OTHER PAIN (A KAYE AND N VADIVELU, SECTION EDITORS)



Systematic Review of Radiofrequency Ablation and Pulsed Radiofrequency for Management of Cervicogenic Headaches

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Abstract

Purpose of Review Cervicogenic headache (CHA) is a secondary headache which has a source in the upper cervical spine. Many traditional analgesic choices lack good efficacy in managing the associated pain. As a result, in management of CHA, radiofrequency ablation (RFA) or pulse radiofrequency (PRF) has been tried with success. Our study investigated the use of RFA and PRF for the management of CHA.

Recent Findings In the present investigation, a review of the literature was conducted using PubMed (1966 to February 2017). The quality assessment was determined using The Cochrane Risk of Bias. After initial search and consultation with experts, 34 articles were identified for initial review and 10 articles met inclusion for review. Criteria for inclusion were primarily based on identification of articles discussing cervicogenic headaches which were previously treatment resistant and occurred without any other pathology of the craniofacial region or inciting event such as trauma.

Summary This systematic review demonstrated that RFA and PRFA provide very limited benefit in the management of CHA. At present, there is no high-quality RCT and/or strong non-RCTs to support the use of these techniques, despite numerous case reports which have demonstrated benefit. This review is one of the first to provide a comprehensive overview of the use of RFA and PRF in the management of CHA.

Keywords Chronic pain · Cervicogenic headache · Radiofrequency ablation · Pulsed radiofrequency ablation

Introduction

Headaches are often classified as primary or secondary. Secondary headaches are headaches caused by pathology that is often non-intracranial in etiology. One type of secondary headache is related to cervical pathology leading to radicular pain. This cervical pathology is associated with muscular, neurogenic, osseous, articular, and vascular structures of the neck [1]. This pathological process is often described as a

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cervicogenic headache (CHA). CHA affects an estimated 4.1% of the population, with a slight male preponderance [2]. The frequency might be as high as 20% in patients with chronic headaches [3]. The mean age of onset is 43 years of age [4•]. These headaches can be extremely difficult to diagnose and to treat not only because of significant overlap between migraines and CHA, but also lack of an easily applicable test or criteria for the diagnosis of CHA [5]. Symptoms such as nausea, vomiting, and throbbing can be present [5]. However, often with CHA, there is a mechanical etiology associated, but it is not required to be present for diagnosis [2]. The Cervicogenic Headache International Study Group (CHISG) Diagnostic Criteria for CHA include the following: (a) unilateral pain (although bilateral CHA may occur); (b) restriction of range of motion of the neck; (c) provocation of head pain by neck movement; (d) provocation of head pain with external pressure over the upper cervical or occipital region on the symptomatic side; (e) vague ipsilateral nonradicular nature neck, shoulder, or arm pain, occasional radicular; (f) confirmatory local anesthetic blocks in the cervical region; (g) marginal response to ergotamines, triptans, or

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indomethacin; and (h) posterior onset of headache pain [2, 6]. This definition has continued to evolve over the past two decades.

The most common source of pain is degenerative changes involving the upper cervical spine [7]. While magnetic resonance imaging (MRI) and computed tomography (CT) myelography can help support the diagnosis, these imaging studies are often more useful in ruling out secondary causes [5]. History and physical are the most useful to diagnose this condition and rule out other systemic illnesses [1]. Diagnostic and therapeutic facet blocks using fluoroscopic guidance are confirmatory to diagnosis and possibly predict responses to treatment [5]. Zygapophyseal joint, cervical nerve, and medial branch blockade (MBB) are utilized to confirm the diagnosis and predict treatment modality efficacy [1].

Because of the complex etiology of the pain, a multidisciplinary approach is required. Pharmacologic treatments include medications which are often used for neuropathic pain, including tricyclic antidepressants, anticonvulsants, or other analgesics. Further, physical therapy may provide long-term improvement. If these techniques are not effective, then radiofrequency ablation (RFA) or pulsed radiofrequency (PRF) can be considered in lieu of surgical management [8]. Many case studies and case series have reported RFA or PRF improving cervicogenic headaches. The purpose of this investigation, therefore, is to evaluate whether this benefit can be seen within a larger study population.

