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Peripheral Nerve

Nonsurgical Treatment of Neuralgia and Cervicogenic Headache: A Systematic Review and Meta-analysis

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Background: Extracranial compression of peripheral sensory nerves is one of many origins of chronic headaches. Identifying these patients can be difficult, and they are often diagnosed with neuralgia or cervicogenic headache. The recent literature provides the outcomes of surgical decompression in patients with these headaches. This study aimed to give an overview of the current literature on the nonsurgical treatment options and to evaluate the effectiveness of these treatments in patients with neuralgia and cervicogenic headache.

Methods: Databases were searched to identify all published clinical studies investigating nonsurgical treatment outcomes in patients with neuralgia or cervicogenic headaches. Studies that reported numerical pain scores, nonnumerical pain scores, headache-free days, or the number of adverse events after nonsurgical treatment were included.

Results: A total of 22 articles were included in qualitative analysis. The majority of studies included patients who received injection therapy. Treatment with oral analgesics achieved good results in only 2.5% of the patients. Better outcomes were reported in patients who received local anesthetics injection (79%) and corticosteroid injection (87%). Treatment with botulinum toxin injection yielded the highest percentage of good results (97%; 95% CI, 0.81–1.00). The duration of headache relief after injection therapy varied from 30 minutes to 5 months.

Conclusions: The nonsurgical treatment of patients with neuralgia or cervicogenic headache is challenging. Injection therapy in patients with these types of headaches achieved good pain relief but only for a limited time. Surgical decompression may result in long-lasting pain relief and might be a more sustainable treatment option.
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INTRODUCTION

Extracranial compression of peripheral sensory nerves is one of many origins of chronic headaches. Patients with an extracranial origin of the headache can identify the pain with one finger and describe that the pain intensifies with applied pressure on the affected nerve area.[1,2] Identifying these patients can be difficult, and they are often diagnosed differently: neuralgia or cervicogenic headache. Neuralgia usually occurs in the occipital region with pain in the greater and lesser occipital nerve distribution. Neuralgia of the supraorbital nerve, supratrochlear nerve, zygomaticotemporal nerve, and auriculotemporal nerve has also been described.[3,4] Cervicogenic headache is caused by a disorder or lesion within the cervical spine, and patients often present with occipital pain.[5] Differentiating cervicogenic headache from occipital neuralgia is difficult due to phenotypic overlap.[6]

Decompression surgery or trigger-site deactivation surgery encompasses the release of extracranial peripheral sensory nerves. The recent literature shows that this procedure constitutes an effective treatment for types of headaches with an extracranial origin, and success rates between 68% and 95% are reported.[7] Before patients with these types of headaches are considered for surgical treatment, they are offered nonsurgical treatment options.[1] There are various nonsurgical treatments, including oral

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treatment and injection therapy.[8] Oral medication used to treat neuralgia and cervicogenic headache includes NSAIDs, tricyclic antidepressants, muscle relaxants, and anticonvulsants.[5,9,10] More often, patients are treated with anesthetic nerve blocks, corticosteroid nerve blocks, or injections with botulinum toxin.[11–13]

The recent literature provides the outcomes of surgical decompression in patients with headaches.[6,7] However, a review describing the efficacy of the nonsurgical treatment of patients is lacking. Therefore, this article aims to overview the current literature on the nonsurgical treatment options and evaluate the effectiveness of these treatments in patients with neuralgia and cervicogenic headaches.

Takeaways

Question: This study aimed to give an overview of the current literature on the nonsurgical treatment options and to evaluate the effectiveness of these treatments in patients with neuralgia and cervicogenic headache.

Findings: Twenty-two articles were included in qualitative analysis. Treatment with oral analgesics achieved good results in only 2.5% of the patients. Better outcomes were achieved in patients who received local anesthetics injection (79%) and corticosteroid injection (87%). The duration of headache relief after injection therapy varied from 30 minutes to 5 months.

Meaning: Injection therapy in patients with neuralgia and cervicogenic headache achieved good pain relief but only for a limited time.

METHODS

Literature Search

A systematic review was conducted to study the nonsurgical treatment of neuralgia and cervicogenic headache. We included all published clinical studies investigating nonsurgical treatment outcomes in patients with neuralgia or cervicogenic headache. The study was performed following the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement (PRISMA guidelines). Databases, such as Embase, MEDLINE, web of science, and Cochrane Central, were searched on May 8, 2020. A second search was performed on May 18, 2021. (**See Supplemental Digital Content 1,** which displays the search terms, **http://links.lww.com/PRSGO/C81**.)

Study Selection

Two independent authors (T.B. and M.H.J.H.) performed the initial search and screened for relevant articles based on title and abstract. All studies were screened for meeting the following inclusion criteria: original articles written in English; study patients aged 18 years or older; patients diagnosed with neuralgia; patients diagnosed with cervicogenic headache; any type of nonsurgical treatment, including oral pharmacologic treatment, injection therapy (anesthetic nerve blocks, corticosteroid nerve blocks, and injection with botulinum toxin), and any other form of nonsurgical intervention. (**See Supplemental Digital Content 2,** which displays an overview of the nonsurgical treatment options, **http://links.lww.com/PRSGO/C82**.)

