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Safety and efficacy of percutaneous pulsed radiofrequency treatment at the C1-C2 level in chronic cluster headache: A retrospective analysis of 21 cases.

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Safety and efficacy of percutaneous pulsed radiofrequency treatment at the C1-C2 level in chronic cluster headache: A retrospective analysis of 21 cases.

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Key words: Cluster headache; retrospective study; pulsed radiofrequency treatment; interventional management; refractory headache.

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ABSTRACT

Objectives — We performed an audit of the safety and efficacy of percutaneous pulsed radiofrequency (PRF) treatment directed at C1 and C2 level as performed at our local pain clinic in refractory chronic cluster headache (CH) patients.

Methods — We identified 21 chronic CH patients treated with PRF (240sec, max. 45V, max. 42°C) directed at the ganglion and/or nerve root of C1 and C2. Data were collected through retrospective analysis of patients' files and include demographic variables, onset and duration of the headache, mean attack frequency and prior pharmacological treatment. Safety and reduction of attack frequency in the first three months after a first PRF treatment was the primary outcome parameter of this audit.

Results — Ten patients suffered from primary chronic CH, 11 from secondary chronic CH (age range 25-62 years). All had been treated with at least two prophylactic drugs and 19 (90%) had previously been treated with verapamil, lithium and topiramate. Ten patients (47,6%) reported no meaningful effect, four patients (19%) reported a meaningful reduction of less than 50% and seven patients (33,3%) reported a reduction in headache burden of at least 50% in the three months following treatment. Two patients reported occurrence or increase in frequency of contralateral cluster attacks. No other adverse events were reported or detected at follow-up.

Conclusion — Upper cervical PRF treatment appears to be a safe procedure that could prove effective in the treatment of patients with refractory chronic cluster headaches and warrants a prospective study.

INTRODUCTION

Cluster headache (CH) is a primary headache with severe headache attacks with ipsilateral autonomous symptoms. (1) The criteria for this disorder have been established by the most recent third edition of the International Classification of Headache Disorders (ICHD). (1) These state that:

- There should have been at least five attacks fulfilling the next criteria.
- Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15 to 180 minutes when untreated.
- There should be either one or both of the following:
    - Ipsilateral to the headache: conjunctival injection and/or lacrimation, nasal congestion and/or rhinorrhoea, eyelid oedema, forehead and facial sweating, miosis and/or ptosis.
    - A sense of restlessness or agitation.
- The attacks occur with a frequency between one every other day and 8 per day.
- Are not better accounted for by another ICHD-3 diagnosis.

Eighty-five to ninety percent of CH patients are episodic were attacks occur in series of weeks to months with remission periods of months to years.(1) Chronic CH patients have no such remission periods. The criteria for chronic CH specify that attacks should be occurring without a remission period, or with remissions lasting less than 3 months, for at least 1 year. Patients may have chronic CH from the onset of their cluster attacks. This is referred to as primary chronic cluster headache. The CH may also become chronic after any period of episodic cluster headache. This is referred to as secondary chronic cluster headache. The most recent version of the ICHD does not make the distinction between primary and secondary chronic CH anymore.(1)

The incidence of cluster headache is 1/1000. (2) The age of onset is usually between 20 and 40 years, men are afflicted 3 times more often than women. (1)

The treatment of cluster headache consists of acute and preventative treatments. The goal of acute treatment is to abort a cluster attack while the goal of preventative treatment is to reduce cluster frequency. (3)

As acute treatment first line treatments are oxygen, subcutaneous (SC) sumatriptan and intranasal (IN) zolmitriptan. (4) The use of oxygen is supported by three controlled trials. (5, 6, 7) The first trial had a non-controlled part in which 39 out of 52 patients obtained complete or almost complete reduction of pain in seven of ten attacks within 15 minutes of starting treatment with 100% oxygen administered through a facial mask at a rate of 7 liters per minute. In the second part of this study oxygen was compared with oral ergotamine. Eighty-two percent of oxygen users obtained complete or almost complete reduction of pain in seven of ten attacks while only 70% of patients in the ergotamine group achieved this outcome. This difference was not significant. (5) A second study with a crossover trial design involving 19 patients found a significant difference of patients' subjective evaluation of cluster headache pain relief between the attacks treated with 100% oxygen versus air inhalation at 6 liters per min. (6) A more recent randomized controlled crossover trial comparing 100% oxygen with high-flow air placebo for 4 attacks in 109 patients. The difference in pain freedom at 15 min (78% for 02 and 20% for air) was significant. (7)