Anatomy

The anatomic basis for CHA lies in the relationship between the afferents of the upper three cervical nerves (C1-C3) and the afferents of the trigeminal nerve [7]. The pars caudalis of the trigeminal nucleus is continuous longitudinally with the outer laminae of the dorsal horns of the upper three to four segments of the cervical spinal cord [9]. This column of gray matter makes up the entirety of the trigeminal cervical nucleus [10]. This structure receives second-order neurons from the upper three cervical nerves and the trigeminal nerve [11]. This convergence is theorized to allow for bidirectional referral of painful sensations between the neck and trigeminal sensory receptive fields of the face and head [12]. Other possible sources might be dorsal roots from C1 to C7, the intervertebral discs down to C7, the zygapophyseal joint from C2-3 and C6–7, and especially the greater and lesser occipital nerve (GON and LON) and the third occipital nerve (TON) [13]. Because of the multiple structures involved in the pathology, diagnostic blockades can be directed at several of the above anatomic structures [14].

Occipital neuralgia, which is pain in the lesser or greater occipital nerves, is often associated with CHA [1]. It is often described as a constant deep or burning pain with superimposed paroxysms of shooting or shock-like pain. Paresthesias and numbness can be present over the occipital scalp. The cause of occipital neuralgia can be multiple, including trauma to or entrapment of the occipital nerve, but also pain within the cervical spine or posterior cranial fossa [1]. In some cases, the pain and symptomology of CHA are worsened related to the presence of occipital neuralgia.

Management

Management of CHA is often multimodal using pharmacologic, non-pharmacologic, and occasionally surgical techniques.

Medical Management

Medical management is often the first-line therapy when patients present with CHA. First-line treatment often involves non-steroidal anti-inflammatory drugs (NSAIDs). Combining NSAIDs with other muscle relaxants with central activity, such as tizanidine and baclofen, often provides increased analgesic efficacy [1]. Opioid-like medications have only a marginal effect and are not recommended for CHA patients related to concern of addiction [15]. Tricyclic antidepressants (TCAs) can also be utilized for management of various neuropathic, musculoskeletal, and head/facial pain syndromes [1]. Further, often times if the above treatments are ineffective, antiepileptic drugs (AEDs) can provide relief in this population. AEDs include divalproex sodium, gabapentinoid preparations, topiramate, and/or carbamazepine. None of these medications have more proven efficacy than the others. However, oxygen or ergotamine is not effective [15].

Further, the combination of multiple medications from different drug classes with or without complimentary mechanisms of action may provide greater efficacy than using individual drugs alone [1].

Therapy

Physical therapy can be important in strengthening the muscles of the upper back and providing rehabilitation for patients to regain lost function. However, there is no proven impact of physical therapy [15-17]. Often times, the headache might initially worse during or after physical therapy, especially if it is aggressive [1].

Physical therapy is often better tolerated when initiated with muscle stretching and manual cervical traction [1]. Sometimes, physical therapy has increasing efficacy if combined with medications or anesthetic blocks [1].

Transcutaneous electrical nerve stimulation (TENS) is often also tried in this population, which functions via the gate control theory; however, it is not particularly effective [15]. The frequency and amplitude can be adjusted continuously to stimulate different pain fibers [15]. Psychotherapy, which includes biofeedback, relaxation, and cognitive behavioral therapy, has also been tried with limited success.

Psychotherapy is often used in conjunction with other therapies to help modify behaviors [1].

Interventional Management

Interventional pain management procedures can be therapeutic or diagnostic. There are several different anesthetic blockades or neurolysis, including as follows: anesthetic blocks to the medial branch of the dorsal ramus (diagnostic), intraarticular z-joint corticosteroid injections (diagnostic), and medial branch of the dorsal ramus area corticosteroid injections (therapeutic). Outside of these specialized interventional pain procedures, cervical epidural steroid injections can also be utilized if there is multilevel disease present. Even trigger point injections can be attempted, and these can help relax the musculature to provide temporary relief or provide an opportunity for physical therapy [1]. There are risks associated with these interventional procedures including as follows: infection, radiation exposure, side effects of corticosteroids, and structural damage from the spinal needle placement. Some of the risk of injury is minimized by use of fluoroscopy guidance [18].

