Contents available at **PubMed**
www.anmm.org.mx

PERMANYER

Gac Med Mex. 2017;153:53-5

GACETA MÉDICA DE MÉXICO

ORIGINAL ARTICLE

Effectiveness of intravenous sedation with midazolam-diphenhydramine in patients who are going to perform an magnetic resonance (MRI)

Lucía Álvarez-Bastidas[1], Enrique Sabag-Ruiz[2] and Alfonso Medina-Soto[3]*

[1]Clinical Coordination of Education and Research in Health, HGR No. 1; [2]Department of Occupational Medicine, High Specialty Medical Unit; [3]Department of Anesthesiology, High Specialty Medical Unit No. 1, IMSS, Obregón, Son. Mexico

Abstract

Introduction: *The requirement of the anesthesiologist for patient care outside the surgical area is constantly increasing. It is an activity that encompasses the different degrees of monitoring, sedation, and anesthesia.* **Objective:** *To compare the safety and efficacy of midazolam midazolam-diphenhydramine against magnetic resonance with level of sedation on the Ramsay scale.* **Materials and methods:** *We performed a study in the Instituto Mexicano del Seguro Social Obregon, Sonora, of patients scheduled for cranial magnetic resonance imaging with sedation, during October and December 2013, comparing two groups: midazolam/diphenhydramine against midazolam groups.* **Results:** *We included 68 patients, 34 in the experimental group (midazolam-diphenhydramine) versus 34 controls (midazolam). The Ramsay scale showed, in the experimental group, an increased sedation effect resulting in one Ramsay 1, at 10 minutes 2.8 2.8 20 minutes and 30 minutes 2.0. In the control group the basal Ramsay was 1, 2.1 to 10 minutes, 20 minutes and 2.1 to 2.0 at 30 minutes (p = 0.0001). The analysis of heart rate, respiratory, and baseline oxygen saturation, at 10, 20 and 30 minutes, was p = 0.0001 for both groups.* **Conclusion:** *The combination of diphenhydramine with intravenous midazolam is safe, with the degree of sedation being better compared with use of midazolam alone, resulting in less failure of sedation during magnetic resonance imaging.* (Gac Med Mex. 2017;153:53-5)

Corresponding author: *Lucía Álvarez-Bastidas, alely27@hotmail.com; lucia.alvarez@imss.gob.mx*

KEY WORDS: *Diphenhydramine. Midazolam. Resonance. Sedation.*

Introduction

The growing diffusion of non-invasive diagnostic and therapeutic techniques and their extension to patients has multiplied the demand for anesthetic actions outside the operating room. It is an activity that encompasses different degrees of surveillance, sedation and anesthesia.

Sedation with midazolam plus diphenhydramine has the advantage that when administered together their effects are synergized without producing respiratory

Correspondence:
*Lucía Álvarez-Bastidas
IMSS
Coordinación Clínica de Educación e Investigación en Salud
Ing. Alberto Zazueta Nieblas, 562
Col. Nainari del Yaqui
C.P. 85130, Ciudad Obregón, Son. México
E-mail: alely27@hotmail.com;
lucia.alvarez@imss.gob.mx

Date of reception: 08-05-2015
Date of acceptance: 27-07-2015

depression[1]. The level of sedation can be assessed with the Ramsay sedation scale[2].

Sedation during MRI studies is indicated in anxious, uncooperative patients or with fear of closed spaces[3]. In a randomized, double-blind trial, comparative of midazolam-diphenhydramine versus placebo, the results showed better sedation quality in favor of the diphenhydramine group ($p < 0.05$)[4]. Therefore, sedation anesthetic techniques with reduced doses of two or more drugs are preferable to those offered by a single drug[5].

The role played by anesthesiologists in the MRI area is increasingly acquiring importance, mainly in anxious or uncooperative adults, who account for up to 10% of patients undergoing this procedure[6].

Material and methods

After authorization was granted by the committee of research and research ethics of the High Specialty Medical Unit (UMAE – *Unidad Médica de Alta Especialidad*) in Obregón, Sonora, a double-blind, randomized, controlled trial was carried out during the months of October through December 2013 including 68 patients of both genders, with ages ranging from 18 to 70 years, programmed for radiodiagnostic study with cranial MRI and with fear to closed spaces. All participants signed an informed consent letter. Treatment group assignment was random, with 2 groups of 34 subjects each being formed: the experimental group (midazolam 0.03 mg/kg plus diphenhydramine 0.5 mg/kg) and the control group (midazolam 0.03 mg/kg).

After insertion of a catheter in a peripheral vein of either upper limb, with saline infusion and vital signs surveillance since the patient was admitted and up to the MRI area by means of a monitor, the drug assigned to each patient, the preparation of which was unknown to the anesthesiologist, was then administered. Each patient had a nasal oxygen cannula placed and the sedation degree according to the Ramsey scale was assessed 10, 20 and 30 minutes after the medication was administered by asking simple questions. If the patient failed to answer the question, the arms were tapped to observe the response to tactile stimulus. Vital signs were closely monitored, with special attention to respiratory rate, oxygen saturation, carbon dioxide total extraction and heart rate. Hemodynamic parameters were recorded at resonator entrance and at 5, 10, 15, 30 and 45 minutes until the completion of the MRI study.

Results

Sixty-eight patients were examined during the time period encompassed between October and December 2013 in the UMAE MRI area, out of which 34 belonged to the experimental group (midazolam-diphenhydramine) and 34 to the control group (midazolam).