Studies including fewer than five patients were excluded. Reviews, case reports, animal studies, conference abstracts, and poster presentations were excluded, as well as nonfull articles. Disagreements between authors were discussed in consensus meetings.

Data Extraction and Quality Scoring

The data from the relevant articles were extracted by two authors (T.B. and M.H.J.H.) using a standardized data collection form.

The primary outcome was the percentage of patients who achieved a good result after the treatment. As various methods to study the outcome of nonsurgical treatments were reported, a standardized outcome was defined to compare individual studies. If reported, a good posttreatment result was defined as “complete pain relief,” “significant pain relief,” or “important pain relief.” In addition, a 50% reduction of pain or a posttreatment Visual Analogue Scale/Numeric Rating Scale (VAS/NRS) of three or less was considered a good result. If the VAS/NRS score was only reported at a group level, the same definitions were applied to the total cohort. Secondary outcomes were headache-free days and the number of adverse events.

The location of the origin of the headache was divided into three subgroups; supraorbital neuralgia or supratrochlear neuralgia was classified as headache arising from the orbital region, occipital neuralgia and cervicogenic headache were classified as headache arising from the occipital region, and zygomaticotemporal neuralgia and auriculotemporal neuralgia were classified as headache arising from the temporal region.

Articles were classified by strength of evidence using the Jovell and Navarro-Rubio classification. Quality assessment was performed using the Study Quality Assessment Tools of the National Institutes of Health.

Statistical Analysis

For each study, the number and proportion of patients who underwent nonsurgical treatment with good results were determined from posttreatment VAS/NRS scores or nonnumerical pain scale scores. Pre- and posttreatment VAS/NRS scores were presented separately as mean with range or SD. From these scores, relative VAS/NRS improvement in percentages was obtained. The proportions of patients with good results were statistically combined in a meta-analysis to generate an overall pooled proportion per treatment with 95% confidence interval. Studies that reported the VAS/NRS only at the group level were not included in the meta-analysis. The meta-analysis was performed in R with a generic inverse variance meta-analysis without Hartung and Knapp adjustments for estimates and confidence intervals. In this model, studies are weighted based on the inverse of the variance of the effect estimate. Heterogeneity testing was performed using a generalized/weighted least-squares extension of Cochran's Q-test, which tests whether the variability in the observed effect sizes or outcomes is larger than one would expect based on sampling variability. Significance was set as $P = 0.05$. The results of the meta-analysis are presented as forest plots.

RESULTS

The first literature search was performed on May 8, 2020 and yielded 1267 publications. After screening the abstracts, 1188 articles were excluded. The full text of 79 articles was assessed. Among these studies, 24 studies met the inclusion criteria. A second literature search was performed on May 18, 2021 and yielded another 252 articles. Of those, two articles met the inclusion criteria. A third literature search was performed on January 5, 2022 and yielded 124 articles; no articles met the inclusion criteria. Four articles were also excluded during the qualitative review because the authors did not report any of our predefined primary or secondary outcomes. In total, 22 studies were included (Fig. 1) (**See Supplemental Digital Content 3**, which displays the Study Quality Assessment Tools of the National Institutes of Health, **http://links.lww.com/PRSGO/C83**.)

Most of the studies were at risk of bias due to the lack of specific inclusion and exclusion criteria, sample size justification, power analysis, or proper statistical methods to adjust for confounders (Fig. 2).

The majority of the studies evaluated the results of treatment with local anesthetics injection (62%).[14–27] Six (23%) articles described treatment with a combination of local anesthetics and corticosteroid,[28–32] three articles described treatment with oral analgesics,[14,17,33] two (7.7%) articles described treatment with botulinum toxin injection,[14,18] and one (3.8%) article described treatment with corticosteroid injection alone.[15] Two (7.7%) articles described other treatments including multifidus cervicis

