

Characteristics and treatment effectiveness of the nummular headache: a systematic review and analysis of 110 cases

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ABSTRACT

Background/objective Nummular headache (NH) is a primary headache disorder characterised by intermittent or continuous scalp pain, affecting a small circumscribed area of the scalp. As there are limited data in the literature on NH, we conducted this review to evaluate demographic characteristics and factors associated with complete resolution of the headache, and effectiveness of treatment options.

Methods We performed a systematic review of cases reported through PubMed database, using Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol and 'nummular headache', 'coin-shaped headache' and 'coin-shaped cephalalgia' keywords. Analysis was performed by using χ^2 test and Wilcoxon rank-sum test. For individual interventions, the response rate (RR%) of the treatment was calculated.

Results We analysed a total of 110 NH cases, with median age 47 years and age of pain onset 42 years. Median duration to make correct diagnosis was 18 months after first attack. The median intensity of each attack was 5/10 on verbal rating scale over 4 cm diameter with duration of attack <30 min. Patients with NH had median three attacks per day with frequency of 9.5 days per month. 40 (57.97%) patients had complete resolution of the headache after treatment. Patients with complete resolution were younger, more likely to be female, and were more likely to have diagnosis within year. Patients with complete resolution more likely to have received treatment with onabotulinum toxin A (botulinum toxin type A (BoNT-A)), and gabapentin compared with patients without complete resolution. Most effective interventions were gabapentin (n=34; RR=67.7%), non-steroidal anti-inflammatory drugs (NSAIDs) (n=32; RR=65.6%), BoNT-A (n=12; RR=100%) and tricyclic antidepressant (n=9; RR=44.4%).

Conclusion Younger patients, female sex and early diagnosis were associated with complete resolution. NSAIDs, gabapentin and BoNT-A were most commonly used medications, with significant RRs.

INTRODUCTION

As per International Classification of Headache Disease-3 (ICHD-3), nummular headache (NH) is a primary headache disorder

characterised by intermittent or continuous scalp pain of highly variable duration, but often chronic, in a small circumscribed area of the scalp and in the absence of any underlying structural lesion.^{1 2} Previously, it was known as 'coin-shaped headache'.¹ The estimated incidence in NH is 6.4 per 100 000.^{3 5}

The pathophysiology of NH is unknown,^{4 5} and the majority of them arise without any precipitating factor. The signs and symptoms of NH are confined to a small area, suggesting a peripheral local process with no evidence of central mechanism as in migraine or tension type headache.⁴ The localisation of pain can be to any part of the scalp, but most commonly parietal area is affected.^{4 6} NH is typically unifocal, with the exception of a few cases of bilateral headache.⁶ The pain is usually mild to moderate in intensity, rarely severe. The duration is highly variable, lasting from as short as a few seconds to daily and continuous pain. Pain is mostly described as pressure, stabbing or occasionally burning.⁴ Sensory disturbances like allodynia, hypo/hyperaesthesia, paraesthesia, hyperalgesia and tenderness commonly occur in the affected area of pain.⁴⁻⁸

Patients with mild pain do not require treatment and reassurance is the only intervention needed. However, treatment is warranted in patients with severe pain. Antiepileptic's and tricyclic antidepressants (TCA) have not been shown to be effective in patients with NH. Analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) have been reported as an effective treatment in 60% of the published cases; especially in cases of acute exacerbation, mild continuous or intermittent pain or as add-on treatment with other drugs.⁴ In patients with inadequate response to other treatments, botulinum toxin type A (BoNT-A) is reported to be a

well-tolerated and effective treatment in few case series^{5,9} but lacks appropriate sample size. It has been reported that gabapentin is only transiently effective for NH and NH eventually becomes refractory to all standard prophylactic and analgesic therapies.^{10–12} Small number of case series and prospective studies have reported NH characteristics and its various treatment therapies but limited by duplication of patients data or inadequate availability of individual patients data.^{3,4,13} To our knowledge, there are no studies that have analysed the individual cases of NH systematically to evaluate the effectiveness of each therapeutic intervention.

The primary aim of this systematic review is to evaluate the demographic characteristics, variation in presentation of NH and effectiveness of therapeutic interventions in individual NH cases published in literature. Our secondary outcomes were to find the characteristics of patients with complete resolution of the headache and effectiveness (response rate (RR)) of the treatment choices used for patients with NH.

METHODS

We performed a systematic review of cases reported on NH. We followed the predesigned Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol and PRISMA checklist¹⁴ (online supplementary file 1) and standard for reporting the systematic review to the extent of our possibilities.

Search strategy

A comprehensive search for case reports and case series on PubMed database was conducted on 30 June 2019 by two independent investigators (AA and SS). The search included case reports, case illustrations, letters reporting human cases and case series from January 2002 to June 2019, by using keywords ‘nummular headache’, ‘coin-shaped headache’ and ‘coin-shaped cephalalgia’.

