

Military Medicine

Treating PTSD in Canadian Special Operation Forces Command with ketamine plus cervical sympathetic blockade --Manuscript Draft--

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Abstract:	<p>Background: Canadian Special Operation Forces Command (CANSOFCOM) operators have been extensively deployed in recent conflicts. They are at risk of trauma and blast exposure as well as the development of post-traumatic stress disorder (PTSD) and blast traumatic brain injury (bTBI). Current psychotherapy and pharmacological approaches provide suboptimal resolution of PTSD and bTBI symptoms. Prior research has shown ketamine infusions (KI) cervical sympathetic blockade (CSB) have reduced PTSD and bTBI symptoms.</p> <p>Aims: To report significant improvement of PTSD and bTBI symptoms in CANSOFCOM operators following concordant use of CSB and KI.</p> <p>Methods: A total of 11 patients, including CANSOFCOM members, were treated and followed. Pre- and post-intervention PCL-5 and NSI scores were recorded. Each patient received a 4 KI and bilateral CSB treatments as per previously published protocol.</p> <p>Results: Two weeks post-intervention, average PCL score reduction of 45.09 (n=11). Two weeks post-intervention, average NSI score reduction of 40.7 (87.0% reduction) (n=6). No other NSI scores were available.</p> <p>Conclusion: KI combined with bilateral CSB can provide a clinically significant reduction of PTSD and bTBI in the CANSOFCOM cohort. Of interest, another study of CSB alone as a treatment of bTBI, which used NSI assessment, showed a reduction of 53% on a one-month follow-up. Our report demonstrated 87% reduction if NSI score at 2 weeks. Possible physiologic explanations are discussed.</p>
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Treating PTSD in Canadian Special Operation Forces Command with ketamine plus cervical sympathetic blockade

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Keywords: ketamine infusion; KI; cervical sympathetic blockade; CSB; PTSD; blast traumatic brain injury; bTBI; traumatic brain injury; CANSOFCOM; SGB

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ABSTRACT:

Background: Canadian Special Operation Forces Command (CANSOFCOM) operators have been extensively deployed in recent conflicts. They are at risk of trauma and blast exposure as well as the development of post-traumatic stress disorder (PTSD) and blast traumatic brain injury (bTBI). Current psychotherapy and pharmacological approaches provide suboptimal resolution of PTSD and bTBI symptoms. Prior research has shown ketamine infusions (KI) cervical sympathetic blockade (CSB) have reduced PTSD and bTBI symptoms.

Aims: To report significant improvement of PTSD and bTBI symptoms in CANSOFCOM operators following concordant use of CSB and KI.

Methods: A total of 11 patients, including CANSOFCOM members, were treated and followed. Pre- and post-intervention PCL-5 and NSI scores were recorded. Each patient received a 4 KI and bilateral CSB treatments as per previously published protocol.

Results: Two weeks post-intervention, average PCL score reduction of 45.09 (n=11). Two weeks post-intervention, average NSI score reduction of 40.7 (87.0% reduction) (n=6). No other NSI scores were available.

Conclusion: KI combined with bilateral CSB can provide a clinically significant reduction of PTSD and bTBI in the CANSOFCOM cohort. Of interest, another study of CSB alone as a treatment of bTBI, which used NSI assessment, showed a reduction of 53% on a one-month follow-up. Our report demonstrated 87% reduction if NSI score at 2 weeks. Possible physiologic explanations are discussed.

KEYWORDS: ketamine infusion; KI; cervical sympathetic blockade; CSB; PTSD; blast traumatic brain injury; bTBI; traumatic brain injury; CANSOFCOM; SGB

1. INTRODUCTION

Canadian Special Operation Forces Command (CANSOFCOM) personnel constitute the most elite members of the Canadian military forces. Military members are exposed to higher rates of trauma, with at least 85.6% of Canadian Armed Forces (CAF) experiencing at least one or more trauma exposures throughout their professional careers.¹ In CAF, lifetime prevalence of PTSD was 6.6%.¹ We predict with even more grueling military careers, CANSOFCOM will develop PTSD at even higher rates. In addition to trauma exposure, special operation forces members develop increased rates of blast traumatic brain injury (bTBI) due to increased deployment rates, extensive operational readiness training, and grueling combat campaigns.²⁻⁶ It was discovered that military veterans with a history of bTBI had greater incidence of comorbid neuropsychiatric issues including PTSD, depression and anxiety.^{7,8} TBI and PTSD present with common neuropsychiatric symptoms including anxiety, irritability, insomnia, personality changes, and memory problems. This overlap complicates diagnostic differentiation. Current psychotherapy and pharmaceuticals provide moderate symptomatic relief with low compliance rates.⁹ In the past, prior research has shown the improvement of PTSD and bTBI symptoms following CSB and KI in US Special Operation Forces cohorts.^{10,11}

