

## Review Article

# Chronic Testicular Pain: A Review of Aetiology and Management

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**Abstract:** Chronic testicular pain affects a growing number of men worldwide. The approach to diagnosis and treatment is variable, resulting in treatment delays of reversible causes that may increase the probability of progression to chronic pain. A large proportion of men have no reversible cause identified and delayed recognition and management of this issue can cause significant morbidity. In this article, an approach to diagnosis and a review of treatment modalities available to manage chronic testicular pain is presented. Randomised control trials and current protocols for management were reviewed, in addition to case series and single-centre experiences of specialists with an interest in managing this condition. It is evident that chronic testicular pain should be managed with a multidisciplinary approach, to address the complex psychosocial elements often co-presenting with chronic pain. Various treatment options are available including medical therapy, non-invasive physiotherapy techniques and invasive surgical techniques. There is good evidence emerging for microsurgical techniques and nerve blocks. More research is required to determine the most effective duration and repetition of treatments. Chronic scrotal pain is physiologically related to other chronic pain syndromes and more research is required to determine the mechanisms behind this and potentially target chronic pain at a cellular level. In summary, chronic testicular pain affects a large number of men and further investigation into aetiology is important to direct treatment. A range of interventions are available -it is recommended that conservative treatments are trialed first in a multidisciplinary setting.

**Keywords:** Testicular Pain, Pelvic Pain, Chronic Pain, Men

## 1. Introduction

Chronic testicular pain is often a diagnostic and therapeutic dilemma for men's health professionals. With increasing awareness of men's health issues in the community, the number of presentations with testicular pain continues to grow [1]. Over 100,000 men in the USA alone suffer from chronic testicular pain, while the estimated incidence in the UK is 1% [1, 2]. It is vital that health professionals are equipped to deal with this growing problem. One estimate suggests patients will see on average 4.5 urologists in seeking help for chronic scrotal pain [3], and the wide variety of treatment options supports the notion that there is no perfect solution for the condition. Although chronic scrotal

pain is often associated with preceding vasectomy, inguinal hernia repair and other scrotal surgery, up to a quarter of patients will have no obvious cause [4]. Reflective of the diverse aetiology, the available treatments include physiotherapy, psychology, pharmaceutical and surgical options.

## 2. Pain Physiology

There are two well-described pathways associated with scrotal pain, both of which may result in chronic pain as a consequence of mechanisms relatively less understood and likely multifactorial [5]. Chronic pain is defined as intermittent or constant pain for at least three months, either

in association with an initial stimulus or when no inciting factor can be identified [6].

Direct stimulation of nociceptors (free nerve endings in somatic and visceral tissues) by any noxious insult leads to transduction and potentiation of this signal via the dorsal horn of the spinal column to various areas of the brain [7]. Brainstem nuclei release neurotransmitters involved in descending modulation of the signal. Beyond the thalamus, pain signals may be distributed to somatosensory cortex, limbic system, insula and frontal lobes [8]. This type of pain is often described as sharp, aching or throbbing.

Neuropathic pain, described as burning, tingling or shooting, is a result of disruption to the peripheral or central nervous system directly -examples include spinal nerve trauma, diabetic neuropathy and herpes zoster infection [8]. Neuropathic scrotal pain has been described in association with damage to inguinal nerves following surgery [9], and with non-scrotal pathologies such as vertebral disc protrusion and sacroiliac joint dysfunction [10].

Wallerian degeneration involves a cascade of events -ultimately, demyelination of the nerve axon distal to the site of injury and establishment of a micro-environment free of debris is the aim, establishing conditions conducive to healing and regeneration of the nerve [11]. There are a range of immune cells and signaling molecules employed during this process which contribute to nerve regeneration. It is thought that immune factors induced by Wallerian degeneration may persist abnormally, resulting in chronic inflammation and neural sensitization. A study retrospectively reviewing 57 tissue biopsies found evidence of Wallerian degeneration in 84% (n=48) of samples from patients with chronic scrotal pain compared with 20% (n=10) of control samples [11].