Definition and classification

NH is a rare kind of primary headache disorder that is defined as, ‘pain of highly variable duration, often chronic pain in a small circumscribed area of the scalp without any underlying cause’. ICHD-3 has described the following diagnostic criteria: (1) continuous or intermittent head pain, (2) exclusively on the scalp with four characteristics of sharply countered, fixed in size and shape, round or elliptical, 1–6 cm in diameter and (3) not met criteria of other headaches of ICHD-3 diagnosis.¹

Eligibility criteria

We used the following inclusion criteria to include cases in systematic review: all case reports and case series of NH (1) where diagnosis was confirmed by clinician as described by the author's judgement, (2) where complete data including demographics and personal information were available, and (3) where mimicking differential diagnosis was ruled out to provide a clear picture. We excluded

articles that were (1) observational studies, review articles, letters to the editor that were not presenting clinical NH case reports, (2) case reports in any language other than English and (3) observational studies, review articles and case series with duplication of patient's data.

Selection of studies and data collection

By using this search strategy, a total of 87 articles were identified and screened. We excluded 21 articles which were non-human, non-full text and outside of January 2002–June 2019 publication. Then, both investigators (AA and SS) independently read 66 articles including abstracts and full manuscript, and selected the articles based on inclusion and exclusion criteria. Any disagreement was reviewed by a third investigator (UKP) and disagreement was resolved by consensus. Twenty-five articles that were excluded were not full articles, incomplete information on demographics or headache characteristics, not well defined, non-English language and difficult to comprehend. This left us with 41 case reports and case series, of which 2 were missing treatment given or effectiveness. So, 41 case reports and case series were considered for qualitative and 39 were considered for quantitative analysis (figure 1).

All eligible studies were reviewed using a standardised web-based form to collect information. All data were summarised descriptively, including country of the patient, age, sex, age at diagnosis, latency, duration, timing and frequency of attack, characteristic of headache (localisation, region, diameter, quality and intensity of pain, tenderness and exacerbating factors), concomitant symptoms, comorbidities and therapeutic interventions.

Outcomes

The primary outcome of our systematic review of cases is to evaluate the demographic characteristics, variation in presentation of NH and treatment interventions as most cases of NH were initially misdiagnosed for other types of headache. Our secondary outcomes were to find the characteristics of complete resolution versus non-resolution of the headache and effectiveness (RR) of the treatment choices. The complete resolution (no headache with ongoing treatment) versus non-resolution (infrequent headache episodes with ongoing treatment) of the headache pain was decided by the patients' response noted by the physicians (within case) with the different medicines.

Statistical analysis

We used Microsoft Excel to collect the data of those 110 cases and SAS (V.9.4) software to evaluate the data (online supplementary file 2). Univariate analysis of differences between categorical variables was tested using the χ^2 test and analysis of differences of median between continuous variables was tested using Wilcoxon rank-sum test. We used proc means, proc freq, proc npar1way and proc univariate procedures to calculate these numbers. Frequency percentage, median and SE of the cohort were calculated from non-missing data. P value of <0.05 was

