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The Efficacy of Botulinum Toxin A in Treating Palmar Hyperhidrosis – a Literature Review

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ABSTRACT

Background: *Palmar hyperhidrosis, a condition characterized by excessive sweating in the palms, considerably impacts the quality of life (QoL). Although various treatment modalities are available, the efficacy and safety of Botulinum toxin type A (BTX-A) needed further investigation.*

Methods: *We conducted a literature review, with open-label, controlled trial, double-blind placebo-controlled and observational designs being eligible for inclusion, according to the PRISMA guidelines.*

Results: *All the six selected studies consistently reported the efficacy of BTX-A in reducing symptoms of hyperhidrosis, without significant side effects. Botulinum toxin type A treatment was found to improve the QoL significantly, to reduce sweat rate and production and to have no detrimental effect on grip strength. The duration of the antisudorific effect also indicated the potential for long-term management of palmar hyperhidrosis with BTX-A.*

Conclusion: *Our findings corroborated the effectiveness and safety of BTX-A in managing palmar hyperhidrosis across diverse patient outcomes and experiences. Botulinum toxin type A emerged as a promising treatment modality for this condition, capable of improving the QoL, reducing symptoms and offering long-term relief without significant side effects.*

Keywords: hyperhidrosis, botulinum toxin type A, BTX-A, quality of life, systematic review, sweat rate, sweat production.

INTRODUCTION

Hyperhidrosis, characterized by excessive and uncontrollable sweating beyond physiological needs, is a chronic dermatological condition that significantly impacts the quality of life (QoL) (1). This ailment subdivides into primary and secondary hyperhidrosis, with the former typically localized to specific body regions such as the palms, soles, axillae, and face (2). Palmar and digital hyperhidrosis, the focus of this review, are particularly debilitating forms of primary hyperhidrosis, causing serious social, psychological, and occupational implications for patients (3).

The pathophysiology of palmar hyperhidrosis (PH), while not entirely elucidated, is generally

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attributed to hyperactivity of the sympathetic nervous system, resulting in overstimulation of eccrine sweat glands (4). Current treatment modalities for palmar and digital hyperhidrosis range from topical antiperspirants, oral medications, iontophoresis, to invasive options like endoscopic thoracic sympathectomy. However, these treatments present a range of side effects and variable efficacy, creating a pressing need for effective and tolerable therapeutic alternatives (5).

Botulinum toxin type A (BTX-A or BoNT-A) has emerged as a promising treatment for hyperhidrosis. BoNT-A is a potent neurotoxin produced by *Clostridium botulinum* that inhibits acetylcholine release at the neuromuscular junction, effectively reducing eccrine sweat gland activity (6). Several studies have reported the successful use of BoNT-A in treating axillary hyperhidrosis, but its efficacy and safety in treating palmar and digital hyperhidrosis remain less well-established (7).

The biological activity of BoNT-A is subject to change, contingent upon the specific toxin subunit and the method employed for its preparation (8). This characteristic contributes to the flexibility of BoNT-A's therapeutic usage, allowing for tailored treatment strategies. The mechanism of action of BoNT-A is primarily through its ability to inhibit the release of acetylcholine and other neurotransmitters from presynaptic vesicles at the neuromuscular junction (4). This effect results in a reduction of involuntary muscle activity, offering a lasting therapeutic impact. Importantly, this action occurs without triggering neurodegeneration, preserving the structural integrity of the nervous system while still delivering the desired therapeutic effect.

Given this background, our literature review aims to systematically analyse the current body of research investigating the therapeutic application of BoNT-A for palmar hyperhidrosis. This review assessed the efficacy, safety, and patient-reported outcomes of BoNT-A therapy, providing a comprehensive overview of its role as a potential treatment modality for this challenging condition. ❑

MATERIALS AND METHODS

Review design

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (9) were used to conduct this literature review. The PRISMA checklist and flow diagram served as the framework for study selection, data extraction, and subsequent synthesis. This ensured a systematic and transparent approach.

The PECO protocol for the present review comprised the following elements:

- Population (P): adults with palmar hyperhidrosis
- Exposure (E): therapy with BTX-A
- Comparison (C): other treatments or control groups
- Outcome (O): efficacy of BTX-A therapy for palmar hyperhidrosis.