2. METHODS

2.1 Patient and Setting

A total of 11 CANSOFCOM were consecutively followed and treated at Stella Center Headquarters in Westmont, IL. 4 patients continued to follow up at 3 months. 3 patients continued to follow up at 6 months.

2.2 Cervical Sympathetic Blockade

Detailed informed consent was obtained prior to all procedures for CSB. The patient was placed in the supine position with the head rotated slightly to the left,

with monitoring per clinic protocol. The skin of the neck was cleaned with chlorhexidine-isopropyl alcohol preparation and 2 g of sterile ultrasound gel was applied. The neck was scanned using a broadband linear transducer (8–13 MHz from the level of the 6th to the 4th cervical vertebrae in transverse view). The skin at the injection site on the lateral neck was anesthetized with 1.5 mL of 1% lidocaine. Utilizing an in-plane approach, under real-time ultrasound guidance, a 22-gauge echogenic needle was placed just dorsal to the ventral fascia of the longus coli, medial to the longus capitus. After attempted aspiration, while monitoring the patient, 0.5 mL of 0.5% bupivacaine was injected, and after observing the patient for 30 s, a second 4 mL aliquot was injected. The patient was monitored for an additional 30 s. After the patient verbally confirmed an absence of any concerning symptoms, an additional 4 mL of 0.5% bupivacaine was slowly injected over 1 min (total injection volume of 8 mL) for a single-level block. A second injection was then performed at the 4th cervical level, with a total of 4 mL of bupivacaine injected. Left-sided CSB was performed the following day in alignment with safety protocols.

2.3 Ketamine Infusion

Detailed informed consent was obtained prior to all infusions following a consultation. The initial infusion of racemic ketamine hydrochloride (0.5 mg/kg) was administered over 45 min. Premedication with ondansetron 4 mg IVP was used for all sessions and an anesthesiologist was present until discharge. During the infusion, a nurse recorded vital signs (heart rate, blood pressure, respirations, pulse oximetry) and clinical status every 5 min. Any concerning or intolerable treatment-emergent side effects (e.g., hemodynamic instability, severe dissociation, worsening depression or anxiety) prompted intervention or discontinuation of the infusion. At the end of each infusion, the patient was clinically monitored for at least 1 h by the nursing staff. Subsequent infusions utilized escalating doses of ketamine of 0.1–0.2 mg/kg titrated to induce mild to moderate dissociation. A total of 4 KI were performed.

2.4 Psychiatric Measure Outcomes

2.4.1 PTSD Checklist for DSM-V (PCL-5)

The PTSD Checklist (PCL-5) is a 20-item self-reported questionnaire that assesses PTSD symptomatology based on 20 symptoms outlined in the DSM-V. The purposes of this test include screening, diagnosis, and monitoring of symptomatology over a period of time. The patient is to self-report a score based on a 5-item Likert scale from 0 to 4, which is described by the following: 0) “Not at all”; 1) “A little bit”; 2) “Moderately”; 3) “Quite a bit”; and 4) “Extremely”. It should be noted that there are a number of differences between PCL-5 and PCL-4 (based on DSM-IV), hence they can neither be compared nor interchanged. The total symptom severity is a sum of the patient responses and may range from 0 to 80. A change in PCL-5 score by 5–10 points is considered reliable, and a change by 10–20 points is considered clinically significant. The optimally efficient minimum cutoff score that is considered diagnostic ranges from 31 to 33.¹²

