Systematic Review of Botulinum toxin injection for Vestibulodynia: Preliminary Results

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Introduction

Provoked vestibulodynia (PVD), the most common cause of sexual pain, affects up to 16% of pre-menopausal women, yet no established standard treatment exists. Although multiple randomized controlled trials (RCTs) have evaluated botulinum toxin for PVD, their findings have not been quantitatively synthesized in a PVD-specific systematic review and meta-analysis. This review aims to evaluate the efficacy and safety of botulinum toxin for PVD, with secondary objectives of examining dose-response effects and complication rates [1].

Methods

The protocol itself has already been published as a Cochrane Review (DOI: 10.1002/14651858.CD016202)[1], and approval for this preliminary report has been obtained from the Cochrane Editorial Board. This systematic review is being conducted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions [2] and following MECIR standards, and is reported in line with PRISMA 2020 guidelines [3]. As this review used previously published data and did not involve human participants or individually identifiable information, IRB approval was not required. CENTRAL, Ovid MEDLINE, Embase, and CINAHL were systematically searched in April 2026 RCTs examining the use of botulinum toxin for the treatment of PVD were included. Two authors independently screened titles, abstracts, and full texts, with disagreements resolved by a third author. Four authors independently extracted data, with disagreements resolved through discussion. Risk of bias was assessed independently by two authors using the Cochrane RoB 2 tool, with disagreements resolved through discussion between the two assessors. Data synthesis for the remaining outcomes is ongoing.

Results



Analysis 1.1: Pain during intercourse, VAS 0–100 at 3 months — BotoxA any dose vs placebo

Study or Subgroup	BotoxA Mean	BotoxA SD	BotoxA Total	Placebo (saline) Mean	Placebo (saline) SD	Placebo (saline) Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F
Haraldson 2020	51.7	25.7	44	59	25	44	53.5%	-7.30 [-17.89 , 3.29]	+ - ? + -
Pelletier 2025	50	30	28	74	22	29	46.5%	-24.00 [-37.70 , -10.30]	+ - - + ? -
Total (Wald [a])			**72**			**73**	**100.0%**	**-15.06 [-31.39 , 1.26]**	
95% prediction interval								[-40.60 , 10.48]	

Test for overall effect: Z = 1.81 (P = 0.07)

Heterogeneity: Tau² (REML [b] , 95% CI) = 100.42 [0.00 , >1004.2090293327365]; Chi² = 3.57, df = 1 (P = 0.06); I² = 72%

Favours botulinum toxin A / Favours placebo (-100, -50, 0, 50, 100)

Analysis 2.1: Pain upon pressure, touch, or other trigger, VAS 0-100 at 3 months

Study or Subgroup	BotoxA Mean	BotoxA SD	BotoxA Total	Placebo (saline) Mean	Placebo (saline) SD	Placebo (saline) Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A B C D E F
Diomande 2019	61.2	22.5	20	65	13.1	12	57.4%	-3.80 [-16.14 , 8.54]	+ + + + ? ?
Pelletier 2025	12	21	28	34	33	29	42.6%	-22.00 [-36.31 , -7.69]	+ + + + ? ?
Total			**48**			**41**	**100.0%**	**-11.56 [-20.90 , -2.22]**	

Test for overall effect: Z = 2.42 (P = 0.02)

Heterogeneity: Chi² = 3.56, df = 1 (P = 0.06); I² = 72%

Favours botulinum toxin A / Favours placebo (-100, -50, 0, 50, 100)

Analysis 3.1: Sexual function (FSFI), 2.0–36.0 at 3 months — any dose

Study or Subgroup	BotoxA Mean	BotoxA SD	BotoxA Total	Placebo (saline) Mean	Placebo (saline) SD	Placebo (saline) Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A B C D E F
Pelletier 2025	18.4	8.4	28	14.9	7.6	29	50.0%	3.50 [-0.66 , 7.66]	+ + + + ? ?
Petersen 2009	17.87	8.14	25	9.18	6.87	25	50.0%	8.69 [4.51 , 12.87]	+ - + + ? -
Total (Wald [a])			**53**			**54**	**100.0%**	**6.09 [1.01 , 11.18]**	

Test for overall effect: Z = 2.35 (P = 0.02)

Heterogeneity: Tau² (REML [b]) = 8.94; Chi² = 2.98, df = 1 (P = 0.08); I² = 66%

Favours placebo / Favours botulinum toxin A (-100, -50, 0, 50, 100)

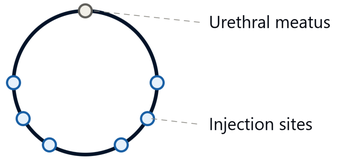
Footnotes

[a] CI calculated by Wald-type method.

[b] Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias



Vulvar vestibule, posterior view
Submucosal injections, bilateral

BoNT-A injection — Vestibular submucosa → **Blocks ACh release** — At nerve terminal → **Muscle relaxation** — Reduces pain

Results

Five RCTs, conducted from 2009 to 2025 in Europe and North America, provided usable outcome data and randomized 305 adult women with clinically diagnosed PVD [4-9]. Meta-analyses were conducted using Review Manager (RevMan).

Pain during intercourse: botulinum toxin may offer a reduction on a visual analogue scale 0-100, but this did not reach statistical significance (MD −15.06, 95% CI −31.39 to 1.26; I^2 = 72%; low-certainty evidence). Heterogeneity may reflect differences in dose, participant characteristics, or outcome assessment.

Pain upon pressure or touch: some improvement appeared at 3 months on a visual analogue scale 0-100 (MD −11.56, 95% CI −20.90 to −2.22; I^2 = 72%; low-certainty evidence). Findings on pain upon pressure or touch were inconsistent: one study showed reduced pain after botulinum toxin A, while other measures (cotton swab and dilator-induced pain) showed little to no clear difference from placebo, limiting confidence in its overall effect on provoked pain sensitivity.

Sexual function: botulinum toxin may improve Female Sexual Function Index scores (MD 6.09, 95% CI 1.01 to 11.18; I^2 = 66%; low-certainty evidence). However, interpretation is limited by the small number of studies and trial heterogeneity, and dose subgroup analysis showed no evidence of a dose-response relationship.

Safety: injection-site pain was the most commonly reported adverse event and was generally transient and mild to moderate.

Quality of life: limited single-study data suggested improvement, but meta-analysis was not feasible.

Discussion

These preliminary findings suggest botulinum toxin may improve pain and sexual function in PVD, but substantial heterogeneity, imprecision, and low-certainty evidence limit confidence in these findings. Early results for provoked pain, quality of life, and adverse events appear inconsistent or imprecise, and synthesis of these outcomes remains ongoing. Given the current evidence base, our findings should be interpreted with caution pending completion of the full review.

Eligibility criteria and outcomes
Overview of included studies and syntheses
Main analyses
References