Observational Trial

Effectiveness of Intermediate Cervical Plexus Block in Whiplash-Associated Disorder: A Prospective Observational Trial in Fifty Patients

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Background: Whiplash trauma can result in a range of symptoms, including chronic neck pain, headache, facial pain, upper back pain, and tinnitus, which comprises whiplash-associated disorder (WAD). Intermediate cervical plexus block (iCPB) is a novel intervention that targets the upper cervical nerves and anecdotal reports suggest benefits in WAD.

Objectives: We hypothesized that the cervical plexus may have a role in the pathogenesis of WAD and blocking the cervical plexus may provide analgesia.

Study Design: Prospective observational trial.

Setting: Tertiary pain medicine unit at a university teaching hospital.

Methods: Adult patients who presented with refractory chronic neck pain following whiplash were included in a prospective observational trial. The pragmatic trial studied the effectiveness of 2 sequential cervical plexus blocks (iCPB with local anesthetic [iCPB-LA] and iCPB with steroid and LA mixture [iCPB-Steroid]) in refractory chronic neck pain following whiplash. Patients who reported < 50% relief at 12 weeks after iCPB-LA were offered iCPB-Steroid. Primary outcome was "neck pain at its worst in the last 24 hours" at 12 weeks. Secondary outcomes included change in neck disability index, employment status, and mood.

Results: After excluding cervical zygapophyseal joint dysfunction, 50 patients underwent the iCPB-LA between June 2020 and August 2022. Five patients reported > 50% relief (durable relief) at 12 weeks and 3 patients were lost to follow-up. Forty-two patients received iCPB-Steroid. iCPB-Steroid was associated with significant reduction in neck pain, neck disability, and improvement in mood at 12 weeks when compared to the block with LA. In addition, iCPB-Steroid was associated with significant reduction in neck pain and disability at 24 weeks. Due to functional improvement, 34 patients (34/50, 78%) were able to maintain employment.

Limitations: This is an open-label, observational, single-center study in a limited cohort under a single physician. Cervical facet joint dysfunction was ruled out clinically and radiologically.

Conclusions: Cervical plexus may play a central role in the pathogenesis of WAD. iCPB could potentially be a treatment option in this cohort.

Key words: Intermediate cervical plexus block, whiplash, trigemino-cervical complex, whiplash-associated disorder, neck pain, chronic headache

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Whiplash-associated disorder (WAD) describes a constellation of symptoms that follows flexion-hyperextension trauma to the neck (1). Neck pain is the commonest presentation and can be associated with headache, periauricular pain, jaw pain, tinnitus, upper back pain, and dizziness (2,3). In a large proportion of patients, these symptoms can persist beyond 3 months causing significant dysfunction (4). In a subset of patients, the underlying pathology has been identified as cervical zygapophyseal joint dysfunction with a well-evidenced treatment, namely, cervical medial branch radiofrequency neurotomy (5,6). However, the underlying pathology remains obscure in many patients with chronic neck pain. Recent evidence (7,8) suggests cervicothoracic muscle dysfunction, which arises from forceful stretch loading of neck muscles during whiplash. The cervical plexus, formed by the upper cervical nerves, have close anatomical relation to the cervicothoracic musculature (9). This plexus is a major part of the trigemino-cervical complex, which has been implicated in the pathogenesis of WAD (10,11). Standard management strategies in chronic neck pain from whiplash include exercise, physiotherapy, acupuncture, pharmacological agents, and trigger point injections (12). Limited treatment options are available in patients who fail to respond. Anecdotal reports (11,13,14) suggest the benefit of intermediate cervical plexus block with steroid (iCPB-Steroid) in treating chronic neck pain, headache, and orofacial pain after whiplash. The objective of this prospective observational trial was to evaluate the effectiveness of 2 sequential interventions (iCPB with local anesthetic [iCPB-LA] and iCPB-Steroid) in the management of patients with refractory chronic neck pain after whiplash.

