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CASE SERIES

Genitofemoral Neuromodulation as a Novel Pain Management Solution for Patients with Chronic Testicular Pain: A Proof-of-Concept Study

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Introduction: Severe chronic testicular pain that has failed medical therapy and physiotherapy poses a treatment dilemma. This study presents a proof of concept for the use of genitofemoral neuromodulation (GFM) as a potential pain management solution for patients with persistent testicular pain unresponsive to conservative and surgical management.

Methods: Patients with chronic testicular pain refractory to conventional treatments were selected for GFM. A total of three patients were included in this proof-of-concept study. Demographic information, prior medical and surgical interventions, and pre- and post-operative pain scores using the Numerical Rating Pain Scale were collected. All patients must have had temporary relief from pain with a spermatic cord block.

Results: Patient 1 (75 years old) had a history of opioid medication use, physiotherapy, radiofrequency ablation, and nerve block. His pain score reduced from 10/10 to 4/10 six months post-operatively. Patient 2 (59 years old) had a history of opioid, nortriptyline, baclofen medication use, and physiotherapy. His pain score reduced from 9/10 to 2/10 six months post-operatively. Patient 3 (36 years old) had a history of opioid medication use and physiotherapy, and bilateral orchidectomy for pain relief. His pain score reduced from 8/10 to 6/10 six months post-operatively.

Conclusion: This study suggests that GFM is effective in reduce pain scores and could be a viable option for patients with chronic testicular pain refractory to traditional interventions. Further research is essential to establish the long-term efficacy and safety of GFM in this cohort.

Keywords: chronic testicular pain, peripheral nerve stimulation, genitofemoral neuromodulation, pain management, opioid

Introduction

Chronic testicular pain is defined as persistent or intermittent scrotal pain lasting at least three months, significantly affecting daily activities and quality of life.[1] In the United States, chronic testicular pain affects approximately 100,000 men annually, accounting for 2.5–5% of urology consultations.[2] Despite its prevalence, up to 25–50% of cases are considered idiopathic, presenting a major challenge in both evaluation and management.[1] Due to the absence of established treatment guidelines, current therapeutic strategies are based on the limited published literature.

Conservative therapy primary involves pelvic floor physiotherapy, and pharmacotherapy, including non-steroidal anti-inflammatory drugs, tricyclic antidepressants, anticonvulsants, and narcotic analgesics for breakthrough pain. Surgical interventions, including orchidectomy as a last resort, may also be considered.[2] However, a significant number of patients remain refractory to these therapies. Managing chronic testicular pain that is unresponsive to physiotherapeutic, medical and surgical treatments is a significant challenge. Given the profound impact on patients' quality of life, alternative innovative approaches are crucial.

Peripheral nerve stimulation (PNS) has shown promise in the management of other chronic pain conditions, by targeting the specific nerves involved in pain transmission.[3] The genitofemoral nerve, which provides somatic innervation to the

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testicle, has been identified as a key contributor to the pathophysiology of chronic testicular pain. This study aims to prove the concept that by modulating the genitofemoral nerve, we can interrupt the pain signals responsible for chronic testicular pain. Proof-of-concept studies test ideas through experimental practice, providing justification for broader clinical application.[4]

To the best of our knowledge, only two case reports have been published regarding the use of PNS for chronic testicular pain, both employing different techniques.[5,6] This case series is the first to describe the successful treatment of chronic testicular pain using GFM, specifically using the technique where the genitofemoral nerve is located via ultrasound and a permanent implantable pulse generator (IPG) is placed in the anterior abdomen. The primary aim of this study is to assess the feasibility and preliminary efficacy of GFM in alleviating chronic testicular pain in patients who have not responded to conservative or surgical treatments.

Materials and Methods

We conducted a retrospective review of all patients undergoing GFM for chronic testicular pain from 1st January 2023 to 31st December 2023. Informed consent was obtained from all participants, and the study was approved by the local ethics board (Ethic Committee Name: Monash Health Human Research Ethics Committee; Approval Code: RES-24-0000-188Q). This study complies with the Declaration of Helsinki.