Another treatment includes botulinum toxin injections. Botulinum toxin has some potential; however, more studies are needed to confirm efficacy [19, 20]. Botulinum toxin can be injected into pericranial and cervical muscles. Surgery can also be attempted; however, it is not recommended unless significant surgically correctable pathology is present. Even in the setting of surgical correctable pathology, it is often considered a last resort because of potential complications and ineffectiveness. One of the major complications is anesthesia dolorosa, which is when pain becomes more intensified after the procedure [1]. Some operations utilized include the following: ganglionectomy, surgical liberation of the occipital nerve from entrapment, surgical transection of GON, ventral decompressive operation and fusion, and dorsal decompressive laminectomy and laminoplasty [15, 18]. Some of these procedures can be temporary, which can make the risks outweigh potential benefits [21].

Because of fewer side effects, RFA and PRF are commonly utilized to manage the chronic debilitating pain associated with CHA. In the present investigation, therefore, a literature review was undertaken to ascertain whether RFA and PRF are efficacious in CHA.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed when conducting and reporting this review and meta-analysis.

Literature Search

A review of the current literature was performed with a systematic literature search performed in the PubMed (1966 to February 2017). The search terms "headache," "cervicogenic," "pulsed radiofrequency," "radiofrequency neurotomy," and "radiofrequency ablation" were combined in different ways to search through this database. Once duplicates were removed, this yielded 66 abstracts for review. The full text of the article was obtained if the title or abstract discussed PRF or RFA for management of cervicogenic headaches. Articles not in English were not included. Articles that included individual patients or case series were included for completeness. Further, if there was any other pathology of the craniofacial region, the article was excluded. This included brain masses, trigeminal neuralgia, previous cranial surgeries, trauma or motor vehicle accidents, or other. A total of 34 articles were obtained and read in their entirety, of which 24 were excluded. Other review articles were reviewed, but excluded because the focus of this analysis was on identifying primary studies to evaluate efficacy. In addition to the electronic search, experts in the field were also contacted for further article suggestions. If articles were missing or if the author team knew of pertinent literature that did not include specific details for inclusion in the review, the corresponding authors were contacted for the relevant information. References from all the included articles were reviewed to ensure that all the articles that met inclusion criteria were included. Ten articles were included in the final analysis (Fig. 1).

Assessment of Study Quality

The Cochrane Risk of Bias was used to measure the methodological quality of the included studies. The Cochrane Risk of Bias System has a list of seven items, which assess the internal validity of the study and are scored by allocating a +, -, or ? to each criterion that is met. The more + signs the lower the risk of bias. Each study was independently assessed (Table 1). Two authors reviewed the studies and discrepancies were settled via discussion.

Data Extraction

The ten included articles were reviewed completely, and the primary etiological theories were extracted to be included in the summary tables. Eight additional articles were also included, which were case reports to provide a more comprehensive analysis. Fig. 1 Literature search methodology. Reviews, metaanalyses, editorials, opinion pieces, and articles that exclusively discussed cervicogenic headache and radiofrequency ablation or pulsed radiofrequency; cervicogenic headaches due to trauma or pathologic brain masses, non-English language articles, and articles that were not available as completely were excluded



10 studies included

articles published previously [18, 40]. Despite these conclusions applying to the overall population, there are subsets of

In this systematic analysis, there were three RCTs, three pro-

spective trials, and four retrospective trials that were evaluated

for the impact of RFA or PRF for CHA. Stovner et al. [24] and

Haspeslaugh et al. [25] demonstrated no benefit. Stovner et al.

the population that have benefited from this treatment.

Results

Summaries of included studies are listed in Table 2 and case reports are summarized in Table 3. The results of the present investigation demonstrate that evidence for RFA is limited and incomplete. Numerous case reports and case series have indicated benefits for RFA. However, only one clinical trial has demonstrated evidence that PRF is effective in managing CHA [28•]. Most of the studies identified do not indicate any benefit or significant complications associated with the procedure. These conclusions are in line with other review

 Table 1
 Cochrane Risk of Bias

 assessment
 Image: Compare Risk of Bias

Article Other Sum van Suijlekom et al. 1998 [22] Govind et al. 2003 [23] Stovner et al. 2004 [24] ? Haspeslaugh et al. 2006 [25] Lee et al. 2007 [26] Halim et al. 2010 [27•] Gabrhelik et al. 2011 [28•] Park et al. 2011 [29•] Chua et al. 2012 [30] Hamer and Parth 2014 [31•]

