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USE OF BOTULINUM TOXIN IN THE MANAGEMENT OF POST-PAROTIDECTOMY COMPLICATIONS: FREY SYNDROME, SIALOCELE AND SALIVARY FISTULA

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ABSTRACT

Background: Parotidectomy is a commonly performed procedure associated with postoperative complications such as Frey syndrome, sialocele, and salivary fistula, which may significantly impair patient quality of life and require additional management. Botulinum toxin is increasingly used as a minimally invasive therapeutic option in this setting.
Aim: The aim of this study was to evaluate current evidence regarding the use of botulinum toxin in the prevention and treatment of complications following parotidectomy.
Material and methods: This study was designed as a narrative review based on previously published scientific literature. A comprehensive search of PubMed, Scopus, and Google Scholar databases was conducted, including studies published up to 2025. Articles addressing the use of botulinum toxin in Frey syndrome, sialocele, and salivary fistula were included and analyzed qualitatively.
Results: The reviewed studies consistently demonstrated high clinical effectiveness of botulinum toxin in the management of post-parotidectomy complications. In Frey syndrome, most patients achieved substantial or complete reduction of gustatory sweating, with therapeutic effects typically lasting 6–12 months. In cases of sialocele and salivary fistula, botulinum toxin reduced salivary secretion, promoted lesion closure, and shortened recovery time compared to conservative management. Reported adverse effects were uncommon and generally mild and transient.
Conclusions: Botulinum toxin is an effective and safe option in the management of post-parotidectomy complications. Despite the need for repeated administration in some cases, it represents a minimally invasive alternative to surgical treatment. Further prospective studies are required to establish standardized protocols and long-term outcomes.

KEYWORDS

Botulinum Toxin; Parotidectomy; Frey Syndrome; Sialocele; Salivary Fistula; Postoperative Complications

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1. Introduction

Parotidectomy remains a cornerstone in the management of both benign and malignant salivary gland tumors, with the parotid gland accounting for the majority of salivary gland neoplasms (Lambiel et al.,2021). Although advances in surgical techniques have significantly improved functional outcomes, postoperative complications continue to represent an important clinical challenge, affecting both recovery and long-term quality of life (Lambiel et al.,2021; Lee et al., 2021).

Among these complications, Frey syndrome, sialocele, and salivary fistula are frequently encountered sequelae following parotid surgery (Lambiel et al., 2021; Kinberg et al., 2022).

Frey syndrome, also known as auriculotemporal syndrome, is characterized by gustatory sweating, flushing, and warmth of the facial skin in response to salivary stimuli (Marchese et al., 2021; Motz et al., 2016; Wang et al., 2005). Its incidence varies widely, with reports ranging from approximately 10% to over 50% of patients following parotidectomy, depending on diagnostic methods and follow-up duration (Motz et al., 2016; Wang et al., 2005; Wood et al., 2019). In many cases, symptoms appear months or even years after surgery and may significantly impair social functioning and quality of life (Marchese et al., 2021; Wood et al., 2019).

The pathophysiology of Frey syndrome is most commonly explained by aberrant regeneration of parasympathetic nerve fibers (Motz et al., 2016; de Bree et al., 2007). Following surgical disruption, postganglionic parasympathetic fibers intended for the parotid gland reinnervate cutaneous sweat glands and blood vessels. As both systems utilize acetylcholine as a neurotransmitter, this misdirected regeneration results in inappropriate activation of sweat glands during mastication (Wang et al., 2005; de Bree et al., 2007). Alternative mechanisms, such as loss of neural insulation, have also been proposed, but the aberrant regeneration theory remains the most widely accepted (Motz et al., 2016).

In addition to Frey syndrome, fluid-related complications such as sialocele and salivary fistula are common postoperative issues (Lambiel et al., 2021; Kinberg et al., 2022). A sialocele represents a subcutaneous collection of saliva without an external fistulous tract, whereas a salivary fistula involves the leakage of saliva through the skin or surgical wound (Send et al., 2019; Jeffe et al., 2015). The reported incidence of sialocele ranges from approximately 4% to over 16%, while salivary fistula occurs in around 3% of patients, although rates vary depending on surgical technique and extent of resection (Lambiel et al., 2021; Kinberg et al., 2022). These complications may prolong hospitalization, require repeated interventions, and negatively impact patient comfort and satisfaction (Kinberg et al., 2022; Yang et al., 2023).