The sedation effect was observed to be higher in the experimental group, with a baseline Ramsey score of 1, 2.8 at 10 minutes, 2.8 at 20 minutes and 2.0 at 30 minutes; in the control group, baseline score was 1, 2.1 at 10 minutes, 2.1 at 20 minutes and 2.0 at 30 minutes. The p-value was significant (0.0001). Table 1 shows the Ramsey scale scores obtained in both study groups.

An analysis of baseline heart rate and at 10, 20 and 30 minutes was made. In the experimental group, heart rate was 86, 74, 70 and 69, respectively; in the control group, heart rate was 88, 82, 79 and 81, respectively. The p-value was significant (0.0001). Important changes in heart rate were generated in both groups. In the experimental group, heart rate decreased more without reaching bradicardia, since it was maintained higher than 60 beats per minute for a 30-minute period.

Discussion

Our results show that the midazolam-diphenhydramine combination can be successfully and safely used in patients requiring sedation for the performance of a MRI, in comparison with the use of midazolam monotherapy, with absolute immobility being achieved during the long period it takes to perform this study, without respiratory depression being produced. The anesthesiologist's goal is to achieve for the patient to cooperate and remain immobile and calmed during the entire procedure using drugs that do not produce respiratory depression.

Cengiz et al.[6] show that sedation with oral midazolam and diphenhydramine achieves successful sedation in 82% in comparison with 52% with midazolam alone, with similar results being shown in our intravenous-route midazolam-diphenhydramine study. The use of both these drugs has the advantage that, when administered together, sedation is synergized and a grade 2 to 3 Ramsey score is achieved without respiratory depression being produced.

Roehrs et al.[7] demonstrated that no significant sedative effects of ethanol, triazolam and diphenhydramine

Table 1. Statistical description of Ramsay scale baseline score and at 10, 20 and 30 minutes in both groups

	Group	Mean	SD	N
Ramsay_baseline	Experimental	1.0000	0.00000	34
	Control	1.0000	0.00000	34
	Total	1.0000	0.00000	68
Ramsay_10	Experimental	2.8235	0.38695	34
	Control	2.1471	0.35949	34
	Total	2.4853	0.50350	68
Ramsay_20	Experimental	2.8235	0.38695	34
	Control	2.1176	0.32703	34
	Total	2.4706	0.50285	68
Ramsay_30	Experimental	2.0000	0.00000	34
	Control	2.0000	0.00000	34
	Total	2.0000	0.00000	68

SD: standard deviation.
Source: patients programmed for MRI between October and December 2013. UMAE Obregón, Sonora.

were observed with regard to placebo in sleep latency and performance measures with the effects being detected over the full 6.5 hours of assessment.

Diphenhydramine has antihistaminic and anticholinergic actions, and is prescribed for the treatment of allergies and Parkinson's disease. It is also commonly used as a sleep aid, both by prescription or OTC, owing to its efficacy as hypnotic sedative[8]. In our study, we have successfully used it as an aid for optimal sedation, with the purpose being to induce deep sedation while minimizing physical discomfort and maximizing amnesia and patient return to previous state[9].

In this studio, sedation is intended to achieve immobility to obtain optimal quality MRI images[10]. The patient may be asleep and often can comply with instructions to remain immobile.

In conclusion, our study indicates that the combination of diphenhydramine plus midazolam by intravenous route is safe, and sedation is efficacious for patients who are to undergo MRI, with the degree of sedation being superior in comparison with midazolam alone, which results in less sedation failure during MRI.

Conflict of interests

There is no conflict of interests.

References

1. Brown RE, Stevens DR, Haas HL. The physiology of brain histamine. Prog Neurobiol 2001;63:637-72.
2. García SMJ, López-Aldrete JA, Martín RJL, Prieto CM. Sedación en pacientes en las técnicas dolorosas diagnosticada y terapéutica: supuestos clínicos. Presentado en: V Reunión Científica de la SED y Jornada de actualización del dolor. Granada; 2001. p. 6-23.
3. Hernández-De la Vega L. Sedación consciente e inconsciente. Rev Mex Anest. 2004;27(Supl 1):395-497.
4. Tu RH, Grewall P, Leung JW, Suryaprasad AG. Diphenhydramine as adjunct to sedation for colonoscopy: a double-blind randomized, placebo-controlled study. Gastrointest Endosc. 2006;63:87-94.
5. Fernández AS, Navarrete ZV, Vallongo MMB, López RM, De la Barrera F. Midazolam-ketaminapropofol vs propofol para sedación en RMN. Costos y beneficios. Rev Cub Anest Rean. 2007;6:20-33.
6. Cengiz M, Baysal Z, Ganidaglis S. Oral sedation with midazolam and diphenhydramine compared with midazolam alone in children undergoing magnetic resonance imaging. Paediatr Anaesth. 2006;16:621-6.
7. Roehrs T, Zwyghuizen-Doorenbos A, Roth T. Sedative effects and plasma concentrations following single doses of triazolam diphenhydramine, ethanol and placebo. Sleep. 1993;16:301-5.
8. Asamblea Mundial de Lisboa. Declaración de Lisboa de la AMM sobre los derechos del paciente. [En línea]. Portugal: WMA. 2005. (Consultado el 11 de julio de 2013.) Disponible en: http://www.wma.net/es/30publications/10policies/l4/index.html.pdf?print-media-type&footer-right=[page]/[toPage]
9. Committee on Drugs. American Academy of Pediatrics. Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: addendum. Pediatrics. 2002;110:836-8.
10. Lawson GR. Controversy: sedation of children for magnetic resonance imaging. Arch Dis Child. 2000;82:150-3.