

## **Pilot study: rapidly cycling hypobaric pressure improves pain after 5 days in adiposis dolorosa**

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### **Abstract**

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### **Introduction**

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Adiposis dolorosa (AD) is considered a rare disorder by the National Institutes of Health and the National Organization for Rare Disease; in Lund, Sweden, 0.1% of the population is affected.<sup>1</sup> The pain associated with AD is in subcutaneous fat, but patients also complain of fatigue, cognitive changes, sleep disturbance, shortness of breath, rapid heart rate, gastrointestinal complaints, and myalgias and arthralgias. Hyperalgesia is prominent, similar to signs and symptoms associated with fibromyalgia,<sup>2</sup> but with the difference that the physical examination is greatly abnormal in AD compared with essentially normal in fibromyalgia. The pain in AD varies in intensity and type, can occur in flares, and is associated with inflammation<sup>3</sup> and fluid in adipose tissue called lipedema,<sup>4</sup> which can progress to lymphedema; seroma formation is common after adipose resection.<sup>3,4</sup>

Current treatments for AD include surgical excision or liposuction,<sup>5–7</sup> intravenous lidocaine,<sup>8</sup> topical analgesics,<sup>9,10</sup> infliximab and methotrexate,<sup>11</sup> and pregabalin combined with manual lymphatic drainage therapy.<sup>12</sup> Intravenous lidocaine is not effective for many patients with AD; topical analgesics provide modest relief; and the immunosuppressive combination of infliximab and methotrexate risks complications, such as infection, and has only shown benefit in a single case to date. External pneumatic compression is known to relieve pain associated with edema.<sup>13,14</sup> Although whole body external pneumatic compression is available,<sup>15</sup> the neck and head are not treated raising a concern for increasing fluid in these areas and exacerbating the fatigue, cognitive changes, and sleep disturbances in AD. Manual lymphatic drainage is also effective for pain relief in AD;<sup>12</sup> however, only small areas of the body can be treated at a time. In addition, individuals with AD may not tolerate external compression because of hyperalgesia.

The Cyclic Variations in Altitude Conditioning™ (CVAC) (CVAC Systems, Inc; Temecula, California, USA) process is an alternative and potentially revolutionary method of touch-free cyclic hypobaric pneumatic compression for treatment of tissue edema and, therefore, edema-associated pain. During the CVAC process, an individual sits within the CVAC altitude simulator while pressure cycles 300 to 500 times in a session simulating altitudes up to 3,200 m. At

higher altitude levels (up to 6,858 m), the dynamic change in hypobaric pressure over a larger range of altitudes provides an intermittent hypobaric hypoxic experience. The CVAC process has been shown to improve blood oxygen saturation up to 6% by pulse oximetry, consistent with a rapid, enduring, and beneficial altitude response.<sup>16</sup> We hypothesized that the CVAC process would improve pain and quality of life in AD patients as measured by validated questionnaires.

## **Results**

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### **CVAC process**

The average number of CVAC sessions completed during days 1–5 was  $9.4 \pm 0.5$ . One participant was able to complete only 1 session daily due to difficulty in equilibrating ear pressure. Another completed only 8 sessions for the same reason. No side effects occurred.

### **Discussion**

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We demonstrated that changing air pressure around participants with AD from ambient altitude (about 60 m above sea level in San Diego, California, USA) to 3,200 m, 300–500 times in a 20-minute session, for up to 2 sessions daily (total of 40 minutes), over 5 days significantly reduced pain perceptions and intensity. The average altitude for the sessions over the 5-day period was approximately 1,828 m. This pneumatic compression benefit on pain reports manifested across several distinct measures including VAS-measured pain intensity, lower current pain levels as captured by the McGill Pain Questionnaire, reduced tendencies to catastrophize pain symptoms on the PCS, and greater quality of life as indicated by improved mental health function scores on the SF-36. Given that both the pain patterns on the average and the low VAS scores had significant linear and quadratic changes, our data suggest that pain changes really did not manifest until day 3 or 4. These data could infer that a 1-day CVAC process intervention would not be sufficient to alter pain status. On the contrary, we saw no evidence of pain scores leveling off during days 4–5, so an even longer CVAC protocol might yield additional benefits. Although these results are limited by the small sample, short-term treatment, and nonrandomized design of this pilot study, the observation that widespread pain-related benefits can be achieved in a brief CVAC process intervention is supportive of further research attention to this novel treatment for AD.

