ORIGINAL ARTICLE

The Efficacy of Propofol vs. Subcutaneous Sumatriptan for Treatment of Acute Migraine Headaches in the Emergency Department: A Double-Blinded Clinical Trial

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■ **Abstract**

Background: In this double-blinded, randomized trial, we hypothesized that propofol is as effective as sumatriptan in treating acute migraine headaches, with better control of nausea and vomiting, and fewer side effects.

Methods: Ninety cases of acute migraine attack admitted to the emergency department were randomly allocated into two treatment groups: (1) 6 mg of sumatriptan subcutaneously or (2) propofol injected intravenously in 30 to 40 mg boluses, followed by 10 to 20 mg intermittent bolus doses to sedate the patients to Ramsey score of 3 to 4. Headache severity was assessed using an 11-point visual analog scale before treatment and 30 minutes, 1 hour, and 2 hours after treatment. Accompanying symptoms, improvement in headache, and the need for anti-emetic therapy were also assessed.

Results: A total of 91 patients were enrolled in this study. One patient in the sumatriptan group was excluded due to severe chest tightness, and 90 patients were included in the final analysis. Pain intensity was significantly lower in the propofol group 30 minutes after treatment ($P = 0.001$); however, after 1 and 2 hours, there were no significant differences between the groups. The need for anti-emetic therapy and the recurrence of symptoms were significantly lower in the propofol group ($P = 0.045$ and $P = 0.001$, respectively).

Conclusion: Propofol is equally suitable as sumatriptan for the acute treatment of migraine headaches in an emergency department setting. Moreover, the use of propofol avoids some of the adverse side effects of sumatriptan while providing better control of nausea and vomiting. ■

Key Words: propofol, sumatriptan, migraine, headache, treatment, emergency department

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Submitted: December 23, 2013; Revised April 18, 2014; Revision accepted: May 26, 2014

DOI. 10.1111/papr.12230

INTRODUCTION

Migraine headaches are responsible for 2.2% of emergency department visits.[1] Triptans, especially sumatriptan, are used as a migraine-specific medication to terminate migraine headache attacks. Although triptans

have been introduced as a safe and effective treatment for migraine attacks, this class of drugs has well-known side effects and contraindications including chest pressure, neck tightness, limb heaviness, and tingling. Contraindications include vascular disease, coronary artery disease, and pregnancy.[2] Several open-label studies and case reports and one double-blinded study have shown that subanesthetic doses of propofol are efficacious as rescue therapy for acute migraine headaches in adults and children.[3–6] In this study, we hypothesize that a subanesthetic dose of propofol is safe, at least as effective as sumatriptan, and alleviates the anti-emetic effect, side effects, and contraindications of sumatriptan.

METHODS

This randomized, double-blinded prospective study was conducted with approval by the university ethical committee and with registration in the Iranian Registry of Clinical Trials (www.irct.ir) by ID number IRCT201008174583N1. A total of 90 known migraine patients meeting the International Headache Society (IHS)[7] criteria were enrolled in this study. The sample size was calculated considering level of confidence = 95%, power = 85%, mean reduction in pain intensity in the propofol group = 95%,[3] and mean reduction in pain intensity in the sumatriptan group = 73%.[8] Considering a 15% failed sample, the minimum sample size was 45 in each group. A similar study[4] also used the same number of patients. The patients aged between 18 and 45 years and were admitted to university hospital emergency department (ED). After obtaining written informed consent, participants were randomly allocated into two groups using a random number table. The exclusion criteria were pregnancy (assessed by a urine βHCG in case of probable pregnancy according to last menstrual period), known or suspected coronary or peripheral vascular disease, allergy to propofol or eggs or soy, self-reported opium addiction, diastolic blood pressure > 105 mm Hg, and the use of ergotamine, or 5-HT (serotonin) agonists within the 24 hours prior to ED admission.