In two randomized controlled crossover trials studying SC sumatriptan with 134 and 49 patients. Headache relief was achieved in about 75% of attacks treated with sumatriptan in both trials and in 26 and 35% of attacks treated with placebo, a significant difference. (8, 9)

As preventative treatment verapamil is first choice. (10) Only one randomized controlled trial has studied its effectiveness in CH. (11) In this trial a dose of 360 mg verapamil was compared to placebo for 14 days. Both the number of daily attacks as the use of rescue medication was significantly reduced in the verapamil group compared to placebo. (11) Other pharmaceutical treatments such as lithium, topiramate, valproate and melatonin are being used but data from prospective trials are very limited and often conflicting. (4)

Invasive and non-invasive ways of neurostimulation have been developed. The most well-known are sphenopalatine ganglion stimulation, occipital nerve stimulation (12, 13), noninvasive vagus nerve stimulation, and deep brain stimulation. Also upper cervical spinal cord stimulation has been tried. (14) All these treatments are investigational and it is

suggested to only consider offering these treatments in intractable headache. (15, 16). Sphenopalatine ganglion stimulation and noninvasive vagus nerve stimulation have been studied in randomized controlled trials. For spenopalatine ganglion stimulation, a trial in 32 patients of which 28 completed the trial period showed superiority to sham stimulation for pain relief at 15 minutes. There was also a reduction in attack frequency, a secondary outcome. (17)

There has been some interest in using the PRF technique for CH patients and a few case series of PRF interventions directed at the pterygopalatine ganglion (18-21) have been published (the largest series reported the results in 16 patients). Studies on PRF treatment directed at the trigeminal ganglion are lacking but limited retrospective data on radiofrequency ablation of this structure is available. (22) An overview of the case series of PRF in CH patients is given in Table 1.

Radiofrequency ablation is a destructive technique that allows to make well-circumscribed lesions by heating the neural tissue adjacent to the uninsulated tip of the electrode. Contrary to the use of continuous radiofrequency signal in radiofrequency ablation, in PRF treatment pulses of radiofrequency signal are administered and the temperature is kept in a non-destructive range. Its main advantages are less pain during the procedure and a lower risk of motor deficits and deafferentiation pain. On electron microscopic analysis some ultrastructural changes such as an increased numbers of vacuoles and enlarged endoplasmic reticulum cisterns are seen after PRF stimulation but the mechanism of action of PRF remains largely unknown. (23, 24)

The three branches of the trigeminal nerve transmit afferent sensory and nociceptive information of the face, the anterior part of the head, and the anterior as well as middle cranial fossa. The cutaneous and deep structures of the back of the head and upper neck are innervated by the greater occipital nerve (GON), the lesser occipital nerve (LON) and the third occipital nerve which project centrally through the upper cervical nerves and dorsal roots. (25) Patients with primary headaches not only report pain from the anterior part of the head innervated by the trigeminal nerve, but also from the back of the head and neck innervated by the upper cervical roots. (26) In the last three decades, through several animal model experiments,(27-29) the concept emerged of a trigeminocervical complex, a functional entity that acts as a major relay for convergent nociceptive afferent input from the supratentorial meninges (innervated by the trigeminal nerve) and cervical structures

(innervated mainly by the GON). (26, 27) It is hypothesized that through this trigeminocervical complex input from the upper cervical nerves can modulate trigeminal nociceptive input. (30) The importance of relay neurons of the trigeminocervical complex in primary headache disorders is the theoretical framework that led to the development of modalities of neuromodulation directed at the afferent input of the upper cervical spine as a means of modifying the disease course of primary headache disorders. Thus far no studies have reported on radiofrequency ablation or pulsed radiofrequency (PRF) treatment directed at upper cervical neural structures.

In this report we present the results from an audit we conducted on the safety and effectiveness of percutaneous PRF treatment directed at the C1 and C2 level in chronic CH patients at our pain clinic.

METHODS:

This audit was approved by our institutional ethical review board. Informed consent was not required for this retrospective clinical audit.
Data collection: A retrospective chart review of patients' medical records was performed of all cluster headache patients who underwent the procedure at the Pain Clinic of the Ghent University Hospital between January 2010 and August 2017. We predefined variables we expected to be consistently available in the medical records including demographic variables, onset and duration of the headache, mean attack frequency at baseline, medication history, medication at baseline and medication changes, previous interventional procedures and adverse events. The main interest was the patients' reported global impression of change in the first three months after treatment, an outcome measure that has been used in other cluster studies.(31)

