

# Intravenous chlorpromazine and promethazine for treating chronic daily headache in cases of unsuccessful analgesic withdrawal\*

*Clorpromazina e prometazina endovenosas para tratamento de cefaleia diária crônica em casos de retirada ineficaz de analgésicos*

João Vitor Feliciano MD<sup>1</sup>, Fabiola Dach MD<sup>1</sup>, Yára Dadalti Fragoso MD, MSc, PhD<sup>2</sup>, Jose G Speciali, MD, MSc, PhD<sup>1</sup>

\* Received from University Hospital, School of Medicine. Ribeirão Preto, SP.

## SUMMARY

**BACKGROUND AND OBJECTIVES:** Chronic daily headache (CDH) may be a particularly challenging condition when the withdrawal of excessive analgesic medication is unsuccessful. Current guidelines suggest hospitalization for these patients, and a variety of pharmacological and non-pharmacological treatments have been reported. This study aimed at presenting our results on hospitalization of cases of CDH associated to medication overuse. The results on the use of intravenous chlorpromazine and promethazine for these patients have not been previously reported.

**METHOD:** Retrospective assessment of medical records from eight patients treated at the Hospital das Clínicas de Ribeirão Preto. In all cases, analgesic withdrawal during hospitalization was associated to intravenous saline containing 25 mg of chlorpromazine and 25 mg of promethazine.

**RESULTS:** All patients obtained at least 70% improvement of their headache. Five to 30 days were necessary to treat these patients in the hospital.

**CONCLUSION:** Hospitalization and intravenous chlorpromazine and promethazine may be a viable alternative to treat CDH when analgesic withdrawal is unsuccessful.

**Keywords:** Headache, Medication overuse, Migraine.

## RESUMO

**JUSTIFICATIVA E OBJETIVOS:** Cefaleia diária crônica (CDC) pode ser uma condição especialmente difícil quando a retirada de excesso de analgésicos é ineficaz. Diretrizes atuais sugerem internação para esses pacientes e uma série de tratamentos farmacológicos e não-farmacológicos tem sido cogitada. O objetivo deste estudo foi apresentar nossos resultados com a internação de casos de CDC associada ao uso excessivo de medicamentos. Resultados sobre o uso de clorpromazina e prometazina endovenosas para esses pacientes não haviam sido apresentados antes.

**MÉTODO:** Avaliação retrospectiva de prontuários médicos de oito pacientes tratados no Hospital das Clínicas de Ribeirão Preto. Em todos os casos, a retirada de analgésicos durante a internação foi associada à solução fisiológica endovenosa contendo 25 mg de clorpromazina e 25 mg de prometazina.

**RESULTADOS:** Todos os pacientes obtiveram ao menos 70% de melhora da cefaleia. Foram necessários de 5 a 30 dias para tratar esses pacientes no hospital.

**CONCLUSÃO:** Internação e clorpromazina e prometazina endovenosas podem ser uma alternativa viável para tratar CDC quando a retirada de analgésicos é ineficaz.

**Descritores:** Cefaleia, Enxaqueca, Excesso de medicação.

## INTRODUCTION

The recent review by Rossi et al.<sup>1</sup> pointed out the difficulties in managing medication overuse headache (MOH), which is an important and very frequent type of chronic daily headache (CDH). In Brazil, the prevalence of CDH is high, reported as 6.9%<sup>2</sup>. Although many patients with CDH can be successfully treated in outpatient clinics, some cases may prove to be very difficult, mainly due to excessive medication usage, with addict-like behavior<sup>3</sup>.

1. University Hospital, School of Medicine, Ribeirão Preto, University of São Paulo. Ribeirão Preto, SP, Brazil.

2. Headache Outpatient Service, Department of Neurology, Metropolitan University of Santos. Santos, SP, Brazil.

No conflicts of interest to declare; no funding for this work. All the authors have received benefits from different pharmaceutical industries in the form of congresses or speaker's grants.

Correspondence to:

Jose G. Speciali

Rua Tucunarés, 735, Quinta da Alvorada  
14110-000 Ribeirão Preto, (SP), Brasil.

Phone: 55 (16) 3623-9743

E-mail: speciali@netsite.com.br

In fact, the “US Headache Guidelines Consortium, Section on Inpatient Treatment”<sup>4</sup> discusses in detail the benefits of hospitalization for these patients.

As Rossi et al.<sup>1</sup> highlighted in their report, the road to evidence is built through experience. Placebo-controlled trials have no place in the assessment of CDH treatment, considering the highly disabling condition of these patients<sup>4</sup>. Therefore, Class I evidence on drugs for hospitalized CDH patients is not likely to ever be obtained. The present paper adds to the discussion of pharmacological approaches to treatment by introducing an alternative combination of chlorpromazine and promethazine. There has not been any previous report on the efficacy and tolerability of this association.

## METHOD

The Ethics Committee of Hospital das Clínicas de Ribeirão Preto approved this study, under the registration number HCRP 968/2008. After two unsuccessful attempts to withdraw excessive medication from confirmed outpatient cases of chronic migraine, hospitalization was proposed. The medical records from eight such patients between January 2005 and March 2005 were systematically reviewed in accordance to the protocol proposed for this study.