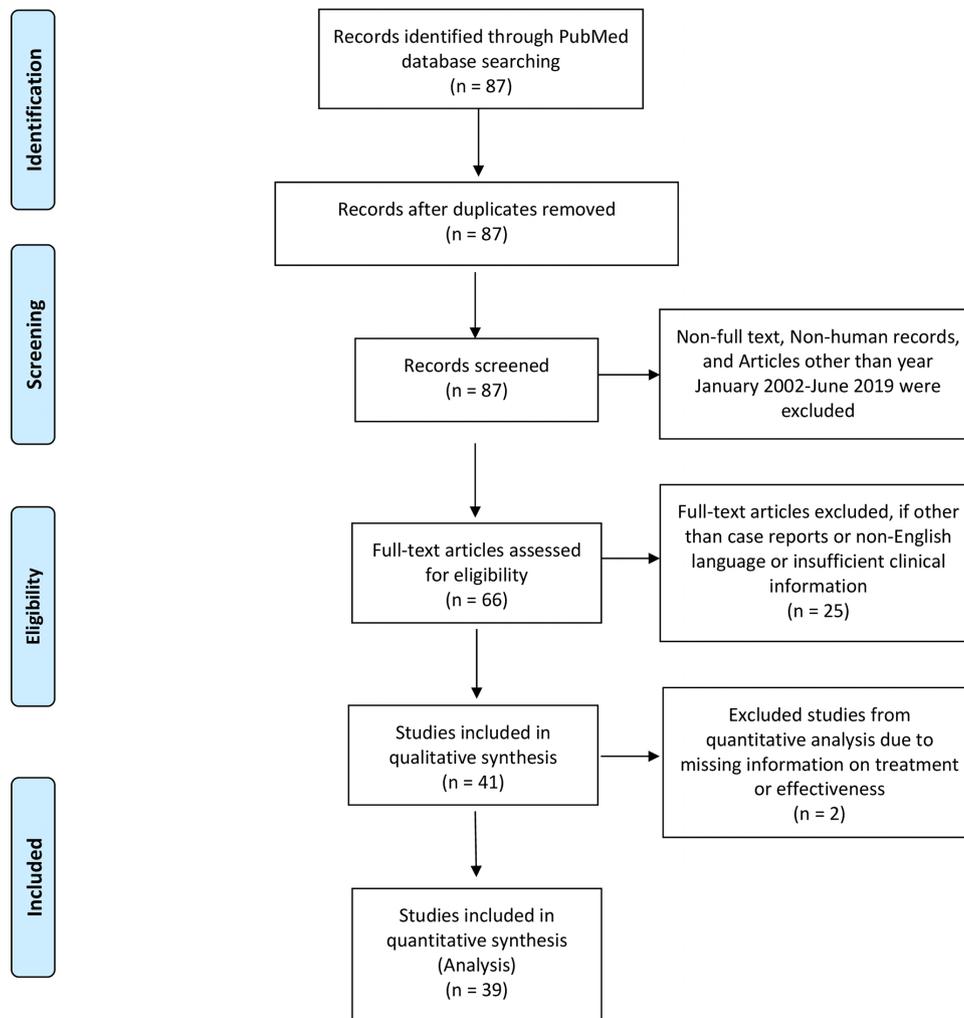


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of literature search and selection process of nummular headache case reports. From Moher *et al.*¹⁴

considered statistically significant. No statistical power calculation was conducted prior to the study and the sample size was based on the available data. For individual interventions, the RR (%) of the treatment was calculated by dividing the number of patients with complete resolution after taking a particular drug to the number of patients who had taken that drug multiplied by 100.

RESULTS

We analysed a total of 110 NH published cases which fulfilled the inclusion criteria for this review. [Table 1](#) represents age-based and gender-based distribution of the cohort.

Epidemiological and clinical characteristics

There were 108 adults (38% male and 62% female) and 2 children (1 boy and 1 girl) diagnosed with NH. The median age of the study cohort was 47 ± 1.7 (SE) years ranging from 4 to 80 years. The median age of onset of pain in patients was 42 ± 1.8 (SE) years ([table 2](#)).

The correct diagnosis of NH was made within 18 ± 12.8 (median \pm SE) months after the first episode of headache

with median intensity of 5 ± 0.2 (SE) on verbal rating scale (VRS) of 1–10 (intensity: 1=least severe to 10=most severe). The median diameter of pain was 4 ± 0.2 (SE) cm. Out of 32 patients with known duration of attack (pain), 17 (53.13%) patients experienced <30 min of attack, 9 (28.13%) between 30 and 120 min duration and 6 (18.75%) patients had >120 min duration of attack.

Patients with NH in the study had 3 ± 2 (median \pm SE) headache attacks per day with frequency of 9.5 ± 3.6 (median \pm SE) days per month. The localisation of pain was observed in 68 patients. Out of 68 patients, 26 (38.24%) patients had pain localised to the left side, 35 (51.47%) patients had right side pain and 7 (10.29%) patients had bilateral pain (two separate area). Forty-three (54.43%) patients had parietal area of the brain affected, 17 (21.52%) had frontal region, 11 (13.92%) had occipital region and 8 (10.12%) had temporal region affected. In the study cohort, 32 (44.44%) patients described pain as pressure like, 12 (16.67%) described it as stabbing pain and 9 (12.50%) patients had burning pain. Out of 68 patients who have reported presence or absence of tenderness associated with pain

Table 1 Distribution of the 110 nummular headache cases based on age and gender

Author; country; year	Number of cases	Age (years)	Gender
Liu and Wei; China; 2018 ²⁴	3	74	F
		46	M
		38	F
Rodríguez <i>et al</i> ; Spain; 2015 ⁸	1	14	F
Camacho-Velasquez; Spain; 2016 ²⁵	1	47	M
Barón <i>et al</i> ; Spain; 2015 ²⁶	1	21	F
López-Ruiz <i>et al</i> ; Spain; 2014 ²⁷	2	67	M
		60	M
Iwanowski <i>et al</i> ; Poland; 2014 ²⁸	1	61	F
Kurian and Solomon; USA; 2014 ²⁹	2	47	F
		49	F
López-Mesonero <i>et al</i> ; Spain; 2014 ³⁰	1	41	F
Mulero <i>et al</i> ; Spain; 2013 ³¹	3	21	M
		45	M
		35	M
Yin <i>et al</i> ; Italy; 2013 ³²	1	52	M
Irimia <i>et al</i> ; Spain; 2013 ³³	1	33	F
Danno <i>et al</i> ; Japan; 2013 ³⁴	3	71	M
		57	F
		39	M
Dai <i>et al</i> ; China; 2013 ⁶	1	63	M
Herrero-Velázquez <i>et al</i> ; Spain; 2013 ³⁵	8	46	M
		60	F
		23	F
		43	M
		53	F
		33	M
Başağrisi <i>et al</i> ; China; 2010 ³⁶	1	59	M
		28	M
		52	M
		52	F
		62	M
		61	M
Guerrero Ángel <i>et al</i> ; Spain; 2011 ⁴¹	6	71	F
		80	F
		30	F
		33	M
		32	F
		47	F
Evans and Pareja; Spain; 2005 ¹¹	1	57	F
Trucco <i>et al</i> ; Italy; 2006 ¹⁰	1	55	F
Evan <i>et al</i> ; Spain; 2006 ⁴³	1	45	F
Trucco <i>et al</i> ; Italy; 2007 ⁴⁴	1	26	F
Guillem <i>et al</i> ; USA; 2007 ⁴⁵	1	60	F
Tayeb <i>et al</i> ; USA; 2008 ⁴⁶	1	47	M