Methods

After obtaining approval from the research ethics committee (REC, 20/EM/0075) and written informed consent from the patients, we included adult patients who presented with WAD to a tertiary pain medicine unit in a prospective observational trial. The trial period was between June 2020 and August 2022.

Inclusion Criteria of Refractory Chronic Neck Pain:

1. Chronic neck pain and history of whiplash preceding onset of pain.
2. Neck pain for at least 6 months.
3. Failed response to anti-inflammatory, weak opioids, and amitriptyline.
4. Failed trial of physiotherapy, acupuncture, and/or trigger point injections.

Exclusion Criteria:

1. Patients with a history of neck pain preceding whiplash injury.
2. Patients with signs and symptoms suggestive of cervical zygapophyseal joint dysfunction.
3. Patients with cervical radicular symptoms.

Cervical zygapophyseal joint dysfunction (i.e., limitation of extension at cervical spine, pain on cervical zygapophyseal joint loading maneuvers, and magnetic resonance imaging of cervical spine, if indicated) was excluded in the pain clinic (15).

Figure 1 shows the study flow chart. Patients first received iCPB-LA agent.

Block 1: iCPB-LA (13).

The block was performed under local anesthesia in the outpatient suite. The skin over the sternocleidomastoid (SCM) muscle was prepared with 2% chlorhexidine solution. A high-frequency (5-10 MHz) ultrasound probe (S-NerveTM; SonoSite Inc., Bothell, WA) was placed across the SCM muscle. The muscle, the underlying vascular structures, and the posterior cervical space (PCS) (i.e., fascial plane between the posterior sheath of the muscle and the prevertebral fascia) were visualized (Fig. 2). Thereafter, a 23-G 50-mm hypodermic needle was inserted in the plane of the ultrasound beam to enter the PCS and 9 mL of 1% lidocaine (90 mg) was injected after negative aspiration. The procedure was repeated on the contralateral side in patients with bilateral symptoms.

The patients completed the Brief Pain Inventory-Short Form (BPI-SF), Neck Disability Index (NDI), and Hospital Anxiety and Depression Scale questionnaires at baseline prior to iCPB-LA and at 12 weeks postprocedure. Patients were reviewed in the pain medicine clinic at 12 weeks.

1. If patients reported 50% improvement at the 12-week review, they were added to the waiting list to receive the iCPB-LA in 7-9 months.
2. If patients reported minimal or no benefit with neck pain returning to the baseline at the 12-week review, they received iCPB-Steroid.
3. If the patient reported clinically significant relief (30% or 2 Numeric Rating Scale points) at 12 weeks, they were given the option to receive iCPB-Steroid. Block 2: iCPB-Steroid.