After assessment of the headache severity by the ED physician using an 11-point visual analog scale (VAS) and evaluation of the accompanying symptoms including phonophobia, photophobia, and nausea and vomiting, the patients were transferred to a dark, quiet room, and an intravenous (IV) line was established with an infusion of 500 mL of normal saline. In the propofol group, 0.5 mL of normal saline was injected subcutaneously (to be similar to the sumatriptan group), followed by a 30 to 40 mg propofol (Lipura®, B. Braun, Melsungen, Germany) bolus injection and then a 10 to 20 mg bolus every 3 to 5 minutes to a maximum dose of 120 mg. This lasted for < 30 minutes sedating patients to a Ramsey score of 3 to 4. In the sumatriptan group, 6 mg of sumatriptan (Migrstop®, Osveh, Iran) was injected subcutaneously, and a 3.5 mL normal saline bolus was infused (to be similar to the propofol group), followed by 1.5 mL every 4 minutes to a final dose of up to 7.5 mL. The therapy was repeated after 1 hour if the pain score was reduced by < 4 points. All syringes were wrapped so that the patients could not identify the contents. All injections were performed by an anesthesiology resident.

The same physician who evaluated them at admission and was also blinded to the therapy assessed patients at 30 minutes, 60 minutes, and 2 hours. Headache severity, VAS score reduction, improvement in accompanying symptoms, and also side effects, including hypotension and bradycardia (defined as a 20% reduction in primary blood pressure and heart rate, respectively), chest tightness, light headedness, and oxygen desaturation to lower than 90% were recorded. Follow-up was conducted 24 hours later by calling the patients and inquiring about headache recurrence. A VAS score reduction of < 4 points was considered a failed response, and patients were prescribed an alternative therapy, including intravenous dexamethasone or an indomethacin suppository. In cases of nausea or vomiting after treatment, patients were treated with a 1 mg infusion of IV granisetron.

Statistical Methods

Quantitative data of the drug effects for both groups (at 30, 60, and 120 minutes after treatment) were analyzed using *t*-test. Baseline nominal data were analyzed using the Fisher's exact test and chi-square test. The analyses were performed using the SPSS, version 16 (SPSS Inc., Chicago, IL, USA). *P* values of < 0.05 were considered as significant difference.

RESULTS

A total of 91 eligible patients were enrolled in this study. One patient in the sumatriptan group could not complete the study because of severe chest tightness. The

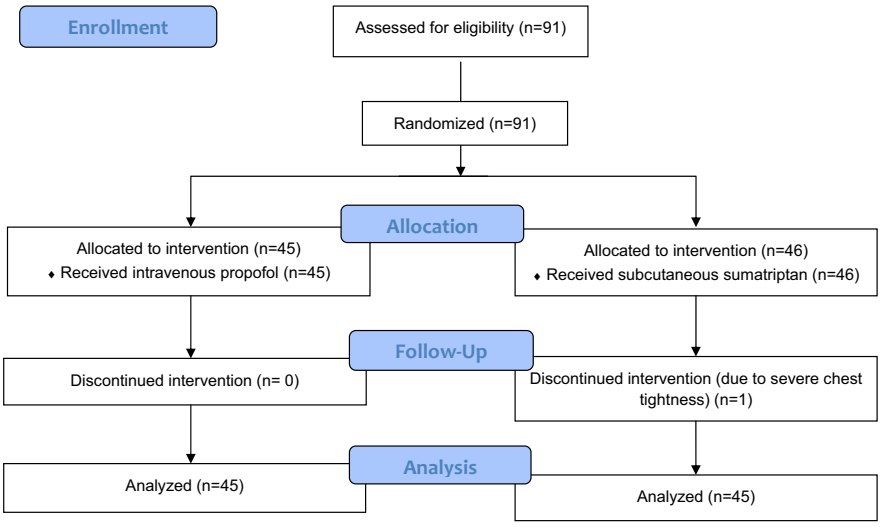

Figure 1. CONSORT flow diagram.