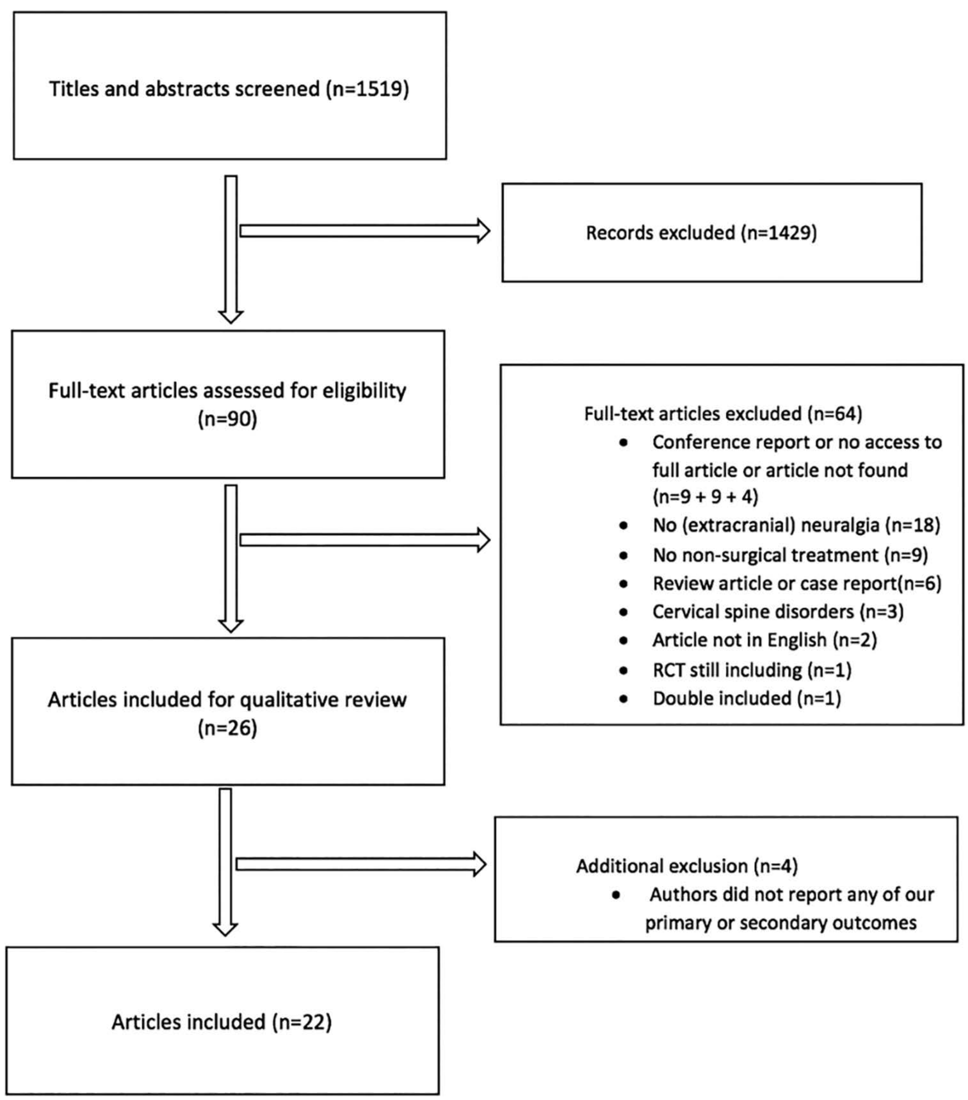

Fig. 1. Flowchart regarding the selection of included articles according to the PRISMA standards.

		Before-after studies with no control group													
Author	Year	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Anthony	1992	Y	Y	Y	Y	N	N	N	N	Y	N	N	NA		
Bovim	1992	Y	Y	Y	Y	N	Y	Y	N	Y	N	N	NA		
Caminero	2001	N	N	Y	NR	Y	Y	N	N	Y	N	N	NA		
De Ru	2009	Y	Y	Y	Y	N	Y	N	N	Y	N	N	NA		
Filipovic	2018	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	NA		
Hascalovici	2017	Y	Y	Y	Y	Y	Y	N	N	Y	N	N	NA		
Juskys	2018	Y	N	Y	NR	Y	Y	Y	N	Y	Y	N	NA		
Madore	2017	Y	Y	Y	Y	Y	Y	N	N	Y	N	N	NA		
Mulero	2012	Y	N	Y	Y	N	Y	N	N	Y	N	N	NA		
Pingree	2017	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	NA		
Sahai-Srivastava	2010	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	N	NA		
Vanterpool	2020	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	NA		
Vincent	1998	Y	N	Y	Y	Y	Y	N	N	Y	Y	Y	NA		
Weibelt	2010	Y	Y	Y	Y	Y	Y	Y	N	Y	N	Y	NA		
		Case series studies													
Pareja	2015	Y	Y	Y	Y	N	N	Y	N	Y					
Pareja	2017	Y	N	Y	Y	Y	Y	Y	N	Y					
		Controlled intervention study													
Cohen	2015	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	NR	Y	Y
Mohamed	2021	N	NR	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Y	Y
Pan	2008	Y	NR	NR	NR	NR	NR	Y	Y	Y	NR	Y	N	Y	Y
Shim	2011	Y	NR	NR	N	Y	Y	Y	Y	Y	NR	Y	N	Y	Y
Terzi	2002	Y	Y	Y	Y	Y	Y	Y	Y	Y	NR	Y	NR	Y	Y
		Observational cohort and Cross-sectional studies													
Martinez	2021	Y	Y	Y	N	N	Y	Y	N	N	N	N	N	Y	N

Fig. 2. Quality assessment of included studies.

plane block and acupuncture followed by acupoint-injection with lidocaine (Table 1).[21,34]

Oral Pharmacologic Treatment

Oral Analgesics

Three articles described treatment with oral analgesics. All three articles included patients with headaches arising from the orbital region. Filipović et al[14] included 19 patients and treated them with paracetamol, ibuprofen tramadol, oxycodone, and oxycontin. Only one (5%) patient reported a good result. The remaining two articles reported no relief after treatment with oral analgesics.[17,33] In total, the mean percentage of patients with good results after treatment with oral analgesics was 2.5%.