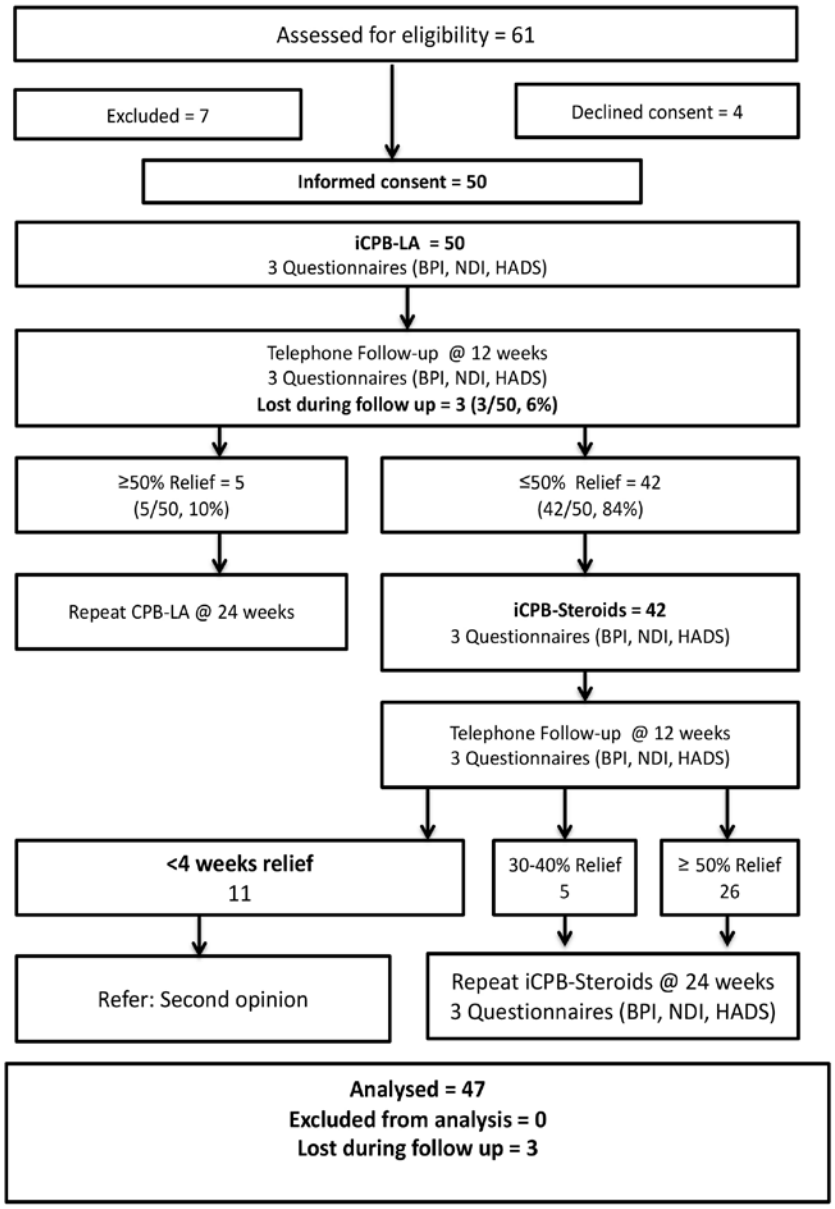

Fig. 1. *Study flow chart.*

The patient was positioned in the lateral decubitus and a 23-G 50-mm hypodermic needle was inserted in the plane of the ultrasound beam to enter the PCS. Once the needle entered the space, 9 mL of a mixture of 1% lidocaine (80 mg) and depot methylprednisolone (60 mg) was injected after negative aspiration. The procedure was repeated on the contralateral side in patients with bilateral symptoms. A total of 80 mg depot methylprednisolone was used for bilateral blocks.

Definition of Outcomes:

1. Clinically significant relief was defined using the "pain at its worst in the last 24 hours" construct in the BPI-SF questionnaire (16). A 2-point change (30%) at 12 weeks posttreatment was considered as clinically significant pain relief (17).
2. Durable relief was defined as a 4-point change (50%) at 12 weeks posttreatment (17,18).
3. Failure of treatment was defined as transient (< 4

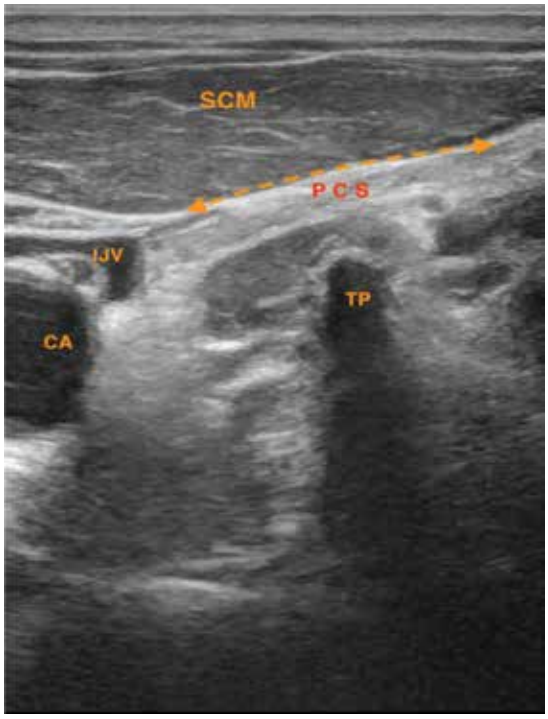

Fig. 2. *The ultrasound image of the neck details the sternocleidomastoid (SCM) muscle, the posterior border of the SCM muscle (dotted line), and the posterior cervical space (PCS).*

weeks) or no benefit with either treatment (iCPB-LA or iCPB-Steroid).