Table 1. Demographic and Baseline Characteristics of the Patients

Characteristics	Sumatriptan Group *N* = 45	Propofol Group *N* = 45	*P* Value
Age	33.36 ± 7.91	33.08 ± 8.12	0.87
Sex	Male = 22.7%	Male = 26.1%	0.80
	Female = 77.3%	Female = 73.9%	
Migraine type	Common = 93.2%	Common = 93.5%	1.00
	Classic = 6.8%	Classic = 6.5%	
Drug usage before admission	88.9%	93.3%	0.71
Accompanying symptoms	91.1%	84.4%	0.52
Nausea and vomiting	77.8%	75.6%	1.00
Photophobia	64.4%	66.7%	1.00
Phonophobia	64.6%	57.8%	1.00

patients' disposition is shown in Figure 1. The patients' demographics and baseline characteristics are summarized in Table 1. There were no significant differences between the two groups in demographic data or baseline characteristics, including migraine type, medications used before admission, and accompanying symptoms. As is seen in Table 2, the primary outcome (pain intensity) was significantly lower 30 minutes after treatment in the propofol group ($P = 0.03$). However, the pain intensity 1 and 2 hours after treatment was similar in both groups. Response to the therapy, which was defined as at least 4 points reduction in VAS score, was similar in two groups. The recurrence rate and need for anti-emetic therapy (granisetron) were significantly lower in the propofol group ($P = 0.001$). Improvements in accompanying symptoms, including photophobia and phonophobia are shown in Table 3 and were similar in two groups at the time of discharge. Table 4 shows adverse effect of therapy. Chest tightness and rash at the site of injection were significantly lower in the propofol group ($P = 0.001$ for both). Figure 2 shows the trend in VAS score reduction at different times (difference between before and after treatment), which is significantly ($P = 0.002$) more in the propofol group (ie, 6.7) than in the sumatriptan group (ie, 5).

DISCUSSION

There are several open-label and case series as well as two randomized double-blinded studies that have investigated the use of propofol for nonorganic headaches.[3–6] However, based on our search, this study is the first randomized clinical trial to compare propofol vs. sumatriptan as a standard rescue therapy for acute migraine management in the ED. This study showed that propofol is as effective as sumatriptan with a faster response time as demonstrated by better pain control 30 minutes after treatment. With the exception of a study by Simmonds et al.,[9] all other studies have demonstrated that propofol has high efficacy in treating migraine headaches.[3–6] However, the Simmonds' study was performed in a different setting, as propofol was

Table 2. Pain Intensity and Response to Therapy in the Patients

Outcome Measurement	Groups		
	Sumatriptan	Propofol	*P* Value
Pain intensity before treatment	8.71 ± 1.20	9.09 ± 1.02	0.111
Pain intensity 30 minutes after treatment	3.69 ± 2.55	2.62 ± 2.12	0.034
Pain intensity 1 hour after treatment	2.36 ± 2.31	2.69 ± 2.63	0.53
Pain intensity 2 hours after treatment	1.36 ± 1.96	1.62 ± 2.04	0.53
Recurrence within 24 hours of discharge	55.3%	17.1%	0.001
Anti-emetic therapy	33.3%	13.3%	0.045
Response to therapy	80%	84.4%	0.78
Response in first attempt	73.3%	64.4%	0.16

Table 3. Accompanying Symptom Improvement at the Time of Discharge

Symptom	Sumatriptan, %	Propofol, %	*P* Value
Nausea and vomiting	91.9	91.2	1.00
Photophobia	84.4	77.4	0.65
Phonophobia	86.7	77.8	0.29