Injection Therapy

Injection with Botulinum Toxin

Two articles described treatment with botulinum toxin injection. Both articles included patients with headaches from the orbital region and found that 31 out of 32 (97%) patients reported good results after injection with Botulinum toxin. The mean headache-free period varied between 7.2 and 7.7 weeks. Two patients reported drooping of the eyebrow, and this adverse effect was transient.[14,18]

Injection with Local Anesthetics

A total of 14 articles examined the results of injection with local anesthetics. Sixty percent of the studies used long-acting anesthetics (120 minutes), and 40% used short-acting anesthetics (30 minutes). Among these, nine studies included patients with headache arising from the occipital region and seven of these studies reported the number of patients with good results.[15,16,20,21,25–27] The remaining two articles only described the rate of adverse events.[19,24] In total, 196 out of 269 (73%) patients with headaches from the occipital region reported good results after injection with local anesthetics. The reported time of headache relief varied; Bovim and Sand[16] and Mohamed et al[21] reported a mean headache-free period of 30 minutes, and Martínez-Pías et al[20] found a mean headache-free period of 3.5 months. Among the studies that included patients with headache arising from the occipital region, an adverse event rate of 0%–9% was reported, including dizziness, blurring of vision, and hypertension.[16,19,24,27]

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Table 1. Outcomes of Nonsurgical Treatments in Patients with Neuralgia and Cervicogenic Headache Stratified by the Location of the Origin of the Headache

Study, Level of Evidence	No. Patients (n)	Diagnostics	Patients with Good Results, n (%)	Follow-up	Headache-free Period, Mean	Adverse Events, n (%)
Oral analgesics						
Orbital region						
Caminero and Pareja[17] VI	14	Diagnostic nerve block supraorbital nerve	0/14 (0)	—	—	—
Filipović et al[14] VI	19	Diagnostic nerve block supratrochlear and supraorbital nerve	1/19 (5)	—	—	—
Pareja et al[33] VI	6	Pain restricted to the internal angle of the orbit that did not show the features of trochlear pain	0/6 (0)		—	—
Botulinum toxin injection						
Orbital region						
De Ru and Buwalda[18] VIII	10	Pain worsened with pressure on the orbital rim near the supratrochlear nerve	9/10 (90)	—	6–10 wk (mean 7.7)	2/10 (20)
Filipović et al[14] VI	22	Diagnostic nerve block supratrochlear and supraorbital nerve	22/22 (100)	3 d	7.2 wk	0/0 (100)
Injection with local anesthetics						
Orbital region						
Caminero and Pareja[17] VI	18	Diagnostic nerve block supraorbital nerve	18/18 (100)	—	1 h–4 mo	—
De Ru and Buwalda[18] VIII	10	Pain worsened with pressure on the orbital rim near the supratrochlear nerve	10/10 (100)	—	30 min	0/10 (0)
Filipović et al[14] VI	22	Diagnostic nerve block supratrochlear nerve and supraorbital nerve	22/22 (100)	Several hours	—	0/22 (0)
Mulero et al[22] VI	8	International Classification of Headache Disorder criteria for supraorbital neuralgia*	8/8 (100)	2–6 mo	3.4 mo	—
Pareja et al[23] VI	14	Patients presenting with pain within the territory of the supratrochlear nerve consistent with supratrochlear neuralgia	14/14 (100) 13/14 (93) 11/14: 79 10/14 (71) 9/14 (64) 6/14 (43) 5/14 (36)	1 h 2 h 4 h 10 h 24 h 2 wk 2 mo	1 wk–5 mo	0/14 (0)
Occipital region						
Anthony[15] VI	50	Circumscribed tenderness over the GON Hypoalgesia, hyperalgesia or dysaesthesiae in the area of distribution of the GON	42/50 (845)	—	—	—
Bovim et al[16] IV	35	Diagnostic criteria for cervicogenic headache (Sjaastad et al 1990)†	20/35 (57)	30 min	30 min	0/35 (100)
Hascalovici and Robbins[19] VI	6	International Classification of Headache Disorders criteria for occipital neuralgia and cervicogenic headache‡§	—	—	—	0/0 (0)
Martínez-Pías et al[20] VI	53	International Classification of Headache Disorders criteria for occipital neuralgia‡	39/53 (73)	—	3.5 mo	—
Mohamed et al[21] IV	30	International Classification of Headache Disorder criteria for cervicogenic headache§	14/30 (47)	—	30 min	—
Sahai-Srivastava and Subhani[24] VI	89	International Classification of Headache Disorders criteria for occipital neuralgia‡	—	—	—	8/89 (9)
Terzi et al[25] III	10	Diagnostic criteria for cervicogenic headache (Sjaastad et al. 1990)†	10/10 (100)	30 min	—	—
Vanterpool et al[26] VI	50	Pain in the distribution of the GON with pain radiating up over occiput to the top of the head or to the eye	31/50 (62)	5 min	—	—
Vincent et al[27] VI	41	Diagnostic criteria cervicogenic headache (Sjaastad et al. 1990)†	100¶	7 d	—	0/41 (0)
Corticosteroid injection						
Occipital region						
Anthony[15] VI	86	Circumscribed tenderness over the GON Hypoalgesia, hyperalgesia or dysaesthesiae in the area of distribution of the GON	75/86 (87)	—	31.5 d (mean)	—
Combination of local anesthetics with corticosteroid						
Occipital region						
Cohen et al[28] III	39	International Classification of Headache Disorders criteria for occipital neuralgia‡ International Classification of Headache Disorders criteria for chronic migraine‖ with a predominance of occipital pain and occipital nerve tenderness that responded to local anesthetic blockade	0¶	2 wk–6 mo	—	6/39 (15)
Juškys and Šustickas[29] VI	44	Anamnesis	35/44 (80)	6 mo	—	1/44 (2)
Madore et al[30] VI	71	Tenderness of the occipital region on examination	—	—	—	0/71 (0)
Pingree et al[31] VI	14	International Classification of Headache Disorders criteria for occipital neuralgia or cervicogenic headache‡§	14/14 (100)	30 min	30 min	0/14 (0)