Collected data included age, gender, duration of symptoms, employment status, presence of other WAD symptoms, including headache, upper back pain, orofacial pain, and tinnitus, as well as any complication with iCPB, including dyspnoea, infection, postprocedural flare-up in symptoms, Horner's syndrome, and dizziness.

Statistical analysis was performed using Stata Version 13.1 (Statacorp LLC, College Station, TX) statistical package for Windows (Microsoft Corporation, Redmond, WA). The first set of analyses compared the changes in outcomes from baseline to 12 and 24 weeks for each block separately and the paired t test was used to compare between time points (Table 1).

A second set of analyses compared the differences in outcomes between the 2 blocks (iCPB-LA and iCPB-Steroid) using linear mixed models (Table 2). The patient was considered as a random effect in this model, with the block taken as a fixed effect. Differences were considered significant for $P < 0.05$. Missing data was imputed using the "last-observation-carried-forward" method.

Results

Over a 27-month period, a total of 61 patients with refractory neck pain were screened. Seven patients were excluded due to preexisting neck pain prior to whiplash (4) or widespread pain (3) and 4 patients refused the intervention due to needle phobia.

Fifty patients reported a history of whiplash prior to the onset of neck pain and were recruited into the study. Cervical zygapophyseal joint dysfunction was excluded in all patients. Forty-eight patients (48/50, 96%) reported additional WAD symptoms. Demographic details, type of trauma, WAD symptoms, and patient characteristics are detailed in Table 3.

iCPB-LA was performed on 50 patients. Bilateral iCPB-LA was performed on 21 patients (21/50, 42%). Three patients were lost to follow-up (3/50, 6%).

At 12-week post-iCPB-LA, 5 patients (5/50, 10%) reported > 50% benefit (i.e., durable pain relief) and were booked to receive repeat iCPB-LA after 24 weeks. Six patients (6/50, 12%) reported to have clinically significant relief at 12 weeks. Thirty-six patients (36/50, 72%) had transient or no relief with neck pain returning to baseline within 12 weeks (Fig. 1).

Forty-two patients (36 patients with transient or no relief following iCPB-LA and 6 patients with clinically significant benefit after iCPB-LA) were offered iCPB-Steroid. At the 12-week review, 5 patients (5/42, 20%) reported clinically significant relief and 26 patients (26/42, 62%) had durable relief that persisted for 24 weeks (Fig. 3).

A second set of analyses compared the scores between the iCPB-LA and iCPB-Steroid groups at baseline and 12 weeks postprocedure and the change in scores between these time points. Differences in outcome are shown in Table 2.

Treatment Failure

Eleven patients (11/50, 22%) reported transient or no benefit with iCPB.

WAD Symptoms

All patients who reported clinically significant improvement with iCPB (LA or Steroid) also reported improvement in associated WAD symptoms, including headache, facial pain, upper back pain, and tinnitus (Table 3).