Table 4. Adverse Effects of Drugs

Adverse Effect	Sumatriptan, %	Propofol, %	*P* Value
Drowsiness	4.4	15.6	0.15
Chest tightness	31.1	2.2	0.001
Hypotension	4.4	2.2	1
Rash at the injection site	33.3	0.0	0.001

used electively in patients suffering from chronic daily headaches rather than as rescue therapy. Another important difference is that in the Simmonds' study, propofol was infused from the start of study, whereas in our study, a propofol bolus was injected as a loading dose. Therefore, a specific therapeutic level may not have been achieved in the Simmonds' study. In our study, propofol had a better side effect profile. In the sumatriptan group, 31% of the patients experienced chest tightness and one patient could not complete the study due to severe chest tightness. This result is in contrast to a study by Kostic et al.,[10] in which no patient in the sumatriptan group complained of chest tightness. In our study, 2.2% of patients in propofol group had chest tightness. It may be related to anxiety accompanying migraine itself. However, the Kostic et al. suggested that this result occurred because of the way they asked about chest tightness. In our study, better control of nausea and vomiting was achieved with propofol, and fewer patients needed anti-emetic therapy (granisetron). In this experiment, granisetron was used because it would not interfere with the study results. Similarly, in a study by Krusz et al.[3], the patients did not require anti-emetic therapy. The anti-emetic properties of propofol have also been demonstrated during the administration of anesthesia.[11,12] No patient in our study had hemodynamic instability or desaturation of < 90%. In both groups, the recurrence rate was higher within the 24-hour follow-up. However, the rate was significantly higher in the sumatriptan group. A previous study by Brandes et al.[13] also demonstrated a high rate of recurrence for sumatriptan. Our main limitation was patients' follow-up, which was conducted only by calling the patients, and not by an appropriate questionnaire. Our follow-up results suggest that a complementary medication is needed to sustain headache relief. Regarding cost-effectiveness, propofol is relatively

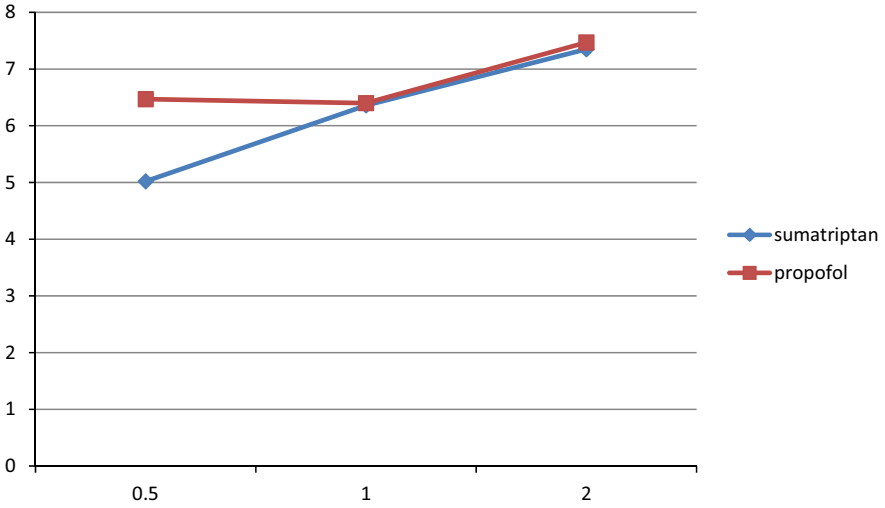

Figure 2. The trend in reduction of visual analog scale score before and after treatment in the two groups. The difference between them is significant only at 0.5 hour after treatment ($P < 0.001$).

expensive and cannot be prescribed in an out-of-hospital setting.

Based on our results, propofol can be an ideal rescue therapy for acute migraine in ED and hospital settings, as it is efficacious with minimal adverse effects. However, a complementary medication is necessary to sustain pain relief.

ACKNOWLEDGEMENTS

This study audits and follow-up were carried out by the Pain Research Center, which is supported financially by Shahid Sadoughi University of Medical Sciences, Yazd, Iran. The authors would like to acknowledge Ms. Sima Valizadeh, MD, for her assistance in writing the article. The authors report no conflict of interest.

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