Continued

Table 1 Continued

Author; country; year	Number of cases	Age (years)	Gender
Pareja <i>et al</i> ; Spain; 2008 ⁴⁷	5	65	F
		50	F
		61	F
		60	M
		34	F
Mathew <i>et al</i> ; USA; 2008 ⁹	4	43	F
		58	F
		35	F
		47	F
Baldacci <i>et al</i> ; Italy; 2010 ⁴⁸	1	40	M
Dach <i>et al</i> ; Spain; 2006 ⁴⁹	3	41	F
		29	M
		64	M
Robbins and Grosberg; USA; 2013 ⁵⁰	1	40	F
Alvaro <i>et al</i> ; Spain; 2009 ⁵¹	4	67	M
		72	F
		50	F
		37	F
Cuadrado <i>et al</i> ; Spain; 2009 ⁵²	3	28	M
		67	F
		51	M
Dabscheck and Ian Andrews; Australia; 2010 ⁵³	1	4	M
Dusitanond <i>et al</i> ; USA; 2008 ⁵⁴	5	24	F
		30	F
		47	F
		55	F
		59	F
Ruscheweyh <i>et al</i> ; Germany; 2009 ⁵⁵	6	25	F
		39	M
		39	F
		49	M
		24	M
		57	F
Jiang <i>et al</i> ; China; 2019 ⁵⁶	2	48	F
		72	M
Grosberg <i>et al</i> ; USA; 2007 ¹⁸	1	55	M
Pareja <i>et al</i> ; Spain; 2004 ^{3*}	14	38 (mean)	3—Male
			11—Female
Pareja <i>et al</i> ; Spain; 2002 ^{2*}	13	50 (mean)	5—Male
			8—Female

*The data from these studies have considered for the analysis of demographic and headache characteristics but have not considered for analysis of treatment effectiveness due to missing accurate treatment.

in the study, 24 (35.29%) patients had tenderness with pain.

There were 47 (69.12%) patients in the study with the temporary relief of the symptoms. Forty (57.97%) patients had complete resolution of the headache after

treatment. Sixty-six patients in the study had received the known therapeutic interventions and rest 14 patients' interventions status were not known. In the study, 34 (52.31%) patients were treated with gabapentin, 11 (16.92%) with carbamazepine, 12 (18.46%) with BoNT-A

Table 2 Demographics and clinical characteristics of the patients with nummular headache

Total number of cases reviewed	n=110
Age group	
Adults	108 (98.18%)
Paediatrics	2 (1.82%)
Age (years) (median \pm SE; IQR)	47 \pm 1.7 (37.5–61.5)
Gender (adults)	
Male	41 (38%)
Female	67 (62%)
Age of onset of pain (years) (median \pm SE)	42 \pm 1.8
The intensity of pain (VRS 1–10) (median \pm SE)	5 \pm 0.2
Latency from the first attack to diagnosis (months; median \pm SE)	18 \pm 12.8
Duration of attacks (min)	
<30	17 (53.13%)
30–120	8 (28.13%)
>120	6 (18.75%)
Diameter of the pain (cm; median \pm SE)	4 \pm 0.2
Number of attacks per day (median \pm SE)	3 \pm 2.1
Frequency (days/month; median \pm SE)	9.5 \pm 3.6
Localisation of pain	
Unilateral—left	26 (38.24%)
Unilateral—right	35 (51.47%)
Bilateral	7 (10.29%)
Region of brain	
Frontal	17 (21.52%)
Temporal	8 (10.12%)
Parietal	43 (54.43%)
Occipital	11 (13.92%)
Quality of pain	
Boring	2 (2.78%)
Burning	9 (12.50%)
Electric	3 (4.17%)
Lancinating	3 (4.17%)
Oppressive	3 (4.17%)
Pressure	32 (44.44%)
Pulsating	2 (2.78%)
Sharp	1 (1.39%)
Stabbing	12 (16.67%)
Throbbing	5 (6.94%)
Tenderness	
Yes	24 (35.29%)
No	44 (64.71%)
Temporary relief	
Yes	47 (69.12%)

Continued

Table 2 Continued

Total number of cases reviewed	n=110
No	21 (30.88%)
Total resolution	
Yes	40 (57.97%)
No	29 (42.03%)
Therapeutic interventions	
Onabotulinum toxin A (BoNT-A)	12 (18.46%)
Triptan	3 (4.69%)
Tricyclic antidepressant (TCA)*	9 (13.6%)
Lamotrigine	8 (12.31%)
Gabapentin	34 (52.31%)
Carbamazepine	11 (16.92%)
Topiramate	3 (4.69%)
Concomitant symptoms	
	Nausea, vomiting, photophobia, phonophobia, allodynia, hyperaesthesia, tearing, itching eye, bilateral trigeminal hyperalgesia, dizziness, blurred vision, hypoaesthesia, paraesthesia, Hyperalgesia
Exacerbating factors	
	Cough, head movements, valsava, cough, sneeze, gym activity, physical activity, poor sleep, cold, combing hair
Comorbidities	
	Aneurysm of the temporal artery, aneurysm of occipital artery, occipital neuralgia, coronary artery disease, hypertension, migraine, myasthenia gravis, type 2 diabetes mellitus, chronic tension headache

Missing data were not considered for the calculation of the frequency percentages.