An association of 25 mg chlorpromazine and 25 mg promethazine was diluted in 500 mL saline and was infused at 14 drops/minute, with the aim of achieving 12 hours of continuous infusion per day, for 5 to 10 days. After hospital discharge, patients received chlorpromazine 30 mg/day for 90 days. Physicians and nurses continuously reinforced the message that withdrawal of pain medication was necessary.

## RESULTS

Eight patients (one male) of average age 42 years, with an average history of 18.8 months of CDH related to medication overuse, entered the study. The positive results from this pharmacological approach are summarized in Table I. No serious adverse events were observed in these patients, although sleepiness was commonly observed during the first days of this treatment. Although postural hypotension leading to fainting and extrapyramidal signs and symptoms were observed in four cases, none was considered to be serious. All adverse signs or symptoms improved immediately after withdrawal of chlorpromazine.

Hospitalization was necessary for five to 30 days (average = 12 days), further demonstrating the difficulty

in managing this medical condition. Patients did not present any signs or symptoms related to adverse effects of medications at the time they were discharged from hospital.

All patients showed at least 70% reduction of their headache when discharged from the hospital (Table 1).

Table 1 – Summary of data on refractory CDH patients, all of them with medication overuse, treated with an association of chlorpromazine and promethazine

Gender	Age	CDH Duration (months)	Hospital Stay (days)	Headache Evolution (% Improvement)
F	50	36	5	>70%
M	22	12	19	>85%
F	41	14	30	100%
F	41	12	7	100%
F	54	48	13	>85%
F	36	8	8	>85%
F	64	3	14	>70%
F	30	18	11	100%

## DISCUSSION

Chronic headache related to medication overuse is a public health problem affecting a large number of individuals worldwide<sup>5</sup>. Aggressive approaches toward detoxification and medication withdrawal involving hospitalization have been recommended by several authors<sup>4,6,7</sup>, although no definite therapeutic scheme can currently be recommended. The present results from an association of chlorpromazine and promethazine for intravenous infusion in more difficult cases of MOH may be worth a proper clinical trial. However, it is unlikely that such trial be performed on a placebo-controlled basis, given the disabling condition created by the disease in question. The experience and the evidence on possible therapeutic approaches to severe cases of CDH will probably continue to be built by reports on case series, such as the present one.

CDH patients with excessive use of medications are the ultimate challenge in tertiary headache units. The inherent difficulties of pharmacological and non-pharmacological approaches toward these patients have often been highlighted<sup>8,9</sup>, although the clinical management of such cases still remains a matter of continual discussion<sup>5</sup>. Results from our open study, despite all limitations, show similar results to those found by Lake, Saper and Hamel<sup>7</sup>, who reported an average of 13 days hospitalization, with 78% headache reduction or remission.

The continuous support provided by physicians and nurses obviously may have had a positive influence on the final results, but it would have been unacceptable to treat these patients without such support<sup>1</sup>.

Patients presented in this case series had been refractory to every attempt of analgesics withdrawal in an outpatient environment. Hospitalization for these patients was our last resource, and the choice of chlorpromazine/promethazine was primarily due to the availability of drugs in our hospital. Injections of dihydroergotamine or tryptans are not currently available in our health public services.

The first days following analgesic withdrawal are known to be crucial for the long-term success of MOH treatment. However, only a few reports discuss the results obtained at the time patients are discharged from hospital.

## CONCLUSION

This work showed that the association of chlorpromazine and promethazine is a valid option for inpatients needing abrupt analgesic withdrawal. An improvement of 70%-100% was obtained in these patients at the time of hospital discharge, increasing the possibility of further success in prophylactic approaches for patients who now are not in excessive use of analgesics.

## REFERENCES

1. Rossi P, Jensen R, Nappi G, et al. A narrative review

on the management of medication overuse headache: the steep road from experience to evidence. *J Headache Pain* 2009;10(6):71-6.

2. Queiroz LP, Peres MF, Kowacs F, et al. Chronic daily headache in Brazil: a nationwide population-based study. *Cephalalgia* 2008;28(12):1264-9.

3. Ferrari A, Cicero AF, Bertolini A, et al. Need for analgesics/drugs of abuse: a comparison between headache patients and addicts by the Leeds Dependence Questionnaire (LDQ). *Cephalalgia* 2005;26(2):187-93.

4. Freitag FG, Lake A 3<sup>rd</sup>, Lipton R, et al. Inpatient treatment of headache: an evidence-based assessment. *Headache* 2004;44(4):342-60.

5. Katsarava Z, Holle D, Diener HC. Medication overuse headache. *Curr Neurol Neurosci Rep* 2009;9(2):115-9.

6. Trucco M, Meinere P, Ruiz I. Preliminary results of a withdrawal and detoxification therapeutic regimen in patients with probable chronic migraine and probable medication overuse headache. *J Headache Pain* 2005;6(4):334-7.

7. Lake AE 3<sup>rd</sup>, Saper JR, Hamel RL. Comprehensive inpatient treatment of refractory chronic daily headache. *Headache* 2009;49(4):555-62.

8. Obermann M, Katsarava Z. Management of medication-overuse headache. *Expert Rev Neurother* 2007;7(9):1145-55.

9. Katsarava Z, Jensen R. Medication-overuse headache: where are we now? *Curr Opin Neurol* 2007;20(3):326-30.

Presented in September 29, 2010.

Accepted in December, 01, 2010.