(*Continued*)

Table 1. (Continued)

Study, Level of Evidence	No. Patients (n)	Diagnostics	Patients with Good Results, n (%)	Follow-up	Headache-free Period, Mean	Adverse Events, n (%)
Shim et al[32] IV	45	Anamnesis	Group S** 100¶ Group B†† 100¶ 0¶	1–4 wk 1 wk 4 wk	—	0/45 (0)
Weibelt et al[35] VI	150	CM by existing ICHD criteria, and all reported that at least 50 of their most severe headaches arose from one side of the occipital skull base or both CM by existing ICHD criteria, and all reported that at least 50 of their most severe headaches arose from one side of the occipital skull base or both CM by existing ICHD criteria, and all reported that at least 50 of their most severe headaches arose from one side of the occipital skull base or both CM by existing ICHD criteria, and all reported that at least 50 of their most severe headaches arose from one side of the occipital skull base or both M by existing ICHD criteria, and all reported that at least 50 of their most severe headaches arose from one side of the occipital skull base or both M by existing ICHD criteria, and all reported that at least 50 of their most severe headaches arose from one side of the occipital skull base or both M by existing ICHD criteria, and all reported that at least 50 of their most severe headaches arose from one side of the occipital skull base or both M by existing ICHD criteria, and all reported that at least 50 of their most severe headaches arose from one side of the occipital skull base or both Chronic migraine criteria (ICHD) with at least 50% of most severe headaches arising from one side of the occipital skull base or both‖	90/150 (60)	1 mo	—	24/150 (16)
Other						
Occipital region						
Multifidus cervicis plane block						
Mohamed et al[21] IV	30	International Classification of Headache Disorders criteria for cervicogenic headache§	24/30 (80)	—	30 min	—
Acupuncture plus acupoint-injection						
Pan and Tan[34] II	84	Obvious tenderness at the outlet of the greater occipital nerve	31/42 (74)	6 mo	6 mo	—

*International Classification of Headache Disorder criteria for supraorbital neuralgia.
†International Classification of Headache Disorders criteria for occipital neuralgia.
‡International Classification of Headache Disorders criteria for cervicogenic headache.
§Diagnostic criteria for cervicogenic headache Sjaastad et al, 1990.
¶Based on VAS/NRS reported at group level.
‖International Classification of Headache Disorders criteria chronic migraine.
**Ultrasound-guided GON block.
††Conventional blind GON block.
GON, greater occipital nerve; ICHD, International Classification of Headache Disorders.

Five articles included patients with headache arising from the orbital region. In total, 72 out of 72 (100%) patients reported good results after injection with local anesthetics. The headache-free period varied between 1 hour and 5 months. No adverse events were reported.[14,17,18,22,23]

Four articles measured the relative VAS or NRS for pain improvement. After a follow-up of 5 minutes, an improvement between 33.3% and 54.6% was reported. Vincent et al[27] found a VAS improvement of 45.6% after a follow-up of 7 days (Table 2).[21,25,26]

Injection with Corticosteroid

One article reported the results of corticosteroid injection. Anthony et al[15] described 86 patients who underwent injection with depomedrol into the region of the greater occipital nerve. A total of 75 (87%) patients reported a good result among these patients. The mean duration of relief was 31.5 days.