Search databases

Four databases – PubMed, Embase, Scopus, and the Cochrane Library – were systematically searched to identify relevant studies. The search was carried out from the inception of the databases until September 2023. The search strategy combined terms related to 'Hyperhidrosis', 'Palmar Hyperhidrosis', and 'Botulinum Toxin Type A'. Both MeSH (Medical Subject Heading)

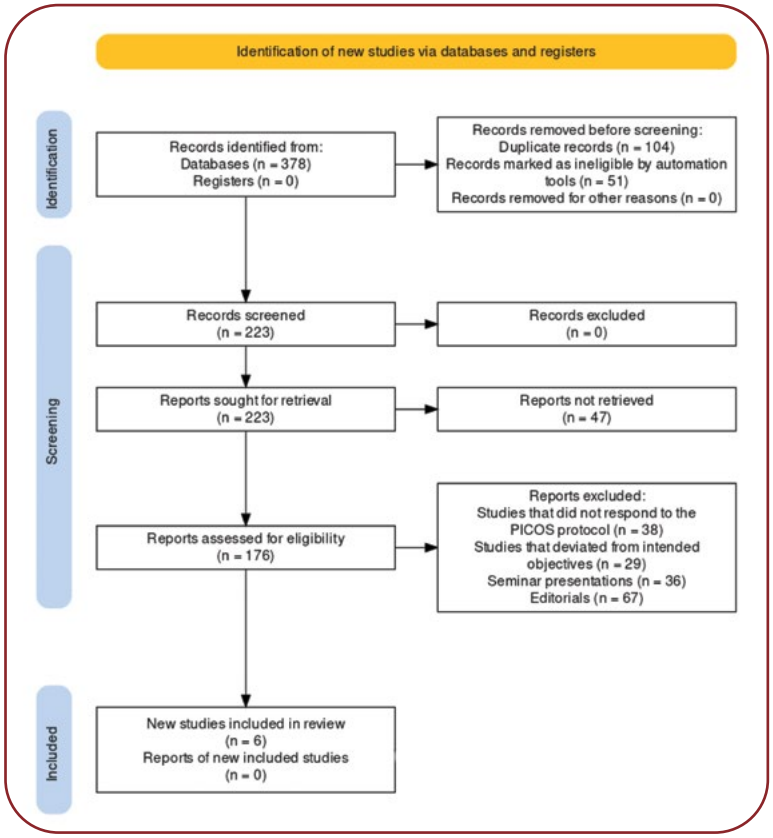

FIGURE 1. PRISMA protocol for the review

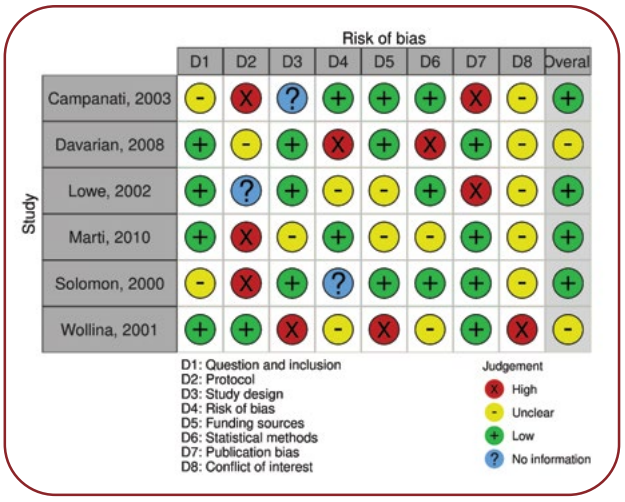

FIGURE 2. Assessment of bias in the selected papers

terms and free-text terms were used to maximize the search sensitivity.

Inclusion and exclusion criteria

Studies were included if they were original research articles (both randomized controlled trials and observational studies) that investigated the efficacy of BTX-A therapy for palmar hyperhidrosis in adults. Studies were excluded if they were case reports, letters, editorials, commentaries, reviews, or if they investigated other types of hyperhidrosis or other types of treatment. Studies not written in English were also excluded. Two independent reviewers screened the titles and abstracts of the identified articles. Any discrepancies between reviewers were resolved by consensus or by a third reviewer.

Bias assessment

The risk of bias in the included studies was assessed using the Newcastle-Ottawa Scale (NOS). The NOS tool (10) was used to evaluate three aspects: the selection of the study groups, the comparability of the groups, and the ascertainment of the outcome of interest as shown in Figure 2. ❑

RESULTS

Following the PRISMA guidelines, we initially identified 378 studies through databases. After removing 104 duplicates and 51 records marked as ineligible by automation tools, we screened 223 records. All 223 were sought for retrieval, but 47 were not retrieved, leaving 176 for eligibility assessment. After exclusion of studies that did not meet the criteria (38 did not adhere to PICOS protocol, 29 deviated from objectives, 36 were seminar presentations, and 67 were editorials), six studies were included in the review.

