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Perspective
Published: 15 Jun, 2017

Radiofrequency Ablation for Treatment of Cervicogenic Headache: Where do we stand?

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Perspective

Cervicogenic headache (CH) is a syndrome characterized by unilateral head pain caused by a disorder of the cervical spine and its component bone, disc, and/or soft tissue elements, usually but not invariably accompanied by the neck pain [1]. It is often a consequence of head or neck injury, but may also occur in the absence of trauma. The prevalence of CH in the general population is between 0.4% and 4.0%. In pain management clinics, however, the prevalence is much greater than - as high as 20% of the patients diagnosed with headaches [2] - and as high as 53% in patients with headache after whiplash injury [3]. The treatment of CH usually requires a multifaceted approach with pharmacologic, physical, manipulative, anesthetic, and surgical interventions [4]. Patients who have not improved with conservative management are considered candidates for interventional pain management, including anesthetic block, intraarticular/medial branch corticosteroid injection, radiofrequency ablation (RFA), and, on occasion, surgical treatment.

Since Sjaastad reported the long term improvement of CH treated with RFA in a more than 4-year follow up [5], evidence has been growing that establish the effectiveness of RFA to treat CH and a technique that is commonly used in chronic pain clinics. However, the evidence is very limited and the results are inconsistent. One recent systematic review reported on a mere 3 randomized clinical trials (RCTs) and 4 non-RCTs investigating RFA [6]. Among the RFA studies are one high quality RCT with an inadequate number of patients [7] and three moderate quality non-RCTs with positive results, but also one RCT and one low quality non-RCT with limited patients with negative evidence [8,9]. Why the conflicting results and can current data guide us in the application of RFA for CH?

One explanation for the inconsistency lies in the nature of CH itself. Even after the Cervicogenic Headache International Study Group (CHISG) updated the diagnostic criteria for CH in 2013, the diagnosis of CH continued to be complicated and another category of headache related to cervical spine structures [10]. Furthermore, there are many potential sources of pain in the neck and these might respond differently to attempted RFA treatments. The C2-C3 z-joint is innervated by the third occipital nerve (TON) and is the most common cause, accounting for 70% of CH, followed by the atlantoaxial (A-A) joint which is the second most common source for CH [11]. This joint and the TON appear most vulnerable to trauma from whiplash of the neck. The other sources of CH include the C2-C3 intervertebral disc, the atlanto-occipital (A-O) joint, and the C3-C4 *Zygapophyseal* -joint [3]. Lower cervical disc prolapse also can cause CH [12]; Michler described one chronic CH patient who experienced long-term improvement after decompression of the left C7 root [13]. So the ablations were performed at different levels and different sites. Common structures include the A-O joint, A-A joint, C2-C3 and C3-C4 z-joints, and the C2-C3 intervertebral disk. In one RCT, Stovner performed RFA of C2-6 on 6 patients selected on the basis of clinical features as opposed to response to diagnostic nerve blocks. They failed to see the benefits from RFA compared with the sham [14]. The results of the observational study by Cohen et al. [15] suggest the factors associated with treatment failure include radiation to the head, opioid use, and pain exacerbated by neck extension and/or rotation. They concluded that selecting patients based on key clinical variables may increase the chance of treatment success for cervical facet RF.

Another concern is the quality of current RCTs. Some RCTs were criticized with blinding and the control group design. Lord proved that RFA of CZJ can provide lasting relief in chronic CH patients in the only reported randomized double-blinded trial to prove the effects of RF on CH [7]. Carragee et al. [16] questioned the blinding methodology, as around half of the treatment group developed long-term anesthetic or dysesthetic areas of skin and none of the patients in the control group developed changes. The small number of patients included in this study is another issue.

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Received Date: *29 Apr 2017*
Accepted Date: *10 Jun 2017*
Published Date: *15 Jun 2017*

Citation:
Sun Z, Martin DC, Dua A. Radiofrequency Ablation for Treatment of Cervicogenic Headache: Where do we stand?. Remed Open Access. 2017; 2: 1069.

Lack of control group in active control trials is a major limitation. However, the control group also varied among studies. In two studies, the control group was designed with the needle placement only [7,14]. In other studies, the control group was designed with injection of anesthetics or steroid on the affected side [8,17]. It is well known that the use of a placebo control in any neural intervention is a difficult task, which adds ethical issues and difficulty with recruitment. The effect of any solution injected into a closed space, such as intra-articular space, epidural space or over a nerve has not been appropriately evaluated. It has been shown that a small volume of local anesthetic or normal saline abolishes muscle twitch induced by a low current (0.5 mA) during electrode location [18,19]. Further, there is direct evidence of spinal cord involvement in placebo analgesia [20]. Epidurally administered normal saline also can provide significant improvement in pain relief and in function [21]. The issues related to placebo have been discussed extensively in recent years, ultimately leading to the opinion that the placebo effect is an inconsistent measure in clinical studies unless it is designed appropriately [22-24].

The majority of radiofrequency neurotomy (RFN) studies were of an observational nature and provided evidence that cervical RF can be very effective when performed in a rigorous manner in appropriately selected patients [25,26]. RFN of CZJ has been shown to significantly reduce CH severity [27,28] and RFN of TON greatly improved CH which with other treatments has had a low success rate [29,30]. However, Hapspeslagh failed to find a difference between RFN and local anesthetic injection of GON in RCT study [17]. The lack of placebo in active control trials is a major limitation. A definitive conclusion about the clinical efficacy of this treatment can only be drawn from a randomized trial and all agree that further prospective trials are required to validate in their conclusion.

The complications from intra-articular injections or radiofrequency ablation in the cervical spine are exceedingly rare in studies [31-33]. Complications of radiofrequency include a worsening of the usual pain, burning or dysesthesias, decreased sensation and allodynia in the skin in the region of the facets denervated, transient leg pain, persistent leg weakness, and inadvertent lesioning of the spinal nerve or ventral ramus, resulting in motor deficits and sensory loss [34]. Although patients with C1-2 joint pain were excluded in some studies because of the technical difficulty of the procedure, in the Halim study of 86 patients, lateral C1-2 joint pulsed RFA for CH was generally safe, except for 1 patient who complained of a worsening occipital headache lasting several hours [9].

In summary, the complex nature of CH, inconsistency among RCTs, and design flaws of both RCTs and non-RCTs resulted in limited evidence for RFA therapy for CH. No meta-analysis was done because of an inadequate number of homogenous studies. Therefore, high quality RCTs and/or consistent non-RCTs without methodological flaws to evaluate the efficacy of RFA treatment on CH are needed.

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