Neuroplasticity describes changes thought to occur in pain pathways and other areas of the brain, where neural sensitization from repetitive stimuli such as injury or inflammation leads to hypersensitivity [12]. This results in pain pathways firing at first in a modulated fashion -small stimuli result in larger magnitude responses than would normally be expected, latency periods are reduced and ultimately nerves may fire in the absence of any stimulus [13]. This is perceived as pain out of proportion to what would be expected from the initial stimulus (hyperalgesia) and pain sensation resulting from stimuli that do not normally cause pain (allodynia) [14].

Another proposed mechanism is impaired inhibition from descending neuromodulators. Upon reaching brainstem nuclei, neurotransmitters including noradrenalin, serotonin and GABA are released, descending the spinal tracts to inhibit further transmission of pain signals [14]. Impaired or reduced release of neurotransmitters is also described in depression, accounts for the therapeutic benefit of antidepressants in chronic testicular pain and may explain the frequent coexistence of depression and chronic pain in the individual [15].

Contribution from affective and emotional pain centres may also affect how pain is perceived and contribute to prolongation of pain perception beyond initial stimulus for some people [16], and there is some evidence that increased sensitivity to alpha adrenergic stimulation could lead to

spasms or pain sensation due to receptors being present in the vas and epididymis [17].

In summary, various biochemical processes including inflammation, neuroplasticity, neuromodulation and Wallerian degeneration, as well as individual factors relating to pain perception may contribute to chronic pain. It is important to identify the source of pain if injury or reversible cause is present, as delays in appropriate treatment can make the evolution to chronic pain more likely through any of the described mechanisms.

### 3. Diagnosis

Many patients with chronic testicular pain will have been dismissed by health practitioners after having multiple normal investigations often including microscopy/culture, bloods and physical examination. Scrotal ultrasound is the initial imaging modality of choice in order to exclude obvious pathology such as testicular malignancies, however it frequently returns no clear causative pathology. It is crucial to establish a good rapport with these patients early [1].

A thorough history and examination is always a part of diagnosis. Once obvious causes have been excluded (trauma, previous surgeries, infection, scrotal contents pathology and non-urological problems), the pain itself should be discussed in detail. Type of pain -nociceptive (dull aching) vs neuropathic (burning, hypo or hyperaesthesia) [18], and the aggravating and alleviating factors can help guide further investigation and may assist in treatment selection, or predict efficacy of certain treatments [19]. Types of pain can overlap and are not fully independent of each other, multimodal treatment is likely to be required for patients with aetiological uncertainty.

MRI is a useful tool in finding causes of pain that may have been missed. These include prostatitis, bony fractures, osteomyelitis, labral tears and anal problems. MRI is an expensive investigation but has shown to change management in 34% of cases, but only 23% of cases when ordered by a urologist [20]. Other imaging modalities such as CTIVP, plain CT, voiding cystourethrogram are of little benefit unless specifically indicated by history or examination [7].

### 4. Treatments

#### *MEDICAL*

Medical treatments have centred around pain relief and neuromodulation. Non-Steroidal anti-inflammatory Drugs (NSAIDs) have been the initial treatment for this condition and along with paracetamol have usually been employed prior to the patient presenting for specialist input [15]. Similarly, antibiotics are often trialled early in the course of treatment, often as first line therapy without objective evidence of infection [15]. There is a large disparity between antibiotic prescribing practices and infection contributing to aetiology of chronic testicular pain. One review of Swiss urologists found that 82% prescribed antibiotics empirically, while of those prescribed antibiotics only 22% were ultimately found to have evidence of infection [21]. Doxycycline and quinolone antibiotics provide the highest

tissue concentrations [7] and are widely used, however they show little benefit long term and do not symptom duration in cases lacking an identifiable infective cause [22].

Neuromodulation drugs such as gabapentin can give a significant improvement in pain with >50% reduction of pain in 61.5% of patients noted in one study [23]. Tricyclic antidepressants have also been found to improve chronic pain (>50% reduction in 66% of patients trialled on nortriptyline) [23]. Both classes likely enhance descending inhibition of pain pathways and have been shown to be effective in patients for whom NSAIDs and antibiotics have failed [23]. In addition, many patients for whom chronic testicular pain coexists with psychiatric disorders such as somatisation disorder and depression can benefit from treatment with antidepressants, improving both mood and pain perception [1].