*TCA includes amitriptyline and nortriptyline.

BoNT-A, botulinum toxin type A; VRS, verbal rating scale (intensity 1=least severe to 10= most severe).

treatment, 3 (4.69%) with triptan, 9 (13.6%) with TCA, 8 (12.31%) with lamotrigine, 3 (4.69%) with topiramate, 2 with metoprolol, 1 with neurotrophin, 1 with duloxetine, 1 with pregabalin, 1 with sodium valproate and 2 underwent nerve block. Besides that, 32 patients had tried NSAIDs, 2 tried acetaminophen and 2 tried acupuncture. Most of the patients received two or more combinations of drugs.

Table 3 Association of characteristics of the nummular headache with complete resolution after treatment

Characteristics	Resolution (yes)	Resolution (no)	P value
Age (years; median \pm SE; IQR)	47 \pm 2.5 (33–56)	49 \pm 2.9 (41–63)	0.1835
Gender			0.1648
Male	14 (35%)	15 (51.72%)	
Female	26 (65%)	14 (48.28%)	
Latency from the first attack to diagnosis (months; median \pm SE)	12 \pm 8.67	24 \pm 32.14	0.0249
Age of onset of pain (years; median \pm SE)	41 \pm 2.73	43 \pm 2.96	0.9337
Intensity of pain (VRS 1–10; median \pm SE)	6 \pm 0.25	5.5 \pm 0.32	0.6991
Diameter of the pain (cm; median \pm SE)	4 \pm 0.23	4 \pm 0.30	0.2054
Number of attacks per day (median \pm SE)	4 \pm 2.9	3 \pm 2.5	0.6191
Frequency (days/month; median \pm SE)	19.5 \pm 5.49	9.5 \pm 1.70	0.1659
Duration of attacks (min)			0.0833
<30	11 (64.71%)	5 (38.46%)	
30–120	5 (29.41%)	3 (23.08%)	
>120	1 (5.88%)	5 (38.46%)	
Temporary relief of headache			<0.0001
Yes	35 (87.50%)	12 (42.86%)	
No	5 (12.50%)	16 (57.14%)	
Onabotulinum toxin A (BoNT-A)			0.0024
Yes	12 (30%)	0 (0%)	
No	28 (70%)	25 (100%)	
Triptan			0.5554
Yes	1 (2.56%)	2 (8%)	
No	38 (97.44%)	23 (92.00%)	
Tricyclic antidepressant (TCA)*			0.1356
Yes	4 (7.50%)	5 (20%)	
No	37 (92.50%)	20 (80%)	
Lamotrigine			0.0002
Yes	0 (0%)	8 (32%)	
No	40 (100%)	17 (68%)	
Gabapentin			0.1163
Yes	24 (60%)	10 (40%)	
No	16 (40%)	15 (60%)	
Carbamazepine			<0.0001
Yes	1 (2.50%)	10 (40%)	
No	39 (97.50%)	15 (60%)	

Note that all percentages are column percentages to compare characteristics between complete resolution and no-resolution groups. Missing data were not considered for the calculation of the frequency percentages.

*TCA includes amitriptyline and nortriptyline.

BoNT-A, botulinum toxin type A; VRS, verbal rating scale (intensity 1=least severe to 10=most severe).

Characteristics of the patients with complete resolution after treatment

Table 3 lists the characteristics of patients with NH with and without complete resolution after treatment. Median age of patients with complete resolution was 47 \pm 2.5 (SE) years compared with 49 \pm 2.9 (SE) years in no-resolution group (p=0.1835). Female gender had higher prevalence of resolution (26 (65%) vs 14

(48.28%); p=0.1648) compared with no resolution, though evidence of significance was weak. Patients with complete resolution were diagnosed early with NH within 12 \pm 8.67 (SE) months from the first episode of headache compared with patients with no resolution being diagnosed within 24 \pm 32.14 (SE) months from the first headache attack (p=0.0249). There was no difference in intensity of pain and diameter of pain between

Table 4 Treatment response of drugs used for nummular headache

Treatment	Number of cases (n)	Complete resolution (A)	Response rate (A/n)*100 (%)
Gabapentin	34	23	67.7%
NSAIDs	32	21	65.6%
Onabotulinum toxin A (BoNT-A)	12	12	100%
Carbamazepine	11	1	9.09%
Tricyclic antidepressant	9	4	44.4%
Lamotrigine	8	0	0%
Topiramate	3	2	66.7%
Triptan	3	2	66.7%
Acupuncture	2	1	50%
Acetaminophen	2	1	50%
Nerve block	2	0	0%
Neurotropicin	1	1	100%
Duloxetine	1	1	100%
Pregabalin	1	0	0%
Sodium valproate	1	0	0%
Metoprolol	2	0	0%

NSAID, non-steroidal anti-inflammatory drug.

the complete resolution and no-resolution groups ($p=0.6991$, $p=0.2054$, respectively).

