

The response to sodium valproate of patients with sinus headaches with normal endoscopic and CT findings

Mohammad Hossein Dadgarnia · Saeed Atighechi ·
Mohammad Hossein Baradaranfar

Received: 29 April 2009 / Accepted: 27 August 2009 / Published online: 16 September 2009
© Springer-Verlag 2009

Abstract The objectives of this study are to evaluate the patients who have sinus headaches, either self-ascribed or physician-diagnosed, and to determinate the response to sodium valproate in a prophylactic treatment of the patients without positive sino-nasal findings. “Sinus headache” is a patient’s complaint or physician-diagnosis that can have a variety of underlying causes. The patients are often treated with multiple courses of antibiotics and occasionally undergo a sinus surgery, often with little or no relief of their symptoms. One hundred and four patients with “sinus headaches” were evaluated prospectively. The patients with a normal rigid nasal endoscopy and a paranasal sinus computed tomography scan were treated with sodium valproate as a prophylactic treatment. After a 3-month follow-up, the patients’ response to the treatment was evaluated. Seventy-two patients (69.2%) did not have any positive sino-nasal findings in the nasal endoscopy and the computed tomography scanning. The response rate to the treatment for these patients was as follows: significant improvement in 44 patients (61.1%), partial response (9.7%), no response (15.3%), and ten patients (13.9%) withdrew or failed to follow-up. According to Wilcoxon test, the patients’ response rate to sodium valproate was statistically significant ($P = 0.001$). In conclusion, a majority of “sinus headache” patients do not show any positive sino-nasal pathologic finding. Therefore, we have to consider migraine headache as a considerable cause and sodium valproate as an effective conservative treatment.

Keywords Sinus headaches · Chronic (rhino) sinusitis · Migraine · Sodium valproate

Abbreviations

EPOS	European Position Paper on Rhinosinusitis and Nasal polyps
IHS	International Headache Society
CT	Computed tomography
L–M score	Lund–Mackay score

Introduction

Headaches associated with a facial pain and pressure are commonly given a nonspecific diagnosis of “sinus headache” [1]. Patients often explain episodes of pain or pressure over the area of their sinuses or around their eyes. Associated symptoms of nasal congestion and drainage often lead to a diagnosis, either self-ascribed or by a physician, as “sinus headache”. These patients have a past history of treatment with multiple courses of antibiotics, decongestants and steroids. They have also occasionally undergone a sinus surgery, with little or no relief of their symptoms [2]. Sinus headache is a common but ambiguous diagnosis, and patients with headache often cite sinus pain and pressure as a cause of their headaches. Couch writes about sinus headache in his review: patients reason that, since the sinuses are close to the eyes, headaches located in the frontal, supraorbital, or infraorbital region are sinus headaches. These headaches are usually recurrent, nonseasonal, and unassociated with fever, localized tenderness, or erythema [3].

There are two principal systems of classification and diagnosis criteria relating to headaches and sinus headaches: The European Position Paper on Rhinosinusitis and

M. H. Dadgarnia (✉) · S. Atighechi · M. H. Baradaranfar
Department of Otolaryngology, Head and Neck Surgery,
Shahid Sadoughi General Hospital,
Shahid Sadoughi University of Medical Sciences, Yazd, Iran
e-mail: drdadgarnia@yahoo.com

Nasal polyps (EPOS) 2007 and the International Headache Society (IHS). In 2007, the EPOS defined rhinosinusitis as inflammation of the nose and the paranasal sinuses characterized by two or more symptoms, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip), \pm facial pain/pressure, \pm reduction or loss of smell; and either endoscopic signs of polyps and/or mucopurulent discharge primarily from middle meatus and/or; edema/mucosal obstruction primarily in middle meatus, and/or CT changes showing mucosal changes within the ostiomeatal complex and/or sinuses. Duration of symptoms in chronic rhinosinusitis is >12 weeks [4]. According to this classification, we have to consider that facial pain or pressure alone is not diagnostic of chronic rhinosinusitis. The original 1988 IHS classification system included the term “acute sinus headache” but did not acknowledge chronic sinusitis as a cause for headache or facial pain [5]. The revised 2004 IHS classification system relates headache to sinus diseases under the classification “headache attributed to rhinosinusitis” with five diagnostic criteria (Table 1). The IHS considers that chronic sinusitis is not creditable as a cause for headache or facial pain unless it relapses into an acute stage. On the other hand, diagnostic criteria for migraines without aura have been published by the IHS as well (Table 2) [6].

It is interesting to note that many patients who experience migraines have associated cranial autonomic symptoms which may resemble sinusitis symptoms and signs. In a series of 177 patients, Barbanti et al. [7] reported that 45.8% of those with a migraine had lacrimation, eyelid edema, rhinorrhea, and nasal congestion in association with their headache. Other studies have also demonstrated that patients who present sinus headache have associated autonomic symptoms that may be mistaken for sinus symptoms [8–10].