Patient Selection

Patients were eligible for GFM if they experienced chronic testicular pain lasting at least three months, despite receiving medical therapies (including opioids), pelvic floor physiotherapy, and consultation with both a pain specialist and psychologist. All patients also underwent thorough medical evaluation, including testing for urinary tract infections and sexually transmitted infections, as well as ultrasonography, cystoscopy and urodynamic studies to exclude other organic causes of pain. Additionally, patients needed to have experienced at least 12 hours of pain relief following a spermatic cord block with 10mL of 1% ropivacaine to qualify for the GFM procedure. This was in hope that a longer-lasting effect would provide a more reliable confirmation of the diagnosis.

Procedure

The GFM procedure was performed by an experienced urologist under sterile conditions and consisted of two stages: trial therapy and implantation of the permanent IPG for those who responded to the trial.

Patients were under general anaesthesia (GA) and positioned supine. Ultrasound guidance was used to identify the genitofemoral nerve near the spermatic cord, just above the inguinal ligament on the affected side. A stimulating stylet was utilized to confirm the nerve's location. An introducer sheath was then advanced over the stimulating stylet, followed by the removal of the dilator. Two leads, each with eight contacts, were inserted approximately 4 mm beneath the dermis along the spermatic cord. Dressings were applied, and patients were discharged the same day.

If the trial period resulted in at least a 50% improvement in symptoms, the leads were removed in an outpatient setting within 1–2 weeks. If pain returned after lead removal, the patient underwent a new lead insertion and IPG implantation approximately one month later. The IPG was implanted in the anterior abdomen, positioned to align with natural skin creases to avoid limiting the patient's range of motion.

Data Collection

Demographic data (age, medical history), prior treatments, and pre- and post-operative pain scores were collected. Pain was evaluated using the Numerical Rating Pain Scale (NRPS), where 0 represents no pain and 10 represents the worst pain imaginable. Pain scores were assessed pre-operatively and at six months post-operatively. Descriptive statistics were used to assess pain scores before and after GFM treatment. Due to the small sample size, formal statistical analysis was not performed.

Results

A total of three patients were included in this proof-of-concept study, all of whom had chronic testicular pain that was resistant to prior medical, physiotherapeutic, and surgical interventions. The patients ranged in age from 36 to 75 years, and each had a history of opioid use along with various other treatments.

The first patient, a 75-year-old male, had previously undergone opioid therapy, physiotherapy, radiofrequency ablation, and nerve blocks for pain management. His pre-operative pain score was 10/10, and six months post-operatively, his pain score decreased to 4/10.

The second patient, a 59-year-old male, had been treated with opioids, nortriptyline, baclofen, and physiotherapy. His pre-operative pain score was 9/10, and six months post-operatively, his pain score decreased to 2/10.

The third patient, a 36-year-old male, had a history of opioid use, physiotherapy, and a bilateral orchidectomy performed for pain relief. He underwent bilateral GFM. His pre-operative pain score was 8/10, and six months post-operatively, his pain score decreased to 6/10.

All patients experienced a reduction in pain scores at the 6-month follow-up, with the most significant pain relief observed in the first two patients. In addition to pain reduction, all three patients were able to discontinue opioid use within three months of the procedure. Each patient continues to receive ongoing follow-up from a pain specialist to ensure comprehensive care.

Discussion

Chronic testicular pain presents a significant clinical challenge, especially when pharmacological interventions, physiotherapy, and even surgery fail to alleviate symptoms. Pulsed radiofrequency ablation (PRF), a minimally invasive treatment, has shown promise, as highlighted in a recent review by Alzahrani et al.[7] Notably, PRF demonstrated a favourable safety profile with no reported side effects. However, the evidence is limited by small patient cohorts and short follow-up durations. PRF was trialed in our first patient but yielded limited success and persistent pain. For such refractory cases, innovative approaches like GFM provide a promising alternative. Our study suggests that GFM has the potential to significantly reduce pain and opioid use in patients with refractory chronic testicular pain.

