Topical Cannabidiol for the Treatment of High Tone Pelvic Floor Dysfunction

Abstract

Pelvic pain can be a debilitating and difficult condition to treat. High tone pelvic floor dysfunction is a known cause of pelvic pain that can be often overlooked. As gynecologists we frequently encounter these patients and currently have limited treatment options. The use of cannabidiol to treat this disorder has not been explored. In this proposal we seek to answer if topical cannabidiol can be used as a treatment for high tone pelvic floor dysfunction. We hypothesize that the use of intravaginal cannabidiol will result in improved pain scores in patients with HTPFD.

Background and Significance

High tone pelvic floor dysfunction (HTPFD) or levator myalgia is a condition characterized by chronic pelvic pain reproducible upon palpation of levator ani and obturator internus muscles at the time of vaginal exam[1]. Pelvic floor physical therapy can be considered the gold standard treatment for this condition, but compliance is low, with a recent study estimating 19.4% full compliance with therapy[2]. Pharmacologic treatments, such as intra-vaginal baclofen, intra-vaginal diazepam, and trigger point injections, have been studied with mixed results[3-6]. Recently the use of cannabidiol (CBD) has been explored as an anti-inflammatory agent and for the treatment of myofascial pain conditions such as temporomandibular disorders (TMD)[7-10]. A study by Nitecka-Buchta et al. concluded that topical application of CBD over the masseter muscle in patients with TMD resulted in reduced muscle activity and reduced pain intensity[9]. Anecdotally, the use of CBD decreases pain in patients with HTPFD but there is a lack of high-quality data. We hypothesize that nightly use of intra-vaginal CBD for 30 consecutive days will result in decreased pain scores and decreased resting pelvic floor tone as determined by surface electromyography.

Study Design

Hypothesis and aims:

Part A*:*

Primary Aim: To detect 15mm difference in baseline pain scores in women with HTPFD using intravaginal CBD compared to placebo.

Secondary Aim:

Part B:

Primary Aim: To compare pro-inflammatory cytokines levels in vaginal secretions of women with HTPFD treated with intravaginal CBD

Secondary Aim: To evaluate systemic absorption of intravaginal CBD

P – women over 18 yrs of age who report persistent pelvic pain of 6 or more on a 10 point visual analogue scale at least 50% of the time over the past 3 months and pain on palpation (6 out of 10) of at least one pelvic floor muscle group

I – CBD 50mg intravaginal suppositories once nightly for 30 days

C – placebo

O – Reduction in pain scores

Methods: Women with a clinical diagnosis of HTPFD will be randomized to CBD 50 mg vaginal suppository nightly vs placebo for 30 days. At initial visit the following baseline assessments will be obtained i) four visual analogue scales (pain level right now, average or typical pain level, pain level at best, and pain level at worst), ii) vaginal exam with modified Oxford scale, iii) vaginal surface EMG measurements using Thought Technology® vaginal EMG sensor (or similar device) and iv) validated questionnaires: Female Sexual Function

Index (FSFI) and Patient Global Impression of Severity (PGI-S). These same measurements will be repeated after completion of treatment (days 30-35) and Patient Global Impression of Improvement (PGI-I) will be added.
The second part of the study, if funding permits, will consist of vaginal swabs collection before and after treatment for assessment of pro-inflammatory cytokines using MILLIPLEX® technology. Plasma will be collected at the second visit to assess systemic absorption of CBD by gas chromatography.

Sample size calculation:
Based on a review of VAS reporting in endometriosis-related chronic pelvic pain trials, a typical mean (SD) baseline pain score is 58.9 (17.3)mm.[11] To detect a 15mm difference in pain score, which is a commonly used MID in pain studies, presuming 90% power and alpha 0.05, and accounting for 15% loss to follow up or withdrawal, we will enroll 33 patients per arm.

Inclusion Criteria	**Exclusion Criteria**
> 18 y/o	Current pelvic floor PT
Non pregnant	Pelvic floor surgery in prior 6 months
Clinical diagnosis of HTPFD	Known gynecological malignancy
Desire for sexual activity	Active PID
	Current cannabis use
	CBD allergy
	Current opioid use
	Breastfeeding

Feasibility:
HTPFD is a relatively common condition seen in practice. In our clinic we see approximately 5-8 patients with high tone pelvic floor per week. Assuming 5 sites and enrollment of 2-3 patients per week per site we anticipate to complete enrollment in 6 months.

Budget:

Part A
CBD suppositories: $5500 (Endoca® or similar) pricing $52/10 suppositories – Endoca willing to donate
Placebo suppositories: $1350 (Coconut oil, can consider hyaluronic acid)
Vaginal EMG: $630 per site (MyoTrac electromyograph plus vaginal probe). Consider surface EMG and use UDS machine if available
Statistical support: $2000
Total budget without molecular analysis: $6,500 (with CBD suppositories donation and 5 sites)

Part B
Vaginal swabs and media: $800
MILLIPLEX 96 well plate with multiple analytes: $20,000 (4 plates needed to run samples in duplicate)
Plasma collection tubes: $500
Patient compensation: $100 per subject: $6,600
Gas chromatography for CBD identification: $20,000
General supplies: $5,000
Total Budget: $59,400

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