Description of the procedure: The treating physician at the pain clinic informed all patients properly about the empirical nature of this treatment. Written informed consent was obtained from all patients prior to the procedure. The PRF application is performed under fluoroscopic guidance. The patient is supine. The C-arm image intensifier is positioned with the intensifier facing the side being treated. It is extremely important to achieve perfect superimposition of both sides of the C1 and C2 vertebrae. The entry point for C1 is at the junction of the upper 2/3 and lower 1/3 of the bony pillar of C1. A 22G 50 mm RF needle is inserted and advanced using tunnel vision until it is firmly gripped by the superficial tissues (as can be seen in Figure 1). The position of the needle is checked in the antero-posterior axis while identifying the lateral margin of the atlanto-axial joint. The needle is advanced to the lateral border of the atlanto-axial joint. At this point the proximity to the ganglion/nerve is confirmed using sensory (50 Hz) and motor (2Hz) stimulation at a level of 0.5V or less. If necessary the needle is advanced further but may never be deeper than the lateral 1/4 of the atlanto-axial joint. The entry point for C2 lies at the junction of the upper 1/3 and lower 2/3 of the bony pillar of C2. A 22G 50 mm RF needle is inserted and advanced using tunnel vision until contact with bone at the target point. After bony contact the needle is angled cranially into the center of the C2 space at the same depth as the bony target. The position of the needle is checked in the antero-posterior axis. At this point the proximity to the ganglion is confirmed using sensory (50 Hz)

and motor (2Hz) stimulation at a level of 0.5V or less. If necessary the needle is advanced but may never be deeper than the lateral 1/3 of the atlanto-axial joint. Finally the radiofrequency pulse is administered at max. 45V for 240 seconds maintaining the temperature below 42°C).

RESULTS:

Subjects. Twenty-one subjects were treated between 2010 and 2017. All patients were referred through our headache clinic and matched the diagnostic criteria for chronic CH (ICHD-III code 3.1.2).(1) Ten patients suffered from primary chronic CH, eleven from secondary chronic CH. The age of patients ranged from 23 to 62 years with a median age of 50 years. The median duration of chronic CH prior to PRF treatment was 5 years with a range of less than a year up to 33 years. All patients had tried at least two prophylactic drugs prior to PRF treatment; all had been on an adequate dose of verapamil, 19 out of 21 on lithium, 19 on topiramate, 11 on gabapentin, 10 on methysergide (which is currently no longer available in Belgium), ten on melatonin and nine on valproate. Two patients had an occipital nerve stimulator in place, two patients a stimulator at the pterygopalatine ganglion (one of those patients also had an implanted occipital nerve stimulator). Seven patients had previously undergone PRF treatment directed to a different structure: 6 patients of the pterygopalatine ganglion, one patient of the Gasserian ganglion, one patient (who had also undergone PRF treatment directed to the pterygopalatine ganglion) of the stellate ganglion.

Efficacy. The results regarding efficacy are summarized in Table 1, along with the self-reported frequency at baseline and the numbers of years suffering from chronic CH. Ten patients (47,6%) reported no meaningful effect after PRF treatment, four patients (19%) reported a meaningful reduction in headache burden of less than 50% and seven patients (33,3%) reported a reduction in headache burden of more than 50% in the three months following treatment. Changes in prophylactic cluster treatment occurred in seven patients in the first three months of follow-up and of these three patients reported a reduction in headache burden of more than 50%. In one out of three medication was reduced; this patient reduced the daily dose of verapamil from 720mg to 480mg because of intolerability. In one patient on a combination therapy of topiramate/verapamil/melatonin/valproate the daily dose of valproate was increased from 1000mg to 2000mg. One patient switched from lithium, topiramate and corticosteroids to gabapentin and long-acting opioids.

Adverse events. One patient with unilateral attacks on both sides of the face received PRF on the preponderant side and experienced more than 50% reduction in headache burden ipsilateral to the procedure but reported an increase in contralateral attacks. A subsequent PRF

treatment directed at the C1-C2 level on this contralateral side had no effect. One other patient with strictly unilateral attacks at baseline and a complete resolution of cluster attacks after ipsilateral PRF treatment reported recurrence of contralateral cluster attacks 11 months after the procedure. No additional adverse events (including bleeding, infection or neuropathic pain) were detected at regular follow-up.

DISCUSSION:

We report on a technique that originated in our local pain clinic. They felt it to be a reasonable and potentially less invasive treatment target alternative to a sphenopalatine ganglion intervention.