There is some evidence that optimising testosterone levels and B12 levels will also result in an improvement in pain. This has been shown to give a significant improvement in 65% of patients [24].

#### PHYSICAL

Transcutaneous electrical nerve stimulation has been shown to improve quality of life for patients with chronic testicular pain. A small randomised control trial of patients with idiopathic testicular pain compared TENS and simple analgesia with the latter alone [25]. The TENS group were found to have significant sustained improvement in quality of life over a short follow up period. Advantages include the non-invasive and low-cost nature of TENS, and the capacity for repeated treatments. Further research regarding optimal timing and duration of treatment is required. In addition, pelvic floor training administered by trained physiotherapists has achieved good results for men with more generalised chronic pelvic pain [26].

#### PSYCHOLOGICAL

Psychological support is integral to patients with all types of chronic pain, as psychiatric conditions may manifest as, or coexist with pain syndromes [7]. Psychosocial history is an important component of evaluation that may reveal potential barriers to pain improvement such as depression, or predisposing factors such as prior sexual abuse [4]. The effect of chronic testicular pain on men's self-esteem, sexual function and relationships lacks standardised assessment and is rarely described in management of the condition, despite increasing suggestion that these issues are common. Of concern is that some men may feel more comfortable addressing the 'physical' component of chronic pain by engaging in invasive procedures, rather than address the contribution of psychosomatic components of pain. This may lead to unnecessary procedures being performed, or limit the success of operative interventions [4].

#### SURGICAL

##### *Nerve blocks*

Genitofemoral and ilioinguinal nerve blocks have been used in both diagnosis and treatment of chronic testicular pain. A mixture of long acting local anaesthetic with steroid has been used in multiple trials with good effect. Local anaesthetic alone may also be used. Therapeutically, blocks aim to break

the pain cycle by downregulating pathways affected by hypersensitivity [27]. Blocks can result in pain relief for up to 12 hours depending on the anaesthetic agent used. Patients have also reported improvements in pain after the effects of the initial injection have worn off, as well as diminishing pain with subsequent treatments. Nerve blocks are an effective short term treatment for chronic scrotal pain, show promising durability with repeated injections [28] and are also useful in predicting the efficacy of more invasive measures such as microsurgical denervation [19].

##### *Microsurgical Denervation*

The microsurgical denervation of the spermatic cord is a well-established destructive technique for the management of testicular pain. Microsurgical denervation is indicated after a nerve block resulting in pain relief. In one of the largest randomised controlled trials, 86.2% of patients had a greater than 50% reduction in pain, with 51.7% achieving complete resolution of pain [29]. This procedure involves the division of all cremasteric fibres and nerves with bipolar diathermy. The aim is disruption of all neural tissue with preservation of lymphatics, vasculature and vas deferens. Risks include ischaemic testis due to inadequate preservation of arteries, hydrocele and haematoma [7].

##### *Neuromodulation*

Both peripheral and spinal neuromodulation has been described in patients with refractory pain, specifically post-surgical intervention eg inguinal hernia repair. The sandwich technique for peripheral stimulation has been shown to decrease pain by at least 50% and has an 85% satisfaction rating. The studies in this area are still small but promising [9] Central (Spinal cord) stimulation has also been used with some effect. The numbers in the studies are still small, but equally promising [30].

##### *Orchidectomy*

The loss of a testicle for pain is always a procedure of desperation. This should never be an initial treatment option. Occasionally, nothing else works and this is the last resort. The role and success rates of orchidectomy vary widely and should only be offered if the patient is fully amenable to the risks [31] There are studies showing pain cure rates as high as 73% [32] but also as low as 20% [33]. It does appear that a high ligation (inguinal approach) provides better relief than a scrotal approach [32].

## 5. Conclusion

Chronic testicular pain is an emerging men's health issue with complex aetiology. Physical and psychosocial evaluations are important for excluding easily reversible causes and establishing a framework for multidisciplinary treatment. Whilst there are many interventions available, a stepwise approach is advised with conservative options explored first. This process is best coordinated by a single treating doctor to avoid unnecessary delays in effective treatment and potentially avoidable perpetuation of pain. More research is required to investigate the pathophysiology of chronic pain and efficacy of available interventions.

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