Discussion

1. Random sequence generation (selection bias)

2. Allocation concealment (selection bias)

3. Blinding of participants and personnel (performance bias)

4. Blinding of outcome assessment (detection bias)

5. No incomplete outcome data (attrition bias)

6. No selective reporting (reporting bias)

7. No other bias

Article	Type of study	Participants	Intervention	Result	Conclusion	Comments
van Suijlekom et al. 1998 [22]	Prospective	15 patients with CHA were treated with follow-up for more than 1 year.	RFN of CZJ	RFN of CZJ significantly reduced headache severity in 80% of patients. Mean VAS decrease was 31.4 at short-term follow-up and 53.5 at long-term follow-up. The average number of headache days per week decreased by 3.	Significant benefit with RZN of CZJ.	
Govind et al. 2003 [23]	Prospective	49 patients suffered from third occipital nerve headaches	RF neurotomy for third occipital headache.	88% achieved successful outcome. Median duration of relief was roughly 300 days.	RF neurotomy shows profound relief of the headache despite having a limitation to its duration.	14 patients underwent repeat neurotomy, with12 of them achieving successful pain control.
Stovner et al. 2004 [24]	Randomized, double-blind trial	12 patients with a disabling, long-standing, and treatment-resistant unilateral CHA randomized to RFN of facet joints C2-C6 v. sham treatment.	RFN of medial branch on facet joints C2–6 on the symptomatic side.	Patients treated with RFN were slightly improved at 3 months, but at a later time, there was no significant difference.	No benefit with the procedure.	Majority of side effects were minor and short lasting.
Haspeslagh et al. 2006 [25]	Randomized, controlled	30 patients with CHA who were randomized to RFN lesion of the medial branches of the posterior primary rami of the C3–C4 facet joints v. injection with local anesthetic of the GON on the affected side.	RFN of the cervical facet joint denervation v. local injections with steroid and anesthetic at GON, followed by TENS when necessary.	No statistically significant differences noted in pain scores.	No evidence that RFN of the cervical facet joints is a better treatment than infiltration of the GON, followed by TENS.	
Lee et al. 2007 [26]	Prospective observational	30 patients suffering from chronic CHA for longer than 6 months	RFN of CZJ	RFN of CZJ significantly reduced the headache severity in roughly 75% of patients at 12 months. Majority of patients had greater than 75% pain relief. Reduced analgesic intake by 70%.	RFN of the CZJ has shown to provide substantial pain relief in patients with chronic CHA.	Patients showed pain relief by greater than 50% from diagnostic and procedural blocks.
Halim et al. 2010 [27•]	Retrospective study	86 patients who underwent later C1–2 joint PRF application for CHA.	C1–2 PRF application was performed using the intra-articular anterolateral approach.	Roughly 50% of patients had > 50% pain relief at 2 and 6 months, and 1 year.	PRF application of the lateral C1–C2 joints is feasible in patients with CHA that is non-responsive to other techniques.	One patient complaint of increased severity of occipital headache lasting several hours.
Gabrhelik et al. 2011 [28•]	Blind, randomized clinical	30 patients with refractory CHA who were randomized into two groups GON block with steroid v. PRF.	GON block with steroid v. PRF.	At 3 months, significant decrease in VAS was identified in both groups. However, at 9 months, there was greater pain control in the PRF group.	PRF provides greater long-term pain control.	No complications. No serious complications.
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Table 2 (continue	ed)					
Article	Type of study	Participants	Intervention	Result	Conclusion	Comments
Park et al. 2011 [29•]	Retrospective observational	 Patients with CHA were treated with follow-up for 6 months. 	RFN of lower cervical (C4–7) medial branches.	VAS score at 6 months decreased by about 60% at 6 months.	Lower cervical disorders can lead to headaches, which can be improved with RFN.	
Chua et al. 2012 [30]	Retrospective observational	45 patients with CHA underwent PRFA with follow-up for more than 1 year.	Anteroaxial Joint PRF.	Lower pain scores at 2, 6, and 12 months of follow-up compared to non-responders. Also reported marked	Anteroaxial Joint PRF improves CHA in patients affected by whiplash.	
Hamer and Parth 2014 [31•]	Retrospective observational	40 patients with refractory CHA and or occipital neuralgia.	RFN of C2 DRG and/or third occipital nerves.	improvements in headache impact and quality of life. 35% of patients reported completed pain relief and 70% reported 80% or greater pain relief.	RFN of the C2 DRG and/or third occipital nerve can provide > 50% of pain relief in the majority of recipients.	