The otolaryngologist should be familiar with the clinical presentation and workup of the patient diagnosed with “sinus headache”. It is because such patients frequently

Table 1 International Headache Society (IHS) diagnostic criteria for headache attributed to rhinosinusitis

A	Frontal headache accompanied by pain in one or more regions of the face, ears, or teeth and fulfilling criteria C and D
B	Clinical, nasal endoscopic, CT and/or MRI imaging, and/or laboratory evidence of acute or acute-on-chronic rhinosinusitis ^a
C	Headache and facial pain develop simultaneously with onset or acute exacerbation of rhinosinusitis
D	Headache and/or facial pain resolve within 7 days after remission or successful treatment of acute or acute-on-chronic rhinosinusitis

^a Clinical evidence may include purulence in the nasal cavity nasal obstruction, hyposmia, anosmia, and/or fever

Table 2 International Headache Society (IHS) diagnostic criteria for migraine without aura

A	At least five attacks fulfilling criteria B–D
B	Headache attacks lasting 4–72 h (untreated or successfully treated)
C	Headache has at least two of the following <ol style="list-style-type: none"> 1. Unilateral location 2. Pulsating quality 3. Moderate or severe pain intensity 4. Aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)
D	During headache at least one of the following: <ol style="list-style-type: none"> 1. Nausea and/or vomiting 2. Photophobia and phonophobia
E	Not attributed to another disorder

refer to the otolaryngologist. The aim of this study is to evaluate the patients who believe that they have sinus headaches and to evaluate how effective conservative treatment with sodium valproate can be for patients with sinus headache with normal endoscopic and CT findings.

Methods

One hundred and four patients with headache complaints who had referred to the ear, nose, and throat clinic were enrolled in a prospective study. The inclusion criteria were as follows: primary complaint of chronic headache or facial pain over the paranasal sinus area and a self or physician-diagnosis of sinus headache. All the patients underwent a complete head and neck examination including a rigid nasal endoscopy. The exclusion criteria were acute rhinosinusitis, sino-nasal polyposis, prior history of sino-nasal surgical operation, and contraindication of sodium valproate prescription especially liver disease. A previous treatment for migraine was not considered as a contraindication to the selection in this study. On entrance, a paranasal sinus coronal computed tomography (CT) scan without contrast was requested for all the patients. The existence of septal deviation, concha bullosa, and contact points was specified, and the chronic paranasal sinus inflammation was assessed with Lund–Mackay (L–M) score sinus CT radiologic staging [11]. The patients with no positive findings in the CT scan of the paranasal sinus were requested to fill out a sinus headache note in which the headache frequency and severity in the past 3 months were recorded. Respectively, these patients were treated with sodium valproate, slow-release tablets (500 mg at bed time) as prophylaxis and followed up for 3 months. They were given headache notes to document the frequency and severity of their headaches and associated symptoms.

The response to treatment was evaluated with a comparison of the frequency and severity of headaches in pre- and post-treatment period that had been recorded by the patients. The prophylactic response to the daily dose of sodium valproate was graded as a significant improvement (greater than 50%), partial (25–50%) and no response (less than 25%). At the end of the follow-up, the patients returned their headache notes. A statistical analysis was done with SPSS software. Wilcoxon test was used for the evaluation of the response rate to the prophylactic treatment, and the level of significance was considered $P < 0.05$.

The patients who did not respond to the prophylactic treatment were referred to a neurologist for further management.

Results

One hundred and four patients entered our study, most of whom were women (63.5%). Their age ranged from 15 to 41 years with a mean age of 35. Seventy-two patients (69.2%) did not present any positive sino-nasal findings in the nasal endoscopy and CT scanning. Thirty-two patients (30.8%) showed abnormalities including chronic inflammation of the paranasal sinuses with L–M score ≥ 5 in 24 cases (23%), concha bullosa and contact points in 10 (9.6%), and septal deviation with nasal obstruction in 13 (12.5%). Some of them had a combination of positive abnormal findings in the nasal endoscopy and CT scan (Tables 3, 4).

After completing the evaluation of the patients for sinus headaches, 32 patients with positive CT were treated with wide spectrum antibiotics for 3 weeks, and for patients

Table 3 Results of sino-nasal evaluation in the patients with sinus headache

Sino-nasal condition	Patient	
	Number	Percent
Normal	72	69.2
Abnormal	32	30.8
Total	104	100

Table 4 Abnormal sino-nasal findings in nasal endoscopy and CT scan of the patients

Finding	Patient	
	Number	Percent
Chronic sinuses inflammation (L–M score ≥ 5)	24	23
Concha bullosa and contact points	10	9.6
Septal deviation with nasal obstruction	13	12.5

without a good response to the medical treatment, a functional endoscopic sinus surgery was done.