The effectiveness of GFM may be attributable to its targeted action on the genitofemoral nerve. The genital branch of the genitofemoral nerve, along with the inguinal nerve, provides the primary somatic innervation of the testicle.[2] The proposed pathophysiology of chronic testicular pain involves hypersensitivity and spontaneous firing of sensory nerve fibres in the spermatic cord, potentially driven by peripheral nerve plasticity or repeated simulation.[8] This phenomenon results in a reduced activation threshold, increased frequency of action potentials, and ultimately autonomous nerve firing without external stimuli.[2] PNS works through the concept of counterirritation, which aligns with the gate control theory of pain. According to this theory, non-painful stimuli delivered through large-fibre neurons could effective "close" the smaller pain fibre "gates", reducing the perception of pain.[9] Thus, the targeted stimulation of the genitofemoral nerve via GFM capitalises on this mechanism by providing such competing sensory input, which subsequently closes the pain gates and reduces the sensation of chronic testicular pain.

PNS is an emerging field in adjunctive analgesic therapies in managing chronic pain conditions. While the concept of PNS has been in practice since the early 19th century, it has experienced a resurgence in popularity driven by the growing demand for non-opioid pain management options. PNS has been well established as a viable option for treating chronic pain conditions such as lower back pain, cervical radiculopathy, and neuropathic pain syndromes.[3] In the context of chronic testicular pain, our study contributes to this body of literature by demonstrating GFM's potential to manage a condition notoriously difficult to treat.

To our knowledge, there have only been two case reports published on the use of PNS for chronic testicular pain. Rosendal et al describes the successful application of PNS, positioned using x-ray guidance and anatomical landmarks, in a 30-year-old male with chronic testicular pain following testicular surgery. In this case, the pain score decreased from 9/10 to 2/10 at seven months post-surgery.[6] Dana et al describes using PNS, positioned using ultrasound guidance, for a 42-year-old male with chronic testicular pain, however, leaving the IPG external to the patient's body. In this case, the patient experienced a pain reduction from 9/10 to 1/10 at five months.[5] Our study expands upon these reports by applying GFM to a small series of patients, further suggesting that GFM may provide consistent pain relief across a broader age range and clinical background.

The significant reduction in opioid use observed in this study is an important consideration, especially in the context of the current opioid crisis. Chronic opioid therapy is associated with numerous risks, including the potential for abuse

and misuse.[10,11] GFM offers a non-pharmacological alternative, which eliminates the risk of dependency and mortality associated with opioids, whilst concurrently managing the patient's pain.[10]

Although this study demonstrates the feasibility and early efficacy of GFM, several limitations must be acknowledged. All GFM procedures were performed under GA, primarily due to patient preference and logistical considerations of our setup. In an Australian context, the availability and accessibility of theatre facilities makes GA a more straightforward and practical option compared to local anaesthesia (LA). While performing GFM under LA is an option that could be explored in future studies, it may require adjustments to infrastructure and patient preparation protocols to ensure comfort and procedural success. The small sample size and absence of a control group limits the ability to generalise these findings. Additionally, the short follow-up period may not capture long-term outcomes, including durability of pain relief, potential complications, or risk of recurrence. Future studies should aim to include larger cohorts and longer follow-up periods to further establish the safety and efficacy of GFM in this patient population. Additionally, while our study used the NRPS as the primary outcome measure, future studies should incorporate additional measures of functional outcomes, quality of life and patient satisfaction to provide a more comprehensive evaluation of GFM's impact.

Conclusion

GFM presents a novel approach to managing chronic testicular pain that has proven resistant to conservative and surgical treatments. The observed reduction in pain scores in this cohort, coupled with the decreased reliance on opioid medications, suggests that GFM may be a viable treatment option. By directly targeting the genitofemoral nerve, GFM offers a promising solution for patients suffering from refractory chronic testicular pain, filling a critical gap in the management of this challenging condition.

Data Sharing Statement

All data generated or analysed during this study are included in this published article.

Ethics Approval and Consent to Participate

Ethics approval and consent to participate obtained from all patients.

Consent for Publication

Consent obtained from all patients for publication.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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