[24] evaluated RFA of facet joints C2–C6 ipsilateral to the pain in comparison to sham treatment. Patients were followed up for 2 years. Only at 3 months was there a benefit for the use of RFA [24]. Despite the lack of benefit, the side effects were also quite minimal. The study attempted to recruit 24 patients, however, only recruited 12, which reduced the overall power of the study [24]. Further, the study did not follow the current criteria for defining CHA, which includes response to diagnostic blocks. Finally, only one patient in the RFA and sham groups had C2–C3 originated pain, while the others had pain generating from lower than the C2 levels [24].

Haspeslaugh et al. [25] evaluated 15 patients with RFA of cervical facet joints and dorsal root ganglion with patients who had local anesthetic block of the greater occipital nerve (GON). There was no statistically significant evidence supporting the use of RFA in patients with CHA. This was despite the criteria for enrollment being quite stringent. Before starting randomized control trial, a similar author team [22] demonstrated in a group of about 15 patients prospectively evaluated that CHA has a positive impact.

Three other prospective non-randomized studies were evaluated. As mentioned above, van Suijlekom et al. [22] evaluated efficacy of RFA of the cervical z-joint in CHA. Patients were evaluated prior to, short term (8 weeks), intermediate term (roughly 8 months), and long term (roughly 17 months). In roughly 80% of patients assessed via the Verbal Rating Scale (VRS), there was a decrease in mean Visual Analog Scale (VAS) of 31.4 and 53.5 mm at short- and long-term follow-up, respectively [22]. The average number of headache days went down by roughly half, and the number of analgesic pills taken went down by 75% [22]. This study revealed positive impact in using RFA for CHA. Despite translating the methods and techniques, a very different conclusion was reached by the same author team in a RCT.

Govind et al. [23] evaluated the role of RFA of the third occipital nerve for the treatment of referred pain from C2–C3 zygapophyseal joints. Successful pain relief was defined as patients being pain free for 90 days associated with restoration of normal activities and no use of drug treatment for the headache. Eighty-eight percent of patients of the 49 patients enrolled in the study achieved a successful outcome [23]. The pain-free interval lasted on average 297 days, with eight patients experiencing continued pain relief [23]. Fourteen patients underwent repeat procedures to experience continued pain relief and 86% of those patients experienced pain relief for 217 days, and six patients had continued pain relief [23]. This study suggests that the ablation has a set duration of efficacy, but repeated ablation can prolong the efficacy as well.

Lee et al. [26] evaluated 30 patients suffering from chronic CHA for longer than 6 months, who demonstrated pain relief of greater than 50% after receiving a C3–C4 cervical median branch block. These patients were treated with RFA of the

Table 3	Case studies	highlighting	impacting	of RFA or PRF
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Case reports	Patients	Conclusion
Sjaastad et al. 1995 [32]	7	RFA of the planum nuchale can treat CHA.
Van Zundert et al. 2003 [33]	18	> 50% pain relief was achieved in > 70% of patients at 8 weeks. However, only 33% of patients had pain relief at 1 year.
Zhang et al. 2011 [34]	2	PRF is effective in the treatment of CHA originating from the C2 nerve.
Bovaira et al. 2013 [35]	3	RF is effective in management of CHA. However, it is often transient.
Kim et al. 2013 [36]	2	PRF is effective in patients with occipital headache and posterior neck pain.
Giblin et al. 2014 [37]	1	RFA can be used to manage CHA+ Right third occipital nerve headache symptoms.
Gorelov et al. 2016 [38]	1	RFA can be used to manage CHA.
Odonkor et al. 2017 [39]	1	RFA showed effective pain management in a patient at 2, 4, 8, and 12 weeks with maximum efficacy at 12 weeks.

cervical z-joints and were assessed at 1 week and 1, 6, and 12 months [26]. The study found that RFA of the cervical z-joints reduced the headache severity in 73% [22] patients at 12 months [26]. The average headache-days per week decreased from 6.2 days a week to 2.8 days a week [26]. The analgesic intake reduced by 70% [26]. There were no major complications; however, four patients experienced ataxia in the immediate aftermath of the procedure [26]. There was no randomization or control group associated with this study. Further, the criteria for inclusion were very specific.

