale.

Correlations

The decrease in pain intensity after the treatment with sedation was higher in patients that were older (Pearson's coefficient, $p = 0.015$). Patients with body pain and high intensity showed more dental pain during treatment and needed high proportion of nitrous oxide (Pearson's coefficient, $p = 0.037$). Finally, patients that needed few sessions received high proportions of nitrous oxide/oxygen (Figure).

DISCUSSION

This study showed evidence of remarkable reduction of chronic body pain complaints in patients that underwent dental treatment with conscious sedation with sedation with nitrous oxide/oxygen. This reduction was not associated with the location of pain, but according to the gender and ages. Women had more pain relief than men, and the older patients had higher decrease in pain intensity than the younger ones.

The doses of analgesic drugs can be reduced after the use of nitrous oxide during surgical procedures^{4,5,6,7,8,9,10,11,12,13,14}. The development of chronic pain after surgeries can also be prevented with this type of sedation¹⁷. However, this is the first study that had showed the effect of nitrous oxide in pain alleviation of chronic symptoms and not in the use as intra-operative anesthetic technique^{10,11,12,13,14,15,16,17}.

The mechanism underlying the analgesic effect of nitrous oxide seems to be its role as an antagonist at the N-methyl-D-aspartate receptor, involved in pain chronification¹¹. Patients with chronic pain show neuroplastic phenomena and altered neural processing that involves NMDA receptors, and they can be a target for anesthesia and analgesic effect that are systemic. In rats, a single exposure to nitrous oxide sedation was capable of alleviate neuropathic pain for a long period, including the reduction of thermal allodynia^{10,18}. Thus, nitrous oxide could be a tool in the treatment of chronic pain conditions.

Nitrous oxide has been used in dentistry since the XIX century for analgesia and it is a safe and effective technique for the control of anxiety and fear. It has been shown that women at labor had less pain and fewer analgesics consume after delivery when exposed to it¹⁹. Its use is regulated and the equipment must prevent proportions higher than 70% of N₂O. Besides its effect in NMDA receptors, the nitrous oxide may cause a release of endorphins and dopamine that modulate

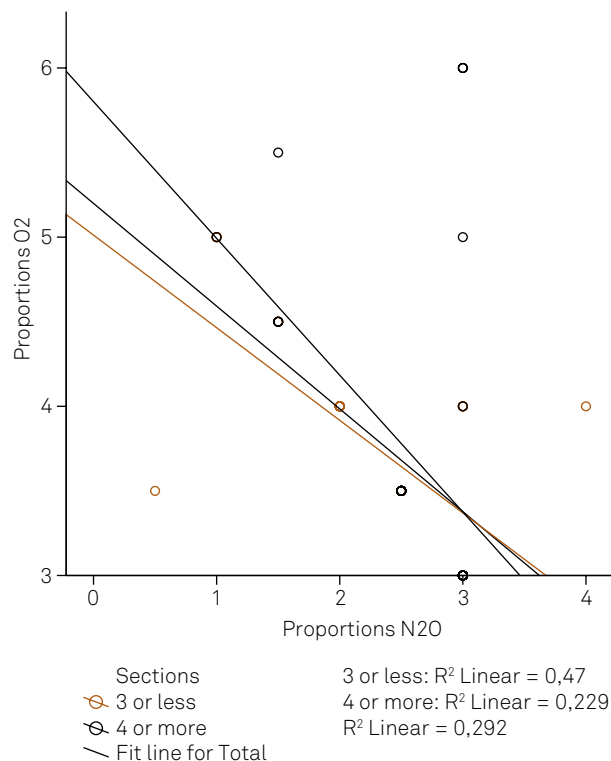


Figure. Negative correlation between the proportion of nitrous oxide / oxygen and the number of sessions (Pearson's coefficient, $p = 0.026$).

the suppressive descendent pathways, however it seems that the relief of chronic neuropathic pain in rats was more associated with the antagonistic effect on NMDA receptors¹⁸. More studies are necessary to clarify the exact pathophysiological mechanism in chronic pain patients, according to the diagnosis, establishing if they are the same as the relief in acute postsurgical pain by nitrous oxide^{19,20}. The role of sexual hormones, genetic differences and aging need to be also investigated in order to understand the associations found. Finally, the patients that were exposed to low proportions of nitrous oxide needed more sessions for the dental treatment, and it is possible that there was a lack in the analgesic effect because of concentration that turned into necessary new appointments to finish the treatment. Therefore, future prospective studies are necessary.

Some limitations of the application need to be further investigated. The sedation with nitrous oxide may be associated with the long-term risk of myocardial infarction, and thus

the patients need to be carefully evaluated in order to indicate this sedation only for those with none or low risks due to this technique^{1,18}. In elderly, other risks such as cancer recurrence, neurotoxicity and long-term cognitive dysfunction need to be investigated and considered.

In conclusion, chronic pain at other parts of the body of patients that underwent dental treatment with nitrous oxide

sedation presented a reduction in their intensity. It was not dependent on the local of pain and more often in women. Nitrous oxide may be a tool to be used in the treatment of chronic pain, and future prospective studies are necessary to understand the underlying mechanisms and the effect of nitrous oxide/oxygen in patients according to the pain diagnosis and other characteristics.

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