Patients with complete resolution had higher prevalence of reported temporary relief of headache compared with patients without resolution (35 (87.50%) vs 12 (42.86%), $p<0.0001$). Patients treated with BoNT-A and gabapentin had a high prevalence of complete resolution of headache than no resolution (12 (30%) vs 0 (0%), $p=0.0024$ and 24 (60%) vs 10 (40%); $p=0.1163$). Lamotrigine and carbamazepine treatment had higher prevalence of no resolution of headache compared with resolution group (8 (32%) vs 0 (0%); $p=0.0002$ and 10 (40%) vs 1 (2.50%); $p<0.0001$, respectively).

RR to treatment

Table 4 mentions RR for the interventions. Most common interventions were gabapentin ($n=34$; $RR=67.7\%$), NSAIDs ($n=32$; $RR=65.6\%$), BoNT-A ($n=12$; $RR=100\%$), carbamazepine ($n=11$; $RR=9.09\%$), TCA ($n=9$; $RR=44.4\%$) and lamotrigine ($n=8$; $RR=0\%$). Other less common interventions were triptan ($n=3$; $RR=66.7\%$), topiramate ($n=3$; $RR=66.7\%$), acupuncture ($n=2$; $RR=50\%$), acetaminophen ($n=2$; $RR=50\%$), nerve block ($n=2$; $RR=0\%$), neurotropicin ($n=1$; $RR=100\%$), duloxetine ($n=1$; $RR=100\%$), pregabalin ($n=1$; $RR=0\%$) and sodium valproate ($n=1$; $RR=0\%$).

DISCUSSION

NH has been reported by Pareja *et al* in the literature since 2002.² According to a survey, NH comprises 0.25% of all headache consultation.¹⁵ According to The International Headache Society's ICHD-III, the name coin-shaped cephalalgia is defined as NH categorised under

primary headaches without an identifiable aetiology, (1) continuous or intermittent head pain, (2) exclusively on the scalp with four characteristics of sharply countered, fixed in size and shape, round or elliptical, 1–6 cm in diameter and (3) not met criteria of other headaches of ICHD-3 diagnosis.¹⁶ Unlike migraine, NH is not associated with nausea, vomiting, lacrimation, rhinorrhoea, sound or light sensitivity or focal neurological symptoms.

NH is most commonly present in the middle age group^{6 17} and the average age of patients in our study group is 47 years with only two paediatric cases. Studies report the predominance of NH in females with a ratio of 1.5–1, consistent with our findings of female to male 0.6/0.4.^{6 18} NH is most commonly unilateral¹⁹ but our study had 10% patients with bilateral pain which is supported by Dai *et al* review⁶ with 12% patients with bilateral pain. Pain mostly occurred on the right side and localised to parietal region, consistent with Rammohan *et al*.¹⁷ Nearly half of our study patients had pressure like quality of pain followed by stabbing and burning, with similar results reported by review by Dai *et al*.⁶ The average intensity of pain is mild to moderate with an average of 5/10 on VRS. The average pain diameter was 4 cm, findings consistent with other studies which reported 2–6 cm of pain.^{6 17 20}

There are no standard treatment guidelines present for NH, but few drugs have been used for the management of NH. These drugs include NSAIDs, gabapentin, carbamazepine, BoNT-A, triptan, TCA and nerve blocks.⁴ A study of 21 patients with NH by Zhu *et al*,²¹ where 14/21 patients with NH were treated with different therapeutic approaches, concluded that NH can be effectively treated with acupuncture or combining amitriptyline with indomethacin,

ibuprofen or carbamazepine. Chirchiglia *et al*²² reported the successful management of one case of NH by adding palmitoylethanolamide to topiramate. Both of these drugs are used for neuropathic pain and suggest that release of algogenic substances like neurokinins, substance-P and calcitonin gene-related peptide (CGRP) causes inflammation and pain. Due to the involvement of cutaneous branches, the pain is superficial. Use of PAE decreases degeneration of mast cells, prevents alteration of nerve fibres and reduces inflammation. Nerve block is used for the treatment of NH and a study by Dach *et al*¹² showed that blocking greater occipital nerve can relieve pain.

Our study found that gabapentin is the most frequently used therapeutic modality, with an RR of 67.7%. Martins and Abreu⁵ and Trigo *et al*²³ concluded that gabapentin is the most frequently used medication with RR >50% in NH treatment and most common dose was 800 mg/day. An interesting finding of our study is the 100% treatment response with BoNT-A therapy. In support of our findings, studies by García-Azorín *et al*¹³ and Cuadrado *et al*⁴ concluded that BoNT-A significantly decreased the frequency of NH and may be a reasonable therapeutic approach for those patients, refractory to gabapentin. Another review study by Dai *et al* proved the effectiveness of BoNT-A treatment in 9/11 cases.⁶

The major strength of our study is that the study population analysed was only individual case reports and precisely evaluated the effectiveness of therapeutic interventions. However, our study has some limitations. First, the sample size is small because of lack of reporting, strict exclusion criteria and excluding other prospective studies with no individual patients' data available. Although this was done to avoid duplicate patients and maintain the quality of article but it further reduced number of patients in the analysis. Second, there were not any randomised controlled studies available to support our study; hence, the evaluated treatment options represent the preferences of the physicians. Third, the treatment response of NH to newer anti-CGRP agents is not known. Nevertheless, given the limited availability of accurate information on this disease, this study shows a relatively large number of patients.