There are some limitations to our audit which is based on retrospective and uncontrolled data; although the necessary relevant data was consistently available in the patients' files, there was no standardized way of reporting. The patients' prophylactic medication changed during the assessment period in a significant proportion of patients This changes are reported in Table 3. Therefore, this analysis provides only preliminary data regarding the efficacy of PRF treatment at the C1-C2 level and does not allow comparison to other available interventional treatments. The number of patients treated is small, however the size of this consecutive case series is comparable to other invasive and non-invasive neuromodulation studies in cluster headache.

A global improvement of at least 50 % reported by a third of this group with difficult to treat chronic CH patients is promising and could be clinically meaningful if confirmed in further prospective (and preferably controlled) studies. There is little data on placebo effect from controlled trials in (refractory) chronic CH patients. In one randomized controlled trial of non-invasive vagus nerve stimulation (nVNS), 40% (18/45) of chronic CH patients in the nVNS group experienced a more than 50% reduction in attack frequency during the last two weeks of the randomized period, which was significantly higher than the 8.3% (4/48) in the control group.(32) Comparison to our results should be done with caution since the patient characteristics in this study could be significantly different from our population as it included chronic CH patients regardless of medication history and no information was provided on previous standard of care prophylactic treatments.

No serious adverse events were reported in this series. The main theoretical safety issue is the close proximity of the intervention to the vertebral artery, a structure that is known to have some anatomical variation and is at risk of damage, especially at the C1 level. (33) This anatomical variation is illustrated in Figure 2.

The major afferent contribution of the occipital and suboccipital deep and cutaneous structures is thought to be mediated by the spinal root and nerve of C2 (25, 26) and the C1 nerve has generally been considered to have no significant sensory function.(34) In a cadaveric study a C1 dorsal root was present in 60% (48 out of 80) of specimens. Only 30% (14 out of 48) of these dorsal roots were found to have a distinct dorsal root ganglion.(35)

This suggests part of this treatment is directed at a structure that is absent in a big part of the population. Interestingly, stimulation of C1 in patients with chronic occipital pain evoked periorbital and frontal pain in the subgroup of six migraine patients only suggesting that C1 has a particular link with migraine; there were no cluster patients included in this study, but a similar phenomenon cannot be excluded.(34)

Overall, the rationale for targeting C1 is less convincing. It seems to be theoretically more dangerous than the other cervical levels, and there is less experience than with targeting C2 which has also been studied in other indications.(36) A suggestion for further research is to consider targeting only C2; or to target C2 and C3 (as nociceptive input of C3 projects to the trigeminocervical complex too).

Since solid data from a prospective study is lacking, we can only speculate on the potential place of PRF treatment at the high cervical level in the interventional treatment algorithm of chronic CH. The way forward is a prospective controlled trail. An overview of a potential future trial design is illustrated in Figure 4.

TABLES AND FIGURES:

Table 1: Retrospective data on PRF in cluster headache.

Author (year)	Target	Outcome parameter	N° cluster patients
Chua (2011)	Sphenopal. ggl	changes in NRS scores, attack frequency/duration, HIT-6 scores	3
Bendersky (2015)	Sphenopal. ggl	Intensity/frequency of pain attacks	3
Fang (2016)	Sphenopal. ggl	Full text not available. Presumably Intensity/frequency of pain attacks	16
Van Bets (2014)	Sphenopal. ggl	Global per- ceived effect	11

Table 2: Overview of results in our patient group.

N	Years chronic	Attack frequency at baseline (per day unless specified)	Patients' estimate of % change in the three months after the procedure
1	7	8	some effect, less than 50%
2	16	less than 1/week	None
3	33	6	More than 50% reduction in ipsilateral attacks
4	10	1 to 2	More than 50% reduction
5	22	1	None
6	5	3 to 4	More than 50% reduction
7	1	0 to 5	More than 50% reduction
8	15	8	More than 50% reduction
9	2	2 to 3	None
10	7	3	Some effect, less than 50%
11	1	5	None
12	1	7 to 8	None
13	7	2 to 3	None
14	2	6 to 7	More than 50% reduction
15	3	2 to 3	None
16	2	1 to 5	None
17	2	1 to 2	Some effect, less than 50% reduction
18	2	4	None
19	12	4 to 5	None
20	7	3 to 4	More than 50% reduction
21	3	5 to 10	Some effect, less than 50% reduction

Table 3: Summary of the medication changes during the assessment period:

N	**Treatment at baseline, daily doses**	**Treatment at 3 months, daily doses**	**Change in medication**	**Patients' estimate of % change in the three months after procedure**
1	Topiramate 400 mg Verapamil 480 mg	Topiramate 400 mg Verapamil 480 mg	None	Some effect, less than 50%
2	Nothing	Nothing	None	None
3	Lithium 500mg Topiramate 25mg Methylprednisolone 32mg	Gabapentin 1800mg Morphin 30mg	Change	More than 50% reduction in ipsilateral attacks
4	Lithium 600mg Verapamil 720mg Topiramate 300 mg	Lithium 600mg Verapamil 720mg Topiramate 300 mg	None	More than 50% reduction
5	Nothing	Nothing	None	None
6	Verapamil 320 mg	Verapamil 320 mg	None	More than 50% reduction
7	Verapamil 720mg	Verapamil 480 mg	Decrease	More than 50% reduction
8	Topiramate 150mg Lodixal 720mg Melatonin 10 mg Na Valproate 1000mg	Topiramate 150mg, Verapamil 720mg Melatonin 10 mg Na Valproate 2000mg	Increase	More than 50% reduction
9	Topiramate 400 mg Melatonin 10 mg	Topiramate 300 mg Melatonin 10 mg	Decrease	None
10	Gabapentin 1200mg Methylprednisolone 24mg Na Valproate 1000mg	Topiramate Verapamil.	Change	Some effect, less than 50%
11	Morphine 20mg Lithium 400mg	Verapamil 360mg	Change	None
12	Verapamil 320 mg Lithium 600 mg	Verapamil 320 mg Lithium 600 mg	None	None
13	Topiramate 75mg Melatonin 10 mg	Topiramate 75mg Melatonin 10 mg	None	None
14	Lamotrigine 50mg/d	Nothing	Decrease	More than 50% reduction
15	Carbamazepine 400 mg Verapamil 480mg Topiramate 200 mg	Carbamazepine 400 mg Verapamil 960mg.	Change	None
16	Verapamil 160mg Gabapentin 1200mg	Verapamil 160mg Gabapentin 1200mg	None	None
17	Verapamil 960 mg Lithium 800 mg	Verapamil 960 mg Lithium 800 mg	None	Some effect, less than 50% reduction
18	Verapamil 960mg	Verapamil 960mg	None	None
19	Verapamil 960mg Gabapentin 3600mg	Verapamil 960mg Gabapentin 3600mg	None	None
20	Verapamil 800mg	Verapamil 800mg	None	More than 50% reduction
21	Nothing	Nothing	None	Some effect, less than 50% reduction

Figure 1: Radiograph made with the C-arm image intensifier showing a lateral view of the cervical spine with the PRF-needle advancing at the C2 level.