The selected studies exhibited varied risk of bias across different domains. For questions and inclusion criteria, most studies showed a low risk, but some concerns were present in the studies by Campanati (2003) and Solomon (2000) (7, 11). Regarding protocols, high risk of bias was noted in the studies by Campanati (2003), Solomon (2000) and Marti (2010) (7, 11, 12). Study design risk of bias was predominantly low, with some concerns in studies conducted by Marti (2010), Lowe (2002) and Wollina (2001) (12, 13, 14). Funding sources, statistical methods, and publication bias mostly reflected low risk, but there were notable exceptions such as high publication bias in studies published by Campanati (2003) (7) and Lowe (2002) (13), high statistical methods bias in a study by Davarian (2008) (15), and high funding sources bias in Wollina's study (2001) (14). Conflicts of interest generally raised some concerns, with an exception of a high risk in Wollina's study (14). Despite these findings, the overall risk of bias was considered low in most studies, except for Davarian's study (15), which was unclear, and Wollina's study (14), which raised some concerns.

Table 1 presents the findings from the six papers, each investigating the effects of BTX-A treatment on palmar hyperhidrosis. In 2003, Campanati *et al* conducted a study with an open-label design which included 41 participants. It evaluated the QoL using Dermatology Life Quality Index (DLQI) scores before and after treatment (7). In 2008, Davarian *et al* conducted a controlled trial involving eight participants. They assessed both the sweat rate, measured *via* gravimetry and iodine-starch tests, and QoL, *via* DLQI scores (15). In 2002, Lowe *et al* performed a double-blind, placebo-controlled trial with 19 participants. They evaluated sweat production through gravimetric measurement, severity rating by the physician and patient, and grip strength (13). ❑

DISCUSSION

Campanati (2003) found that BTX-A treatment significantly improved the QoL in patients

TABLE 1. Selected studies and their drawn inferences

Study ID	Study design	Sample size (n)	Parameters assessed	Results observed	Overall inference drawn
Campanati, 2003	Open-label	41	QoL (DLQI scores) before and after treatment	QoL improved significantly post BTX-A treatment regardless of the number or types of sites involved (P<0.001).	BTX-A treatment significantly improved the quality of life (QoL) in patients with axillary and palmar hyperhidrosis.
Davarian, 2008	Controlled trial	8	Sweat rate (gravimetry, iodine-starch tests), QoL (DLQI scores)	Significant reduction in sweat rate observed post BTX-A treatment for up to three months in the right hand and up to four weeks in the left hand (P<0.05). No notable side effects reported.	Iontophoresis of BTX-A effectively reduced sweating rate for at least three months without causing any pain, muscle weakness, or other side effects.
Lowe, 2002	Double-blind, placebo-controlled	19	Sweat production (gravimetric measurement), severity rating by physician and patient, grip strength	Significant reduction in sweat production with BTX-A versus placebo at day 28 (P<0.05). All patients reported successful treatment with BTX-A. No change in grip strength. Only mild adverse events reported in 21% of patients.	BTX-A was effective and safe for treating palmar hyperhidrosis, reducing sweat production significantly without affecting grip strength.
Marti, 2010	Observational	52	Clinical profile (age, sex, profession, family history, site of hyperhidrosis, accompanying symptoms), time to BTX-A effect, side effects, severity of hyperhidrosis pre- and post-BTX-A	BTX-A treatment significantly reduced hyperhidrosis severity two months after treatment (P<0.001). The majority of patients were women (75%), with onset during puberty (61.5%) and familial hyperhidrosis history (36.5%).	BTX-A was effective in reducing the severity of primary hyperhidrosis, with the treatment being well-tolerated.
Solomon, 2000	Observational	20 (19 completed the study)	Sweat production, duration of anhidrosis, side effects	BTX-A significantly reduced sweat production. Anhidrosis duration varied from four to nine months. Mild thumb weakness occurred in four patients, lasting 3-6 weeks.	Subepidermal injections of BTX-A were effective in reducing sweat production in patients with recalcitrant palmar and digital hyperhidrosis.
Wollina, 2001	Observational	10	Sweat reduction, duration of antisudorific effect, side effects	BTX-A significantly reduced sweating within one week in all patients. The antisudorific effect lasted 12.3 ± 5.5 months with a maximum of 22 months. Repeated treatment retained efficacy. The only side effect was tolerable pain from intracutaneous injections.	Intracutaneous injections of BTX-A were effective and safe in treating severe palmar hyperhidrosis, inducing long-term remission without significant acute and long-term side effects.