Seventy-two of 104 cases (69.2%) who were without positive findings in the physical examination and CT scan filled in a sinus headache note and then a prophylactic treatment began. After 3-month follow-up for all the patients, 62 out of 72 (86.1%) completed the study and returned their headache notes.

The majority of patients reported having headaches that occurred several times per week or per day and lasted hours prior to the beginning of the treatment. Regarding the reduction of the frequency and severity of the headache, the prophylactic response to the daily dose of sodium valproate was as follows: out of 72 patients that were followed up, 44 (61.1%) had a significant improvement, 7 (9.7%) a partial response, 11 (15.3%) no response and 10 (13.9%) did not complete the course of prophylactic treatment (Table 5). According to Wilcoxon test, the patients’ response rate to sodium valproate was statistically significant ($P = 0.001$). Among those patients who completed follow-up period, none had any complaint of drug-induced side effects.

Discussion

“Sinus headache” is a common diagnosis both self-ascribed and physician-diagnosed in the absence of any clinical or radiographic evidence for sinus disease [12]. The similarity of symptoms with migraine complicates the diagnostic evaluation of sinus headaches.

In a migraine situation, the presence of what some have described autonomic symptoms such as nasal congestion, rhinorrhea, lacrimation, and eyelid edema, often leads patients to believe that their headache is due to a sinus disease [7]. Although both historical and new data show that nasal symptoms frequently accompany a migraine, these symptoms are not part of the IHS diagnostic criteria for a migraine [13].

Wolff conducted a number of experiments demonstrating the fact that traction on numerous regions of the meninges

Table 5 Results of patients’ response to prophylactic treatment with sodium valproate

Response	Patient	
	Number	Percent
Significant	44	61.1
Partial	7	9.6
No response	11	15.3
Failed to follow-up	10	13.9
Total	72	100

$P = 0.001$

produced a referral pain into the face and the sinus area, suggesting that sinus pain could be referred from meningeal irritation that occurs in a migraine [14, 15]. Ishkanian et al. [16] have recently reported in a randomized, double-blind, placebo-controlled study that sumatriptan is effective and well tolerated in the treatment of patients with self-described or physician-diagnosed “sinus headache”.

Migraine affects about 3–8% of males and 11–18% of females in developed countries [17]. Despite this high prevalence and according to the fact that over 90% of sinus headaches meet the IHS criteria for migraine, it is under-recognized by both “sinus headache” patients and their physicians [18]. The treatment of “sinus headache”, when treated as a sinus disease, often leads to medical and surgical interventions that do not relieve the patients’ headaches. Therefore, an appropriate recognition of migraine in patients who complain about sinus headaches may help minimize the suffering and unnecessary interventions.

Our study demonstrates that of 104 patients with “sinus headache” complaints, only 32 (30.8%) had symptoms and signs compatible with EPOS criteria for the diagnosis of chronic sinusitis. It means that most patients presenting a “sinus headache” may not actually have a rhinosinusitis-associated headache. In a series of 51 patients, Shields et al. [19] demonstrated that facial pain and headache did not correlate with disease severity on the CT scan of the paranasal sinus.

The significant response to sodium valproate (61.1%) as a prophylactic treatment in our data supports the findings of other researchers in that migraine headache should be considered as a principle cause in the evaluation of a patient who complains about a sinus headache. Schreiber et al. [8] have recently conducted a large multicenter study of sinus headaches (2,991 patients), predominantly in a primary care setting. They found that 80% of the cases completely satisfied the criteria for migraine. An allergy and migraine study in 2007 reported that out of 100 subjects with self-diagnosed “sinus headache”, 52% met IHS criteria for migraine [10]. Paulson and Graham described 104 patients who made a primary complaint of facial pains. These patients who had a normal nasal endoscopy and sinus CT scan were referred to a neurologist for further evaluation. Thirty-seven percent of those that followed up were diagnosed with migraine headaches, 17% rebound headaches, 17% chronic daily headache, and 16% obstructive sleep apnea [20].

The treatment efficacy of sodium valproate in our study demonstrates the diagnostic utility of response to sodium valproate in diagnosing migraine headaches, particularly in individuals who may not have had the IHS criteria for migraine. Kari and DelGaudio [12] reported that among 55 patients with self-described “sinus headache”, 82% had a significant response to an empiric treatment for sinus headaches with triptans. Cady and Schreiber report similar

findings with self-diagnosed sinus headaches in which the patients were requested to treat their headaches with sumatriptan. It demonstrated that 66% of patients’ headaches were reduced to mild or no pain. The authors concluded that the patients who respond to migraine-specific therapy are actually those suffering from migraine headaches [13].