Table 1. *Changes in outcomes from baseline to 12 and 24 weeks following iCPB.*

Outcome	Group	Time Point	n	Baseline Mean ± SD	Subsequent Time Mean ± SD	Change Mean (95% CI)	*P* value
BPI "Worst pain in last 24 hours"	LA	12 weeks	47	7.8 ± 0.9	7.0 ± 1.8	-0.8 (-1.3, -0.3)	0.002
	Steroid	12 weeks	42	8.0 ± 0.9	4.3 ± 2.2	-3.8 (-4.6, -2.9)	< 0.001
	Steroid	24 weeks	42	8.0 ± 0.9	5.6 ± 2.1	-2.4 (-3.1, -1.7)	< 0.001
NDI	LA	12 weeks	47	50 ± 16	45 ± 16	-4 (-7, -1)	0.005
	Steroid	12 weeks	42	47 ± 15	25 ± 14	-23 (-28, -18)	< 0.001
	Steroid	24 weeks	42	47 ± 15	34 ± 16	-13 (-18, -15)	< 0.001
HADS Anxiety	LA	12 weeks	43	10.4 ± 4.7	10.1 ± 5.0	-0.2 (-1.0, 0.5)	0.55
	Steroid	12 weeks	37	9.9 ± 5.0	7.4 ± 4.2	-2.6 (-3.7, -1.5)	< 0.001
	Steroid	24 weeks	36	9.8 ± 5.0	7.7 ± 4.0	-2.2 (-3.1, -1.3)	< 0.001
HADS Depression	LA	12 weeks	43	7.8 ± 4.5	7.8 ± 4.7	0.0 (-0.9, 0.8)	0.96
	Steroid	12 weeks	37	8.2 ± 4.7	6.0 ± 3.4	-2.2 (-3.2, -1.3)	< 0.001
	Steroid	24 weeks	36	8.3 ± 4.7	6.8 ± 3.6	-1.4 (-2.3, -0.5)	0.003

Abbreviations: iCPB, intermediate cervical plexus block; n, number; SD, standard deviation; CI, confidence interval; BPI, Brief Pain Inventory; NDI, Neck Disability Index; HADS, Hospital Anxiety and Depression Scale; LA, local anesthetic.

Table 2. *Differences in outcome between iCPB-LA and iCPB-Steroid.*

Outcome	Measurement	LA		Steroids		Difference (*)	*P* value
		n	Mean ± SD	n	Mean ± SD	Mean (95% CI)	
BPI "Worst pain in 24 hours"	Baseline	47	7.8 ± 0.9	42	8.0 ± 0.9	0.2 (0, 0.4)	0.01
	12 weeks	47	7.0 ± 1.8	42	4.3 ± 2.2	-2.7 (-3.5, -1.9)	< 0.001
	Change (+)	47	-0.8 ± 1.7	42	-3.8 ± 2.7	-2.9 (-3.8, -2.0)	< 0.001
NDI	Baseline	47	50 ± 16	44	47 ± 14	-3 (-5, 0)	0.02
	12 weeks	47	45 ± 16	42	25 ± 14	-21 (-26, -17)	< 0.001
	Change (+)	47	-4 ± 10	42	-23 ± 16	-18 (-24, -13)	< 0.001
HADS Anxiety	Baseline	45	10.3 ± 4.6	39	9.9 ± 4.9	-0.2 (-0.9, 0.5)	0.55
	12 weeks	43	10.2 ± 5.0	39	7.0 ± 4.4	-2.7 (-3.8, -1.7)	< 0.001
	Change (+)	43	-0.2 ± 2.5	37	-2.6 ± 3.2	-2.4 (-3.6, -1.1)	< 0.001
HADS Depression	Baseline	45	7.9 ± 4.6	39	8.0 ± 4.6	0.2 (-0.6, 1.1)	0.63
	12 weeks	43	7.8 ± 4.7	39	5.7 ± 3.6	-2.2 (-3.1, -1.3)	< 0.001
	Change (+)	43	0.0 ± 2.7	37	-2.2 ± 2.8	-2.2 (-3.4, -1.0)	< 0.001

(*) Differences calculated as value for Steroid minus value for LA. Calculated using mixed model.
(+) Change in outcome values from Baseline to 12 weeks.
Abbreviations: iCPB-LA, intermediate cervical plexus block with local anesthetic; iCPB-Steroid, intermediate cervical plexus block with Steroid; n, number; LA, local anesthetic; SD, standard deviation; CI, confidence interval; BPI, Brief Pain Inventory; NDI, Neck Disability Index; HADS, Hospital Anxiety and Depression Scale.