CONCLUSION

This is the first systematic study to report the effectiveness of treatment options after analysing the individual cases published in literature. The median age of diagnosis of NH was 47 years. Patients with NH had median three attacks per day with frequency of 9.5 days per month. Sixty-nine per cent of patients had temporary relief and 60% of patients had complete resolution of the headache after treatment. Female sex and early diagnosis were associated with complete resolution of NH. NSAIDs, gabapentin and BoNT-A were most commonly used medications, with RRs increasing in that order.

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REFERENCES

- Headache Classification Committee of the International Headache Society (IHS). The International classification of headache disorders, 3rd edition (beta version). *Cephalalgia* 2013;33.
- Pareja JA, Caminero AB, Serra J, *et al*. Nummular headache: a coin-shaped cephalgia. *Neurology* 2002;58:1678–9.
- Pareja JA, Pareja J, Barriga FJ, *et al*. Nummular headache: a prospective series of 14 new cases. *Headache* 2004;44:611–4.
- Cuadrado ML, López-Ruiz P, Guerrero Ángel L. Nummular headache: an update and future prospects. *Expert Rev Neurother* 2018;18:9–19.
- Martins IP, Abreu L. Nummular headache: clinical features and treatment response in 24 new cases. *Cephalalgia Reports* 2018;1:1–8.
- Dai W, Yu S, Liang J, *et al*. Nummular headache: peripheral or central? one case with reappearance of nummular headache after focal scalp was removed, and literature review. *Cephalalgia* 2013;33:390–7.
- Queiroz LP. Unusual headache syndromes. *Headache* 2013;53:12–22.
- Rodríguez C, Herrero-Velázquez S, Ruiz M, *et al*. Pressure pain sensitivity map of multifocal nummular headache: a case report. *J Headache Pain* 2015;16:38.
- Mathew NT, Kailasam J, Meadors L. Botulinum toxin type A for the treatment of nummular headache: four case studies. *Headache* 2008;48:442–7.
- Trucco M, Mainardi F, Perego G, *et al*. Nummular headache: first Italian case and therapeutic proposal. *Cephalalgia* 2006;26:354–6.
- Evans RW, Pareja JA. Nummular headache. *Headache* 2005;45:164–5.
- Dach F, Éckeli Alan L., Ferreira KdosS, Ál Éckeli, KdS F, *et al*. Nerve Block for the Treatment of Headaches and Cranial Neuralgias - A Practical Approach. *Headache* 2015;55:59–71.
- García-Azorín D, Trigo-López J, Sierra Álvaro, *et al*. Observational, open-label, non-randomized study on the efficacy of onabotulinumtoxinA in the treatment of nummular headache: the prenumabot study. *Cephalalgia* 2019;39:1818–26.