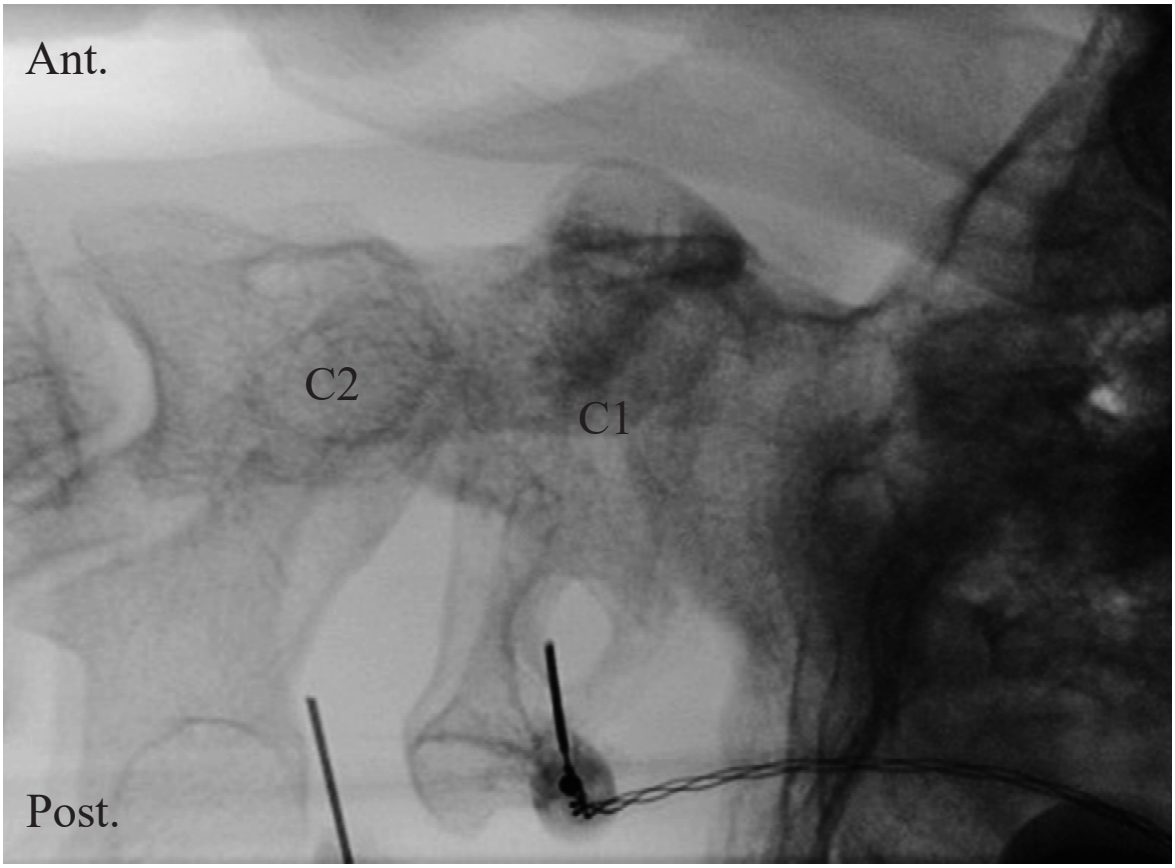


Figure 2: Overview of the vertebral artery at the higher cervical spine. (Adapted from Katoh ea. Spine. 1990 Nov; 15 (11): 1085-7)

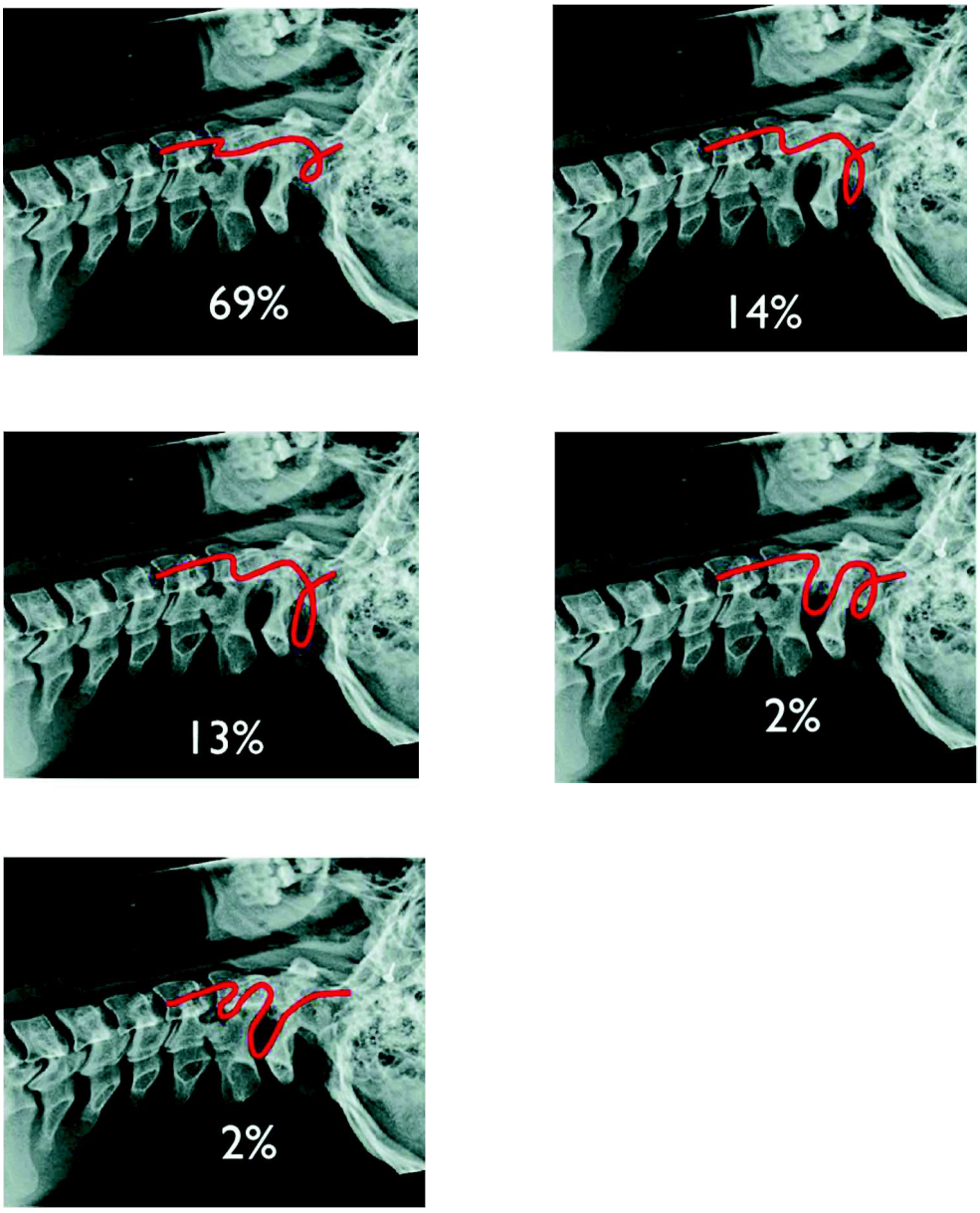
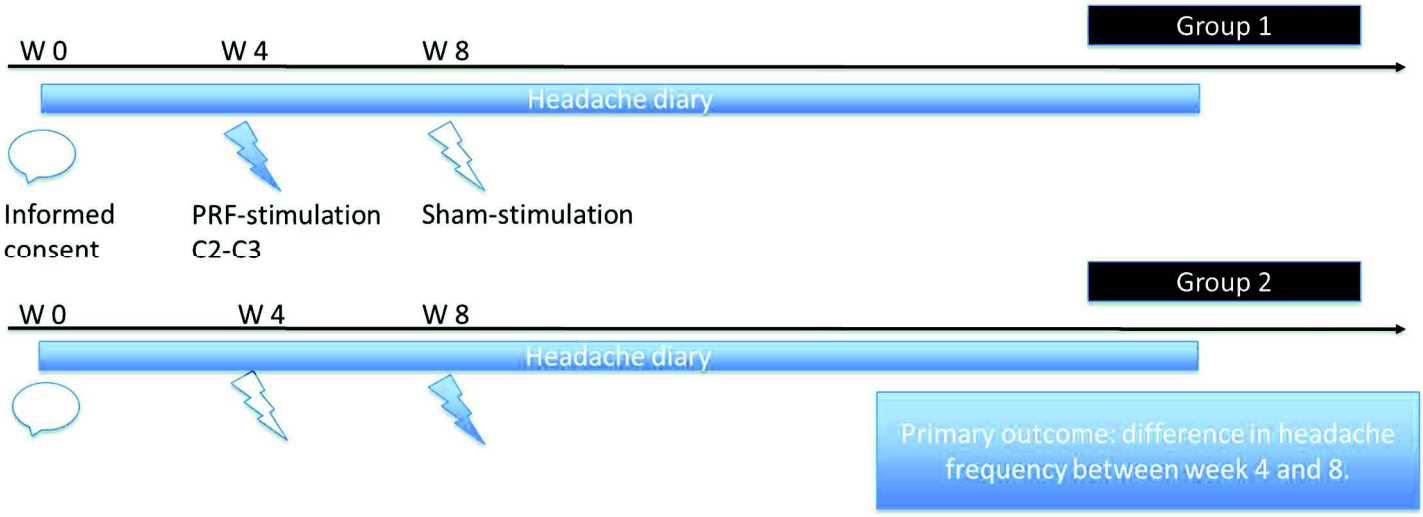