Studies that reveal the efficacy of anti-convulsants drugs in migraine prophylaxis have demonstrated that sodium valproate in comparison with a placebo causes a $\geq 50\%$ reduction in migraine frequency [21]. Our study identified a significant response by comparing the frequency and severity of headaches that were recorded by the patients before and after the treatment. There is, however, a potential weakness; the study was not designed as a randomized one with a placebo control for the evaluation of sodium valproate treatment efficacy. This has to be considered by further studying the subject.

Conclusion

Although “sinus headache” is a commonly made diagnosis, it has a difficult clinical presentation. Our study demonstrates that the majority of the patients do not have any positive sino-nasal findings. Our findings suggest that we have to consider migraine headaches in a differential diagnosis of patients suffering from “sinus headaches”. The study also reveals the efficiency of the conservative treatment with sodium valproate as a prophylactic treatment for patients with sinus headache with normal endoscopic and CT findings. Although a prospective randomized controlled study is needed in order to confirm if valproate is being effective or if it was the placebo effect.

Conflict of interest statement This study was not a sponsored research and we had no financial relationship with any sponsor.

References

1. Levine HL, Setzen M, Cady RK et al (2006) An otolaryngology, neurology, allergy and primary care consensus on diagnosis and treatment of sinus headache. A literature review. *Otolaryngol Head Neck Surg* 134:516–523
2. Schor DI (1993) Headache and facial pain—the role of the paranasal sinuses: a literature review. *Cranio* 11:36–47
3. Couch JR (1988) Sinus headache: a neurologists viewpoint. *Semin Neurol* 8:298–302
4. Fokkens WJ, Lund VJ, Mullol J et al (2007) European Position Paper on Nasal polyps. *Rhinology* 45(Suppl 20):1–139
5. Headache Classification Committee of the International Headache Society (1988) Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Cephalalgia* 8(Suppl 7):1–96
6. Headache Classification Subcommittee of the International Headache Society (2004) The international classification of headache disorders, 2nd edn. *Cephalalgia* 24(Suppl 1):9–160

7. Barbanti P, Fabbrini G, Pesare M, Vanacore N, Cerbo R (2002) Unilateral cranial autonomic symptoms in migraine. *Cephalalgia* 22:256–259
8. Schreiber CP, Hutchinson S, Webster CJ, Ames M, Richardson MS, Powers C (2004) Prevalence of migraine in patients with a history of self-reported or physician-diagnosed “sinus” headache. *Arch Intern Med* 164:1769–1772
9. Mehle ME, Kremer PS (2008) Sinus CT scan findings in “sinus headache” migraineurs. *Headache* 48:67–71
10. Eross E, Dodick D, Eross M (2007) The Sinus, Allergy and Migraine Study (SAMS). *Headache* 47:213–224
11. Scadding GK, Lund VJ (2004) *Investigative rhinology*. Taylor and Francis, London, p 96
12. Kari E, DelGaudio JM (2008) Treatment of sinus headache as migraine: the diagnostic utility of triptans. *Laryngoscope* 118:2235–2239
13. Cady RK, Schreiber CP (2002) Sinus headache or migraine? Considerations in making a differential diagnosis. *Neurology* 58:S10–S14
14. Wolff H (1948) *Headache and other pain*. Oxford University Press, New York
15. Cady RK, Schreiber CP (2004) Sinus headache: a clinical conundrum. *Otolaryngol Clin North Am* 37:267–288
16. Ishkanian G, Blumenthal H, Webster CJ, Richardson MS, Ames M (2007) Efficacy of sumatriptan tablets in migraineurs self-described or physician-diagnosed as having sinus headache: a randomized, double-blind, placebo-controlled study. *Clin Ther* 29:99–109
17. Dowson A, Dahlof A, Tepper S et al (2004) The prevalence and diagnosis of migraine in a primary care setting—insights from the landmark study. *Headache Care* 1(2):137–139
18. Tepper SJ (2004) New thoughts on sinus headache. *Allergy Asthma Proc* 25(2):95–96
19. Shields G, Seikaly H, LeBoeuf M et al (2003) Correlation between facial pain or headache and computed tomography in rhinosinusitis in Canadian and US subjects. *Laryngoscope* 113:943–945
20. Paulson EP, Graham SM (2004) Neurologic diagnosis and treatment in patients with computed tomography and nasal endoscopy negative facial pain. *Laryngoscope* 114:1992–1996
21. Mulleners WM, Chronicle EP (2008) Anticonvulsants in migraine prophylaxis: a cochrane review. *Cephalalgia* 28:585–597