At least 3 potential mechanisms may account for the observed improvements in pain reports in this study. First, tissue edema likely decreased, as supported by a significant decrease in weight in participants and a significant decrease in impedance; a decrease in impedance indicates less water in tissue. The multiple changes in external pressure during the CVAC process exposure may cause the lymph fluid to move out of the tissue similar to external compression;<sup>21</sup> this pneumatic displacement of fluid improves pain in lymphedema.<sup>22</sup> Another possible mechanism to explain improved pain in participants with AD could be through improved blood flow by the intermittent pneumatic compression,<sup>23</sup> consistent with the CVAC process; this could allow for a secondary decrease in tissue edema. The CVAC process has also been demonstrated to increase arterial oxygen saturation.<sup>16</sup> Muscle contraction improving lymph flow and oxygenation also occurs with exercise.<sup>24</sup> Pain in lipedema is thought to result from hypoxia, inflammation, and necrosis of adipocytes;<sup>25</sup> therefore, improved blood flow and oxygen saturation may decrease hypoxia in the painful adipose tissue.<sup>26</sup> If these mechanistic theories are confirmed, the CVAC process may also hold

treatment potential for other chronic pain conditions in which impaired blood flow and tissue edema are contributing factors. For example, improved blood flow may be a mechanism through which exercise improves pain and quality of life among fibromyalgia patients.<sup>27</sup> To date, however, the CVAC process has not been tested in fibromyalgia populations, although 5 of 10 participants in this study had a diagnosis of fibromyalgia. Future work could focus on pain relief after CVAC process exposure compared with exercise or combined with exercise. Pain pathways could also be assessed systematically as they relate to pneumatic compression or exercise.

In contrast to our observations of consistently favorable changes in pain reports following the 5-day CVAC process intervention, there was no evidence to suggest improvements in areas of pain disability, sleep, or physical function from this protocol. Although it is possible that the lack of improvement in these areas represents limitations in CVAC process treatment, an alternative interpretation is that the absence of changes in the latter dimensions was a result of the brevity of the intervention. A longer measurement protocol may be required in order to assess the potential for meaningful change in the areas of sleep quality and quantity, family, social and sexual relationships, occupational functioning, and self-care. Additional research will be required to compare the merits of these interpretive hypotheses.

We also observed some preliminary evidence for CVAC process-induced body weight changes as measured by bioimpedance technology. Weight significantly decreased for the participants in this pilot study over 5 days. Interestingly, although weight significantly decreased after CVAC process exposures, fat mass and fat percent increased and FFM significantly decreased as measured by BIA. Bioimpedance analysis is a widely used method to estimate body composition. When a current is passed through the body, the water-containing tissues primarily conduct the electrical current so that impedance is higher with increased FFM, which is 73% hydrated;<sup>28,29</sup> impedance is also increased in lymphedema.<sup>30</sup> In other words, impedance increases with increased water in tissues. In BIA, higher TBW results in a measure of lower body fat percentage; less water increases the percentage of body fat and decreases calculated FFM. There is currently no algorithm for BIA that provides a volume in liters.<sup>29</sup> In our participants, although weight significantly decreased after CVAC process exposures, fat mass and fat percent increased and FFM decreased consistent with a significant decrease in impedance. These data suggest that the CVAC process decreases tissue fluid in AD accounting for a significant decrease in weight loss. The CVAC process of gentle pneumatic compression cycled 300–500 times in a 20-minute period repeated on an average of 9 times in 1 week, therefore, decreased tissue fluid weight in our participants with AD while decreasing pain. These changes in BIA measures would best be confirmed by the use of dual X-ray absorptiometry for body composition, perometry for limb volume measurements, and deuterium isotope dilution as a measure of TBW before and after the CVAC process.

In conclusion, the CVAC process, which is touchless, cycled, pneumatic, hypobaric compressions administered via a high-performance altitude simulator, may decrease tissue fluid and improve oxygen saturation resulting in decreased pain in people with AD. Although randomized, controlled trials are needed to confirm these data, the CVAC process could potentially help in treating AD, related chronic pain disorders, and painful lipedema.