- 14 Moher D, Liberati A, Tetzlaff J, *et al.* Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6:e1000097.
- 15 Janjua MS, Singh P. *Nummular headache*. StatPearls. Treasure Island (FL), 2019.
- 16 Belvis R, Mas N, Roig C. [Changes introduced into the recent International Classification of Headache Disorders: ICHD-III beta classification]. *Rev Neurol* 2015;60:81–9.
- 17 Rammohan K, Mundayadan SM, Mathew R. Nummular headache: Clinico-epidemiological features in South Indian population. *J Neurosci Rural Pract* 2016;7:532–6.
- 18 Grosberg BM, Solomon S, Lipton RB. Nummular headache. *Curr Pain Headache Rep* 2007;11:310–2.
- 19 Schwartz DP, Robbins MS, Grosberg BM. Nummular headache update. *Curr Pain Headache Rep* 2013;17:340.
- 20 Dach F, Éckeli Alan L., Ferreira KdosS, *et al.* Nerve Block for the Treatment of Headaches and Cranial Neuralgias - A Practical Approach. *Headache* 2015;55:59–71.
- 21 Zhu K-yun, Huang Y, Zhong S-sheng, *et al.* [Nummular headache: 21 new cases and therapeutic results]. *Zhonghua Yi Xue Za Zhi* 2008;88:2935–7.
- 22 Chirchiglia D, Della Torre A, Signorelli F, *et al.* Administration of palmitoylethanolamide in combination with topiramate in the preventive treatment of nummular headache. *Int Med Case Rep J* 2016;9:193–5.
- 23 Trigo J, García-Azorín D, Martínez Pias E, *et al.* Clinical characteristics of nummular headache and differentiation between spontaneous and posttraumatic variant: an observational study. *J Headache Pain* 2019;20:34.
- 24 Liu Y, Wei T. First three cases of scalp temperature change in symptomatic areas affected by nummular headache: a case report. *BMC Neurol* 2018;18:223.
- 25 Camacho-Velasquez JL. Nummular headache associated with linear scleroderma. *Headache* 2016;56:1492–3.
- 26 Barón J, Rodríguez C, Ruiz M, *et al.* Atypical nummular headache or circumscribed migraine: the utility of pressure algometry. *Pain Research and Management* 2015;20:60–2.
- 27 López-Ruiz P, Cuadrado M-L, Aledo-Serrano A, *et al.* Superficial Artery Aneurysms Underlying Nummular Headache - 2 Cases and Proposed Diagnostic Work-Up. *Headache* 2014;54:1217–21.
- 28 Iwanowski P, Kozubski W, Losy J. Nummular headache in a patient with ipsilateral occipital neuralgia—A case report. *Neurol Neurochir Pol* 2014;48:141–3.
- 29 Kurian M, Solomon GD. Can temporal course of pain determine patient response to specific medication in nummular headache? *Headache* 2014;54:1058–61.
- 30 López-Mesonero L, Porta-Etessam J, Ordás CM, *et al.* Nummular headache in a patient with craniosynostosis: one more evidence for a peripheral mechanism. *Pain Medicine* 2014;15:714–6.
- 31 Mulero P, Matarazzo M, Pedraza MI, *et al.* Nummular headache related to exercise or Valsalva maneuver. clinical characteristics of 3 cases. *Headache* 2013;53:1167–8.
- 32 Yin H-L, Chui C, Tung W-F, *et al.* Nummular headache after trans-sphenoidal surgery: a referred pain-based headache syndrome. *Neurol Neurochir Pol* 2013;47:398–401.
- 33 Irimia P, Palma J-A, Idoate MA, *et al.* Cephalalgia alopecia or nummular headache with trophic changes? a new case with prolonged follow-up. *Headache* 2013;53:994–7.
- 34 Danno D, Kawabata K, Tachibana H. Three cases of nummular headache effectively treated with Neurotropin®. *Intern Med* 2013;52:493–5.
- 35 Herrero-Velázquez S, Guerrero AL, Pedraza MI, *et al.* Nummular headache and Epicrania fugax: possible association of Epicranias in eight patients: table 1. *Pain Medicine* 2013;14:358–61.
- 36 Man Y-H, Yu T-M, Li L-S, *et al.* A new variant nummular headache: large diameter accompanied with bitrigeminal hyperalgesia and successful treatment with carbamazepine. *Turk Neurosurg* 2012;22:506–9.
- 37 Yamazaki Y, Kobatake K. Successful treatment of nummular headache with Neurotropin®. *J Headache Pain* 2011;12:661–2.
- 38 Rocha-Filho PAS. Nummular headache: two simultaneous areas of pain in the same patient. *Cephalalgia* 2011;31:874.
- 39 Porta-Etessam J, Lapeña T, Cuadrado M-L, *et al.* Multifocal Nummular headache with trophic changes. *Headache* 2010;50:1612–3.
- 40 Chen W-H, Li T-H, Lee L-H, *et al.* Varicella-Zoster virus infection and nummular headache: a possible association with epicranial neuralgia. *Intern Med* 2012;51:2439–41.
- 41 Guerrero Ángel L., Cuadrado ML, García-García ME, *et al.* Bifocal nummular headache: a series of 6 new cases. *Headache* 2011;51:1161–6.
- 42 Campbell WW, Sartori RJ. Nummular erythema in a patient with chronic daily headache. *Headache* 2003;43:1112.
- 43 Evans RW. Case studies of uncommon headaches. *Neurol Clin* 2006;24:347–62.
- 44 Trucco M. Nummular headache: another case treated with gabapentin. *J Headache Pain* 2007;8:137–8.
- 45 Guillem A, Barriga FJ, Giménez-Roldán S. Nummular headache secondary to an intracranial mass lesion. *Cephalalgia* 2007;27:943–4.
- 46 Tayeb Z, Hafeez F, Shafiq Q. Successful treatment of nummular headache with TENS. *Cephalalgia* 2008;28:897–8.
- 47 Pareja JA, Cuadrado ML, Fernández-de-las Peñas C, *et al.* Nummular headache with trophic changes inside the painful area. *Cephalalgia* 2008;28:186–90.
- 48 Baldacci F, Nuti A, Lucetti C, *et al.* Nummular headache dramatically responsive to indomethacin. *Cephalalgia* 2010;30:1151–2.
- 49 Dach F, Speciali J, Eckeli A, *et al.* Nummular headache: three new cases. *Cephalalgia* 2006;26:1234–7.
- 50 Robbins MS, Grosberg BM. Menstrual-related nummular headache. *Cephalalgia* 2010;30:507–8.
- 51 Álvaro LC, Garcí JM, Areitio E. Nummular headache: a series with symptomatic and primary cases. *Cephalalgia* 2009;29:379–83.
- 52 Cuadrado ML, Valle B, Fernández-de-las-Peñas C, *et al.* Bifocal nummular headache: the first three cases. *Cephalalgia* 2009;29:583–6.
- 53 Dabscheck G, Ian Andrews P. Nummular headache associated with focal hair heterochromia in a child. *Cephalalgia* 2010;30:1403–5.
- 54 Dusitanond P, Young W, Type BT. Botulinum toxin type A's efficacy in nummular headache. *Headache* 2008;48:1379.
- 55 Ruscheweyh R, Buchheister A, Gregor N, *et al.* Nummular headache: six new cases and lancinating pain attacks as possible manifestation. *Cephalalgia* 2010;30:249–53.
- 56 Jiang L, Li M, Liu Q, *et al.* Nummular headache: 2 cases with good beta blocker responses and a narrative review. *Headache* 2019;59:593–602.