Injection with a Combination of Local Anesthetics with Corticosteroid

Six studies reported the treatment results with a combination of local anesthetics with corticosteroid. All studies included patients with headaches arising from the occipital region. Among these, five out of six studies reported the number of patients with good results. In total, the mean percentage of patients with good results after injections with local anesthetics and corticosteroids was 60%. The time of headache relief varied between 30 minutes and 6 months. The adverse event rate was reported in all articles. In total, 31 out of 363 (8.5%) patients reported an adverse event, including dizziness, nausea, symptoms of vasovagal syncope, hypophonia, dysphagia increased swelling at the injection site, temporary worsening of the headache, vomiting, and blurred vision.[28–32,35]

Four studies reported relative VAS or NRS improvement after local anesthetics and corticosteroids treatment. They found an improvement between 27.8% and 64.1% within a follow-up of 4 weeks. At a follow-up of 6 months, a relative VAS/NRS improvement between 6.8 and 69.4 was reported (Table 2).[28,29,31,32]

Other Treatments

Two articles described other treatments, including multifidus cervicis plane block and acupuncture followed by acupoint-injection with lidocaine in the greater occipital nerve. Both articles included patients with headache arising from the occipital region. Mohamed et al[21] treated

Table 2. Overview of Studies Reporting Pretreatment and Posttreatment Pain Scores according to VAS/NRS

Reference	No. Patients	Pretreatment VAS/NRS [mean (range)]	Posttreatment [VAS/NRS (mean, SD)]	Follow-up	Relative VAS/NRS Improvement (%)
Oral analgesics					
Orbital region					
Filipović et al[14]	19	8.1±0.2	6.5±0.2	—	20.7
Botulinum toxin					
Occipital region					
Filipović et al[14]	22	8.1±0.2	2.9±0.4	—	64.2
Local anesthetics					
Orbital region					
Terzi et al[25]	10	6.6 (0.8–0.3)	4.4 (1.2–1.0)	5 min	33.3
			3.1 (1.0–0.3)	10 min	53.7
			1.7 (1.6–0.5)	30 min	74.4
Occipital region					
Vanterpool et al[26]	50	6.0±2.6	2.7±2.2	5 min	54.6
Vincent et al[27]	41	3.8±0.3	2.0±0.3	7 d	45.6
Mohamed et al[21]	30	7.7±1.6	3.7±2.2	2 wk	52.1
			4.4±2.2	4 wk	42.3
Combination local anesthetics with corticosteroid					
Occipital region					
Cohen et al[28]	39	5.1	3.7	2 wk	27.8
			3.7	6 wk	26.9
			4.4	3 mo	13.2
			4.8	6 mo	6.8
Juškys and Šustickas[29]	44	7.2±0.9	1.9±1.6	24 h	73.0
			2.2±1.7	6 mo	69.4
Pingree et al[31]	14	4.7; median, 5; IQR, 3–6	0.9 (median, 0.5; IQR, 0–1)	30 min	80.3
			2.1 (median, 2; IQR, 0–3.5)	2 wk	56.1
Shim et al[32]	45	Group S: 6.4±0.2*		Group S	
			2.3±0.2	1 wk	64.1
			2.3±0.2	4 wk	64.1
		Group B: 6.5±0.2†		Group B	
			3.0±0.3	1 wk	53.8
			3.8±0.3	4 wk	41.5
Other					
Occipital region					
Mohamed et al[21]	30	7.9±1.9	2.5±2.1	2 wk	68.5
			3.8±2.6	4 wk	52.0

*Ultrasound-guided GON block.
†Conventional blind GON block.

30 patients with a multifidus cervicis plane block and reported good results in 24 (80%) patients and a headache-free period of 30 minutes. Pan and Tan reported good results in 74% after treating patients with acupuncture plus acupoint-injection. The mean headache-free period was 6 months.[34]

Meta-analysis

A meta-analysis was performed to compare the different nonsurgical techniques. Only techniques including two or more studies were included in the analysis; local anesthetics, botulinum toxin, the combination of local anesthetics with corticosteroid, oral analgesics, and "other." Overall, the pooled proportion of patients with good results was 0.87 (0.59–0.85). Treatment with botulinum toxin yielded the best results with a pooled proportion of 0.97 (0.81–1.00). Local anesthetics, botulinum toxin, combination of local anesthetics with corticosteroid, and "other" showed significantly better results than oral analgesics [0.03 (0.00–0.16)] (Fig. 3).

DISCUSSION

The aim of this systematic review and meta-analysis of the literature was to evaluate the effectiveness of the nonsurgical treatment in patients with neuralgia or cervicogenic headache. We found that the effectiveness varied between the different types of treatments; treatment with oral analgesics achieved good results in only 2.5% of the patients. Better outcomes were achieved in patients who received local anesthetic injection (79%), corticosteroid injection (87%), or botulinum toxin injection (97%).