Employment

There were 40 patients (40/50, 80%) who were struggling to maintain employment due to severity of neck pain and were considering either reduction of working hours or resignation. Thirty-four patients (34/50, 78%) who responded to iCPB (LA or Steroid) were able to maintain employment (Table 3).

Complications

Twenty-six patients (26/50, 52%) reported postprocedural flare-up for 1-2 weeks. There was no incidence of dyspnoea secondary to phrenic nerve palsy despite over a third of patients receiving bilateral iCPB. None of the patients developed overt signs of a cervical sympathetic block (e.g., Horner's syndrome).

Table 3. *Demographic data, employment status, and patient characteristics.*

Demographics	n = 50
Age, y (mean ± SD)	45 ± 12.1
Gender, n (%)	
Men	15 (30%)
Women	35 (70%)
Duration, y (median [P25, P75])	11 (5, 16)
Employment, n (%)	
Employed	40 (80%)
Unemployed	6 (12%)
Retired	4 (8%)
Trauma, n (%)	
Motor Vehicle Accident	35 (70%)
Sports Injury	5 (10%)
Other Trauma	10 (20%)
Associated WAD Symptoms, n (%)	
Headache	37 (74%)
Orofacial Pain	27 (54%)
Upper Back Pain	43 (86%)
Tinnitus	28 (56%)

Abbreviations: SD, standard deviation; n, number; y, years; WAD, whiplash-associated disorder.

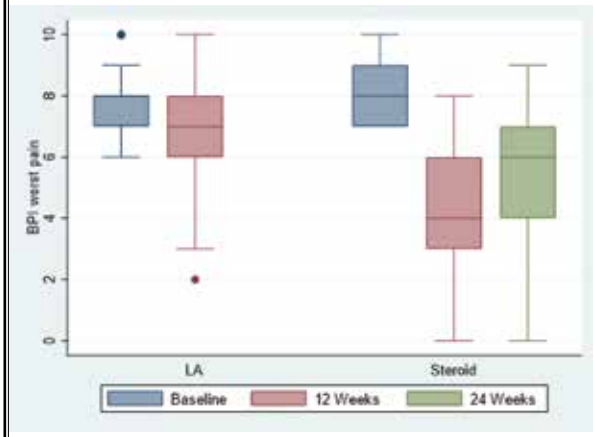

Fig. 3. *Changes in outcomes from baseline to 12 and 24 weeks following intermediate cervical plexus block (iCPB) with local anesthetic (LA) and iCPB with steroid.*

Missing data was imputed in 9 patients in the iCPB-LA group. Nine nonresponders had the 24-week post-iCPB-LA BPI missing and the 12-week observations were imputed.

Discussion

The authors present the first study on the effectiveness of iCPB in the management of refractory chronic neck pain after whiplash.

Patients received 2 sequential interventions (iCPB-LA and iCPB-Steroid). When compared to iCPB-LA, iCPB-Steroid provided a significant reduction in neck pain, NDI, anxiety, and depression at 12 weeks. In addition, iCPB-Steroid provided durable analgesia in 62% of patients (26/42, 62%). Over a third of patients were able to maintain employment.

In the United Kingdom, 1,500 whiplash claims are made daily with many requiring health care input (19). The incidence of WAD in the United Kingdom is estimated to be around 400,000 per year (20). Two decades ago, the estimated cost from WAD was £ 3.1 billion that was attributed to chronic symptoms and loss of work (21). Neck pain is the commonest chronic WAD symptom affecting 40% to 60% of patients with whiplash and can be a challenge to manage (2,22). Neck-related disability has considerable impact on costs and health care utilization (23). There is increasing evidence that patients with chronic neck pain post-whiplash have poorly functioning cervicothoracic muscles (7,8). Treatment guidelines and protocols in the management of chronic neck pain secondary to cervicothoracic muscle dysfunction are vague, having little supporting evidence, and are based on expert opinion (1,24,25). These include analgesics, physiotherapy, acupuncture, and trigger point injections. In addition, current management of chronic pain from whiplash is suboptimal and a research priority is to establish the effectiveness of available treatments for neck pain (26).