Figure 3: Diagram of a potential future prospective trial:



NEDERLANDSE SAMENVATTING:

Cluster hoofdpijn (CH) is een primaire hoofdpijnaandoening met ernstige hoofdpijnaanvallen met ipsilaterale autonome symptomen. De overgrote meerderheid van de patiënten heeft de episodische vorm van CH met aanvallen die voorkomen in series van weken tot maanden met remissie periodes van maanden tot jaren. Chronische CH patiënten hebben geen dergelijke remissieperiodes. Er bestaan verschillende preventieve behandeling maar een deel van de patiënten is hieraan refractair. Voor deze groep van patiënten werden invasieve en niet invasieve neuromodulatietechnieken ontwikkeld. Sommige van deze technieken zijn gericht naar de afferente input van het bovendeel van het cervicale ruggenmerg.

De theoretische onderbouwing voor het ontwikkelen van neuromodulatietechnieken gericht naar de afferente input van het bovendeel van het cervicale ruggenmerg als een manier om het ziekteverloop van primaire hoofdpijnaandoeningen te proberen beïnvloeden is het trigeminocervicaal complex. In de voorbije dertig jaar ontstond door verschillende proeven met diermodellen het concept van een trigeminocervicaal complex. Dit is een functionele entiteit die een majeur schakelpunt vormt voor convergente nociceptieve afferente input van de supratentoriële meningen (geïnnerveerd door de nervus trigeminus) en cervicale structuren (geïnnerveerd door de nervus occipitalis major). Er wordt gedacht dat trigeminale nociceptieve input kan beïnvloed worden door de afferente input van het cervicale ruggemerg.