As mentioned above, we found that injection with botulinum toxin yielded the highest proportion of good results (97%). The literature describes that injection with botulinum toxin A into the irritation site of the nerve reduces the neurogenic inflammation and inhibits the central sensitization of the nerve.[36] These processes lead to a less sensitive nerve and a reduction of the pain.[37] In this review, only two studies that reported the use of botulinum toxin were analyzed. Both studies included patients

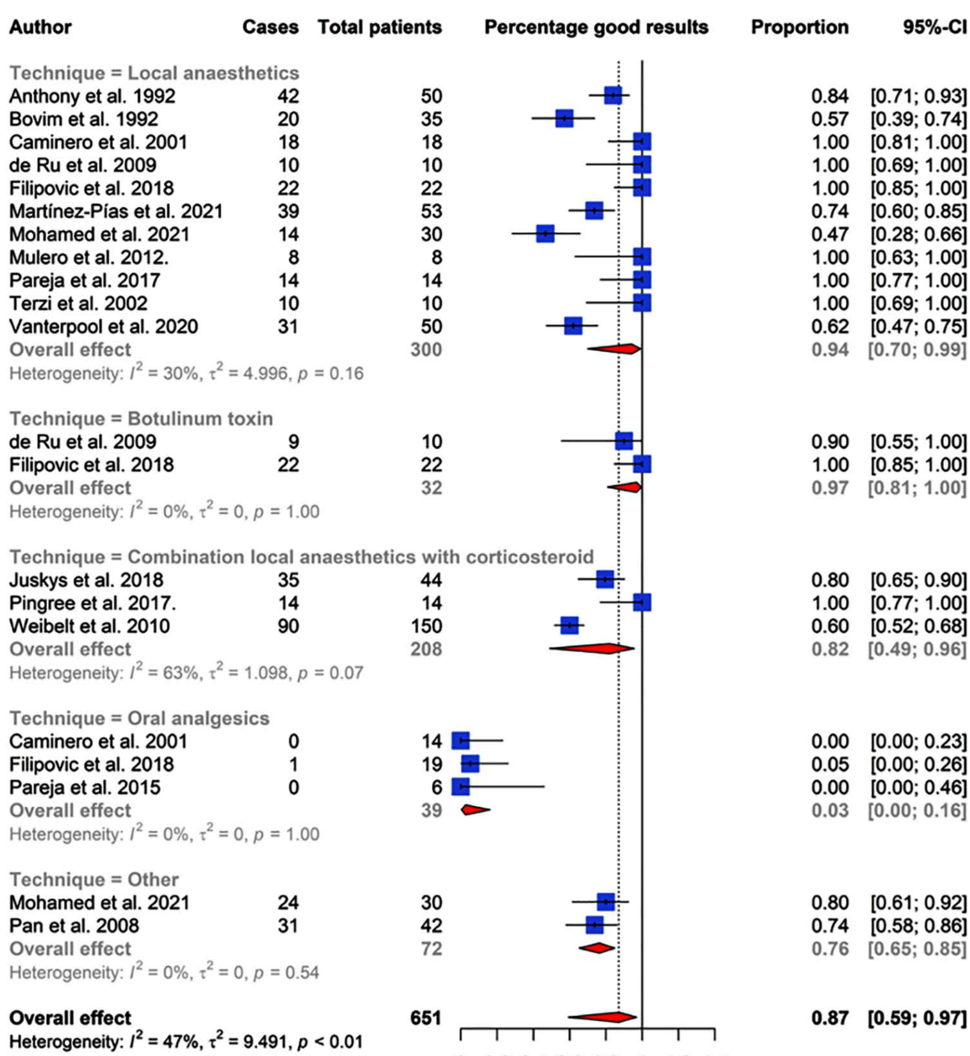

Fig. 3. Meta-analysis comparing the different nonsurgical techniques.

with headache arising from the orbital region.[14,18] There is only a paucity of studies investigating botulinum toxin's use in occipital neuralgia and cervicogenic headache. A case report by Volcy et al[37] described that injection with botulinum toxin was effective in the local treatment of occipital neuralgia. In addition, a case report on a patient with cervicogenic headache reported a reduction of headache after injection with botulinum toxin as well.[38]

In this review, most of the studies described treatment with local anesthetics. Overall, 73% of the patients with headaches from the occipital region and 100% of those from the orbital region reported good results after injection with local anesthetics. The duration of headache relief varied from 30 minutes to months. Theoretically, it could be expected that the headache relief maintains as long as the duration of action of the used anesthetic. However, we observed that injection with anesthetics yields extended relief for 5 months.[23] There are two factors described that are associated with a prolonged time of pain relief. First, Naja et al[39] show that repeated injections with anesthetics may reduce hypersensitivity and cytokine expression, leading to long-lasting pain-free periods. Second, the ability to detect and block the greater occipital nerve precisely by using ultrasound rather than simply infiltrating its general location contributes to this prolonged pain-free period as well.