Rationale for Study Methodology

The study was conducted during the COVID-19 pandemic. Various regulatory bodies had advised against the use of corticosteroids in pain interventions (27-29). These guidelines risked denying an effective treatment to patients who often have limited options to manage persistent pain. We have previously reported on the ineffectiveness of LA interventions and the effectiveness of steroid interventions in chronic abdominal pain and facial pain (18,30). In addition, we have reported on the safety of depot steroid interventions during the COVID-19 pandemic (31). At our center, the waiting period for interventions reached 12-18 months due to reallocation of resources, which lead to the conclusion that it would be suboptimal practice to offer interventions with questionable efficacy. Based on the above

rationale, the present study design offered a pragmatic pathway that had the scope to identify an effective and safe intervention for the individual patient.

Rationale for iCPB in WAD

A well-recognized cause of pain in a subset of patients with whiplash is the cervical zygapophyseal joint dysfunction and these were excluded in the present study (5). Alternate pain generators identified in WAD include the cervicothoracic muscles and upper cervical nerves (i.e., cervical plexus) (7,8,11). There is robust evidence of neurophysiologic and structural convergence of cervical sensory and muscle afferent inputs into the trigeminal subnucleus caudalis neurons (29,32-34). Thus, persistent symptoms following whiplash could involve a nociceptive drive from the upper cervical afferents with subsequent activation and sensitization of the trigemino-cervical complex (10,11,13). Anecdotal reports (11,13,14) have shown the benefit of iCPB-Steroid in patients presenting with chronic neck pain, headache, orofacial pain, and upper back pain after whiplash (11,13,14). During iCPB, the injectate that is deposited in the PCS permeates through the porous prevertebral fascia and blocks the deep cervical plexus (35,36). Although, none of our patients showed the clinical signs of a cervical sympathetic block (e.g., Horner's syndrome), the possibility of suppression of sympathetic activity still exists. Thus, a single ultrasound-guided injection has the potential to target multiple cervical neural pathways, which, in turn, could dampen the sensitized trigemino-cervical complex (14). This may explain the benefit of iCPB in neck pain, headache, and facial pain following whiplash. In the present study, there was an improvement in associated symptoms, including headache, facial pain, upper back pain, and tinnitus following iCPB (Table 3).

Limitations

The authors are aware of the limitations of the open-label, observational, single-center study in a limited cohort under a single physician. Cervical zygapophyseal joint dysfunction is a recognized cause of chronic neck pain following whiplash in a subset (37). We used clinical and radiological signs to exclude cervical zygapophyseal dysfunction instead of diagnostic median branch blocks as it would have subjected the patient to a fluoroscopy-guided procedure with attendant risks that required a theatre setting (38). In addition, the use of depot steroids in the cervical region raises potential concern. However, the procedure is performed under real-time ultrasound guidance, and negative aspiration was performed prior to injecting the mixture into a fascial plane (i.e., PCS). Our unit has been performing ultrasound-guided interventions in the head and neck region with depot steroids without adverse effects for over a decade (11,13,14,30,31). Over a third of patients with bilateral symptoms required bilateral iCPB and the phrenic nerve block is a potential concern. The phrenic nerve is safely encased in the deeper prevertebral fascia and the drugs are deposited in the PCS superficial to this fascia (36). None of the patients in this study reported dyspnea suggesting diaphragmatic palsy after bilateral blocks in concordance with recent evidence (9,13,14,36). iCPB with depot steroids has a good safety profile, can be performed in an outpatient setting, provides durable relief, and therefore mandates evaluation (9,14,35,36).

Conclusions

The cervical plexus could play a key role in the persistence of symptoms after whiplash. iCPB-Steroid may have a role in the management of refractory neck pain after whiplash. The authors recommend trialing iCPB-Steroid in patients with refractory chronic neck pain post-whiplash. Further studies are required to confirm this observation from our trial.

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