Radiofrequentie ablatie is een destructieve techniek die toelaat om welomschreven lesies te maken door het verhitten van zenuwweefsel dat tegen de niet geïsoleerde tip van de elektrode aanligt. Bij radiofrequentie ablatie wordt een continue radiofrequent signal toegediend. Bij een gepulseerde radiofrequentie behandeling (PRF) worden slechts impulsen gegeven en wordt de temperatuur in een niet destructief gebied gehouden. De belangrijkste voordelen hiervan zijn minder pijn tijdens de procedure en een lager risico op motore uitval en deafferentiatie pijn. Bij analyse met elektronenmicroscopie zijn er na PRF ultrastructurele veranderingen te zien zoals een toegenomen aantal vacuolen en vergrote cisternen van het endoplasmatisch reticulum. Het exacte werkingsmechanisme is niet gekend.

Er was eerder reeds enige interesse voor het gebruik van PRF bij CH. Er werden bij deze patiëntengroep enkele gevallenreeksen gepubliceerd van PRF interventies gericht naar het

ganglion pterygopalatine. De grootste reeks betreft 16 patiënten. Er zijn geen studies over PRF interventies gericht naar het ganglion trigeminale bij clusterhoofdpijn. Wel zijn er beperkte retrospectieve data over radiofrequentie ablatie gericht naar deze structuur.

We voerden een audit uit over de veiligheid en de effectiviteit van een percutane gepulseerde radiofrequentie (PRF) behandeling gericht naar het C1 en C2 niveau. Dit is een behandeling die verricht wordt in de pijnkliniek van het UZ Gent bij patiënten met refractaire cluster hoofdpijn.

Er werden 21 patiënten met chronische cluster hoofdpijn met deze techniek behandeld van januari 2010 tot augustus 2017. Er werd een PRF behandeling gedurende 240 seconden met een maximum van 45 V verricht waarbij een maximale temperatuur van 42°C werd bereikt. De behandeling was gericht naar het ganglion en/of de zenuwwortel van C1 en C2. De data werden bekomen door een retrospectieve analyse van het dossier van de patiënt. Hierbij werden demografische gegevens, gegevens over het begin en de duur van de hoofdpijn en de gemiddelde aanvalsfrequentie en voorafgaande medicamenteuze en interventionele behandelingen verzameld. De primaire uitkomstparameters van deze audit waren veiligheid en vermindering van de aanvalsfrequentie in de eerste drie maanden na de eerste PRF-behandeling die een patient onderging (sommige patiënten ondergingen meer dan één behandeling).

Van de 21 patiënten hadden 10 patiënten primair chronische clusterhoofdpijn en 11 patiënten secundair chronisch clusterhoofdpijn. Patiënten waren tussen 25 en 62 jaar oud. Alle patiënten werden reeds met minstens twee profylactische medicamenten behandeld en 19 patiënten werden reeds behandeld met zowel verapamil, lithium als topiramaat. Tien patiënten hadden geen klinisch betekenisvol effect, vier patiënten rapporteerden een klinisch betekenisvolle vermindering van de hoofdpijn met minder dan 50% en zeven patiënten rapporteerden een reductie in hoofdpijn met meer dan 50% in de drie maanden volgend op de behandeling. Twee patiënten rapporteerden het optreden of een toename in frequentie van contralaterale cluster aanvallen. Er werden geen andere bijwerkingen of complicaties gerapporteerd of opgemerkt bij de verder opvolging.

Een PRF-behandeling gericht naar de sensibele input hoog cervicaal lijkt een veilige procedure te zijn die effectief zou kunnen blijken in de behandeling van refractaire chronische

clusterhoofdpijn. Voorzichtigheid blijft echter geboden, zeker gezien de nabijheid van de vertebrale arteriën tot het behandelingstraject. Er is een prospectieve studie nodig om zowel de veiligheid als de effectiviteit verder te bestuderen zodat duidelijk wordt welke plaats deze behandeling kan hebben bij chronisch clusterhoofdpijn. De rationale voor het richten van de behandeling naar C1 is zwak. Theoretisch is dit niveau gevaarlijker dan de andere cervicale niveaus en er is minder ervaring op dit niveau dan met het richten van de behandeling naar C2 (waarvan de radiofrequentiebehandeling ook bestudeerd is in andere indicaties). Een suggestie voor verder onderzoek is het overwegen van de behandeling enkel naar C2 te richten of naar C2 en C3 (gezien de nociceptieve input van C3 ook projecteert naar het trigeminocervicaal complex).

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