with palmar hyperhidrosis, signifying a positive impact beyond symptom management (7). In 2008, Davarian reported that the iontophoresis of BTX-A effectively reduced the sweating rate for at least three months without causing any pain, muscle weakness, or other side effects (15). This underscores the safety and efficacy of a non-invasive BTX-A application method. Lowe's study (13) confirmed that BTX-A was effective and safe for treating palmar hyperhidrosis. It reduced sweat production significantly without affecting grip strength, indicating that the treatment could control symptoms without compromising function.

In 2010, Marti reported that BTX-A was effective in reducing the severity of primary hyperhidrosis, with the treatment being well-tolerated (12). This highlights the patient acceptability and efficacy of BTX-A in managing primary hyperhidrosis. Solomon's study (11) showed that subepidermal injections of BTX-A were effective in reducing sweat production in patients with recalcitrant PH. This suggests that BTX-A could be a viable treatment option even for stubborn cases of hyperhidrosis. Wollina (2001) found that intracutaneous injections of BTX-A were effective and safe in treating severe palmar hyperhidrosis, inducing long-term remission without significant acute and long-term side effects. This study provides evidence of BTX-A's long-term effectiveness and safety profile (14).

Management of severe PH presents a unique set of challenges. Traditional, non-invasive strategies often fail to deliver satisfactory results, while surgical sympathectomy, although efficacious, carries risks of specific complications and even mortality (16). More recently, intradermal BTX-A injections have gained traction as a viable treatment option. By chemically denervating the sweat glands, this approach, initially proposed by Bushara and colleagues, offers both safety and high efficacy, making it a preferred choice for many practitioners in the management of moderate to severe PH (17).

The task of quantifying treatment impacts in PH has been the focus of numerous research attempts, given that indices of patient satisfaction and QoL are inherently subjective (18). Some methods have been employed intraoperatively to real-time monitor the disruption of sympathetic activity. Minor's starch-iodine test, for instance, is a valuable tool to identify hyperhidrosis areas and monitor treatment progress. However, this semi-quantitative method can be cumbersome and time-consuming, particularly in outpatient settings (19).

Gravimetry is another method favored by some researchers, despite its drawbacks including high variability in sweat production measurements and challenges in quantifying smaller sweat volumes (20). More advanced tools, such as transepidermal water loss equipment and evaporation cameras, offer precise quantification of sweat excretion, albeit they are expensive and can only evaluate a small area at a time (21). Therefore, the quest for an optimal, cost-effective, and comprehensive method to evaluate PH treatment outcomes remains a crucial area of research (16).

This review, while informative, has several limitations. The first limitation is the variability in study designs, ranging from open-label, controlled trial, double-blind placebo-controlled, to observational studies. This heterogeneity might have influenced the consistency and comparability of the results. Moreover, the double-blind, placebo-controlled study, regarded as the gold standard in clinical research, was represented by only one study in the present review. Moreover, the sample sizes across the studies were relatively small, with the largest involving only 52 participants. The small sample sizes may limit the generalizability of the findings to the wider population of individuals with hyperhidrosis. Also, the parameters assessed across the studies were varied. While this allowed for a comprehensive evaluation, it also made direct comparison challenging. Furthermore, not all studies assessed the same outcomes, making it difficult to draw firm conclusions on certain aspects such as long-term safety and effectiveness of BTX-A. ❑

CONCLUSION

The findings provided extensive evidence for the beneficial role of BTX-A in managing palmar hyperhidrosis. Despite the differences in study design and parameters assessed, all the studies consistently reported a significant decrease in sweating and improved the QoL following BTX-A treatment, without notable side effects. These results were consistent across a variety of patient experiences and outcomes, suggesting a robust therapeutic effect of BTX-A.

Furthermore, the studies indicated the potential of BTX-A for long-term management of palmar hyperhidrosis. The duration of the observed antisudorific effects suggests that BTX-A not only offers immediate relief from excessive palm sweating but also contributes to sustained improvement over time. However, it is critical to consider the identified limitations when interpreting these results. These include the variability in study designs, small sample sizes, diverse assessed parameters, and potential confounding factors. While the findings strongly support the efficacy and safety of BTX-A for palmar hyperhidrosis, future research should address these limitations to further strengthen our understanding of BTX-A's role in treating this condition. ❑

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