2.4.2 Neurobehavioral Inventory Scale (NSI)

The Neurobehavioral Inventory Scale (NSI) is a highly reliable, 22 item self-reported questionnaire that assesses bTBI and post-concussive symptoms based on 22 unique symptoms.^{13,14} The purposes of this test include screening, diagnosis, and monitoring of symptomatology over a period of time. The patient is to self-report a score based on a 5-item scale from 0 to 4, which is described as the following: 0) “None”; 1) “Mild”; 2) “Moderate”; 3) “Severe”; 4) “Very Severe”. The total symptom severity is a sum of the patient responses and may range from 0 to 88. A NSI score change by greater to or equal than 7 is considered clinically significant.¹⁵

3. RESULTS

In a total of 11 patients (n=11), pre-PCL average scores were 51.73. Post-PCL average scores at 2 weeks post-treatment were 6.64 (Δ 45.09, 87.0% reduction) (Table 1).

In a total of 6 patients (n=6), pre-PCL average scores were 50.3. Post-NSI average score was 9.7 (Δ 40.7, 81% reduction) (Table 2).

In total, 4 patients followed-up at 3 months (n=4). The average pretreatment PCL score of this cohort was 49.25. Post-treatment average PCL scores at 3 months were 7.75 (Δ 41.50, 82.9% reduction) (Table 3).

In total, 3 patients followed-up at 6 months (n=3). The average pretreatment PCL score of this cohort was 52.0. Post-treatment average PCL scores at 3 months were 11.0 (Δ 41.0, 79.0% reduction) (Table 4).

Table 1:

2-Week Follow Up				
# of Patients	Pre-PCL Score	Post-PCL Score	Δ PCL	% Reduction
11	51.73	6.64	45.09	87.00

Table 1: 2-week follow-up PCL-5 scores

Table 2:

2-Week Follow Up				
# of Patients	Pre-NSI Score	Post-NSI Score	Δ NSI	% Reduction
6	50.3	9.7	40.7	81.00

Table 2: 2-week follow-up NSI scores

Table 3:

3-Month Follow Up				
# of Patients	Pre-PCL Score	Post-PCL Score	Δ PCL	% Reduction
4	49.25	7.75	41.50	84.00

Table 3: 3-month follow-up PCL-5 scores

Table 4:

6-Month Follow Up				
# of Patients	Pre-PCL Score	Post-PCL Score	Δ PCL	% Reduction
3	52.00	11.00	41.00	79.00%

Table 4: 6-month follow-up PCL-5 scores

4. DISCUSSION

Ketamine infusion and cervical sympathetic blockade have both been shown to treat PTSD individually. Together, the two treatments appeared to have synergistic effects with the mechanism discussed in further detail in Lipov et al., 2023, and were presumed to have a positive impact on symptoms of bTBI.¹⁰ In a cohort of 5 US SOF who received KI with bilateral CSB, an average PCL score reduction of 28 points was maintained 6 months post-treatment.¹¹ Recent report by Dr. Mulvaney demonstrated that out of 23 patients, 22 showed improvement in their NSI scores when treated by bilateral CSB.¹⁶ NSI baseline average score was 42.7; the average score at 1-week post-treatment was 18.8; 1-month post-treatment was 20.1.¹⁶ This represents a 53% improvement in the NSI score between baseline and 1 month.¹⁶ This contrasts with our findings of NSI change two weeks post-intervention using KI and CSB and an average NSI score reduction of 40.7 (87.0% reduction) (n=6). Many reasons for this difference can be conceived, such as

a small N, a difference in follow-up, and others. Yet, this significant difference may be due to the synergetic impact of KI and CSB.

Thus, KI and CSB together provide a promising and hopeful healing modality to achieve PTSD and bTBI symptom reduction in the elite CANSOFCOM, special operator forces United States, and global militaries and should be further investigated.

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Table 2:

2-Week Follow-Up				
# of Patients	Pre-NSI Score	Post-NSI Score	Δ NSI	% Reduction
6	50.3	9.7	40.7	81.00

Table 2: 2-week follow-up NSI scores

Table 3:

3 Month Follow-Up				
# of Patients	Pre-PCL Score	Post-PCL Score	Δ PCL	% Reduction
4	49.25	7.75	41.50	84.00

Table 3: 3-month follow-up PCL-5 scores

Table 4:

6-Month Follow-Up				
# of Patients	Pre-PCL Score	Post-PCL Score	Δ PCL	% Reduction
3	52.00	11.00	41.00	79.00%

Table 4: 6-month follow-up PCL-5 scores