Hamer and Purath [31•] retrospectively evaluated 40 patients with refractory CHA and/or occipital neuralgia. Patients were followed for 6 months to a year with the majority receiving a bilateral C2 ganglion RFA. Thirty-five percent of patients reported 100% pain relief, while about 70% reported greater than or equal to 80% pain relief [31•]. The duration of pain relief was on average 22.35 weeks [31•]. Ninety-two percent of patients reported satisfaction with the procedure and would undergo the procedure again if necessary [31.]. Of note, the symptoms of the patients included in this study were more diverse than those in other studies, since some patients had migraine headaches and others had experienced whiplash. Twelve to 13% of patients experienced complications, which were predominantly hyperesthesia along the greater and lesser occipital nerves [31•]. In a follow-up study of 23 patients, the authors evaluated patients who needed a repeat RFA. 86.5% of patients reported pain relief which lasted on average 25.4 weeks [41•]. However, a greater percentage (roughly 41%) reported side effects including hyperesthesia and/or discomfort [41•]. Most of these side effects were mild. Despite this significant population, 95% reported willingness to have the procedure again if necessary [41•]. The one patient who did not want a repeat procedure had headaches associated with post-traumatic stress disorder [41•]. Fifty-nine percent of patients reported that the repeat RFA had the same effect as the first one, and about 32% reported the repeat RFA was the most effective [41•].

Among the PRF studies for CHA, Gabrhelik et al. [28•] performed a pilot study evaluating 15 patients who underwent a blockade of the GON, with administration of local anesthetics and corticosteroids, while another 15 patients had a PRF to the GON. In this randomized control trial, both groups had a decline of roughly 50% in the VAS scores at the 3-month mark [28•]. However at 9 months, the beneficial effect of the PRF seemed to reduce [28•]. This trend was accompanied by changes in the patient satisfaction score [28•]. These changes were also accompanied by a significant decline in analgesic medication consumption, with a greater decline in the PRF group [28•].

In a retrospective study of 86 patients, Halim et al. [27•] evaluated patients who underwent a lateral C1–C2 joint PRF for CHA. On average, the pain was present for about 9.5 years prior to the procedure, and the baseline pain score was 8.5 [27•]. The percentage of patients who had 50% pain relief at 2 and 8 months and 1 year were 50, 50, and 44.2%, respectively [27•]. Long-term pain relief at 6 months and 1 year was predicted by pain relief at 2 months [27•]. Minimal complications or side effects were seen in the participants. Only one patient reported worsening occipital neuralgia [27•]. Some of the limitations of this study included the retrospective nature and short follow-up period.

There are limitations to this systematic review. There were differences in the structure and inclusion criteria associated with the RCTs, leading to differences in outcomes. In addition, several procedures utilized slightly different techniques or distributions of ablation, which may place another variable in developing an overarching conclusion. Further, most studies included in this analysis were not RCTs. There were very few side effects in the included studies. However, the studies did not utilize extended follow-up periods in all the studies. Clearly defined inclusion and exclusion criteria may help clarify outcomes and develop more consensus for the use of RFA or PRF.

Conclusion

At present, there are numerous case reports and a few older retrospective studies that have suggested efficacy of RFA and PRF in the treatment of CHA. Some studies indicate benefit of RFA or PRF for a short duration of time. Few clinical trials were conducted in reviewing the literature, and therefore, there is a need for more RCTs to confirm the efficacy of RFA and PRF in the treatment of CHA.

Compliance with Ethical Standards

Conflict of Interest Ravi K. Grandhi and Alaa Abd-Elsayed declare that they have no conflict of interest. Alan D. Kaye is a speaker for Depomed, Inc. and Merck, Inc.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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