In this review, the location of the origin of the headache was divided into three subgroups: the orbital region, the occipital region, and the temporal region. No studies reporting the results in headaches arising from the temporal region were available. Patients with headaches arising from the orbital region seem to report more effective pain relief compared with patients with headaches arising from the occipital region following injection with local anesthetics (100% versus 73% good results). Unfortunately, the number of patients included was too small to perform subgroup analysis on the headache location.

The outcome of this review shows that injection therapy is effective in patients with headaches due to extracranial compression of peripheral sensory nerves. However, evidence in the literature indicates that injection therapy demonstrates efficacy in patients with primary headache disorders.[40–42] These primary headache disorders include migraine, tension-type headache, or cluster headache and are conditions in which the pathophysiological basis is in the central nervous system.[40,43] For example, injection with botulinum toxin has been approved to prevent migraine following the demonstration of good results in two large controlled trials.[44] In addition, blocks of the greater occipital nerve with an anesthetic and corticosteroid have proven effective in patients with cluster headaches and migraines.[45,46]

Theories have been described explaining the effectiveness of peripheral nerve treatments in patients with primary headache disorders. Tang et al[46] describe that a greater occipital nerve block causes pain relief in migraine patients by modulation of the nociceptive afferent nerves reaching the trigeminal nucleus caudalis. The proximity of sensory neurons in the upper cervical spine to the trigeminal nucleus caudalis neurons and the convergence of sensory input to trigeminal nucleus caudalis from both trigeminal and occipital afferents leads to a relief of headache following a greater occipital nerve block.[47] Additionally, diagnosing headache patients correctly is challenging due to phenotypic overlap within the different types of headache disorders. We theorize that a few patients diagnosed with migraine might have headaches with an extracranial origin or experience a combination of both, resulting in headache relief following peripheral nerve treatments.

The results of this review show that the nonsurgical treatment of headaches is effective in patients with an extracranial origin of the headaches. However, headache relief is only temporary and often repeated treatment is necessary. As mentioned in the introduction, current literature shows that surgical decompression may result in enduring pain relief in patients with an extracranial origin of the headache, with positive outcomes in 68%–95% of cases.[1,7] Guyuron et al[48] reported the long-term outcomes following surgical decompression and found that 88% of the patients experienced beneficial results after 5 years. These outcomes show that surgical intervention may result in long-lasting pain relief and might be a more sustainable treatment option. Based on the results of this review, we have modified our consent process on nonsurgical treatment, and we inform patients about our preference for decompression surgery as we believe that conservative treatment is a less sustainable treatment option.

A recent article published by Gfrerer et al[49] shows that primary decompression surgery sometimes fails when the nerve appears severely damaged, leading to recurrent or persistent symptoms. In this situation, most experienced surgeons will offer secondary transection of the nerve combined with advanced techniques to address the proximal nerve stump. We believe that, when patients have a clear diagnosis and are adequately informed, they should be referred sooner for surgery. Earlier surgery could positively influence the outcome of nerve decompression surgery and provide long-lasting pain relief. In addition, earlier surgery could possibly reduce the risk of reoperation.

The effectiveness of injection therapy in primary headache disorders could be interpreted as a limitation to this review, as it is difficult to determine whether the effect is extra or intracranial. A second limitation of this study is that randomized controlled trials with large study populations were hard to achieve. Although most included studies were observational studiezs, two randomized controlled trials could be included in this analysis.[25,34] Furthermore, the methods of outcome reporting varied between numerical and ordinal pain scale scores. We combined the various outcome measures into a clinically meaningful "good posttreatment result." However, a standardized set of valid, reliable, and easily interpretable outcome measures should be applied in future research. In addition, the percentage of patients who experienced good pain relief varied among the included studies. We theorize that this could be explained by the possibility of improper diagnosis. The inclusion criteria differed between the included studies. In numerous studies, the International Classification of Headache Disorders (ICHD) classification or the diagnostic criteria of Sjaastad were used. Some studies included patients based on their symptoms and others included patients based on an effective diagnostic injection. This could lead to incorrect diagnosis. Second, it is not clear whether assessment of the right trigger site was performed in all studies. In addition, in a majority of the studies, the diagnosis is based on the classification of headaches (ICHD). In this classification, there is no specification of nerves in the occipital region with cervicogenic headache. This could have led to improper or too few injection points as well. Also, considering the fact that the authors are plastic surgeons, there could be a possibility of a conflict of interest recommending surgical treatment. However, by reporting the results of this review, we hope to show colleagues from all hospital departments that the effect of the nonsurgical treatment is only temporary and that referral of patients with a clear diagnosis for nerve decompression surgery might offer them long-lasting pain relief.

CONCLUSIONS

This systematic review and meta-analysis demonstrates that the nonsurgical treatment of patients with neuralgia or cervicogenic headache is challenging. Injection therapy in patients with these types of headaches achieved good pain relief but only for a limited time. Injection with botulinum toxin yielded the highest proportion of good results. Surgical decompression may result in long-lasting pain relief and might be a more sustainable treatment option.

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