Despite the availability of numerous preventive and therapeutic strategies, including compression therapy, aspiration, anticholinergic medications, and surgical interventions, no consensus has been established regarding optimal management (Lambiel et al., 2021; de Bree et al., 2007; Chow et al., 2003). Many conventional approaches are associated with limitations, such as discomfort, aesthetic concerns, or risk of additional morbidity (de Bree et al., 2007; Chow et al., 2003). Furthermore, surgical solutions for persistent fistulas may carry a significant risk of facial nerve injury and are not always effective (Send et al., 2019; Pendolino et al., 2018).

In recent years, botulinum toxin (BoNT) has emerged as a promising minimally invasive therapeutic option for the management of parotidectomy-related complications (Send et al., 2019; Maharaj et al., 2020; Graillon et al., 2019).

By inhibiting acetylcholine release at cholinergic nerve endings, BoNT effectively reduces glandular secretion and suppresses aberrant neural signaling (Safarpour, et al., 2023; Marchese-Ragona et al., 2006). This mechanism directly targets the underlying pathophysiology of both Frey syndrome and salivary complications (de Bree et al., 2007; Safarpour, et al., 2023). Numerous clinical studies have demonstrated the efficacy of botulinum toxin in treating Frey syndrome, with significant reduction or complete resolution of gustatory sweating in the majority of patients (Beerens et al., 2002; Jansen et al., 2017; Arad-Cohen et al., 2000; Dulguerov et al., 2000; Laskawi et al., 1998). Similarly, botulinum toxin has been successfully used in the management of salivary fistulas and sialoceles, promoting healing by reducing salivary flow and allowing tissue recovery without the need for invasive procedures (Send et al., 2019; Chow et al., 2003; Marchese-Ragona et al., 2006; Pantel et al., 2013; Laskawi et al., 2013). Additionally, emerging evidence suggests that BoNT may play a role not only in treatment but also in the prevention of these complications following parotid surgery (Lee et al., 2021; Sheykhveisi et al., 2025).

Given the growing evidence supporting its safety, efficacy, and minimally invasive nature, botulinum toxin represents an increasingly important tool in the management of post-parotidectomy complications (Send et al., 2019; Maharaj et al., 2020; Graillon et al., 2019).

However, variability in treatment protocols, dosing, and long-term outcomes highlights the need for a comprehensive evaluation of its clinical utility (Maharaj et al., 2020; Graillon et al., 2019; Alimohammadi et al., 2025).

Therefore, the aim of this review is to summarize current evidence regarding the use of botulinum toxin in the prevention and treatment of Frey syndrome, sialocele, and salivary fistula following parotidectomy, with particular emphasis on mechanisms of action, clinical effectiveness, and future therapeutic perspectives.

2. Materials and methods

This review was conducted in accordance with the principles of narrative and structured literature review methodology. No human participants were directly involved. A comprehensive search of the PubMed, Scopus, and Google Scholar databases was performed to identify studies evaluating the use of botulinum toxin in the management of complications following parotidectomy, including Frey syndrome, sialocele, and salivary fistula.

The following search terms and their combinations were used: “botulinum toxin”, “parotidectomy”, “Frey syndrome”, “gustatory sweating”, “sialocele”, “salivary fistula”, and “postoperative complications”. After removal of duplicate records, titles and abstracts were screened for relevance. Full-text articles were subsequently assessed according to predefined eligibility criteria.

Studies were included if they evaluated complications following parotidectomy, investigated the use of botulinum toxin as a therapeutic or preventive intervention, were original studies, case series, case reports, or review articles and were published in English with full-text availability. Studies unrelated to parotid gland surgery, articles not involving botulinum toxin, conference abstracts without sufficient data, and non-English publications were excluded.

Due to the heterogeneity of study design, treatment protocols, outcome measures, and patient populations, a quantitative meta-analysis was not feasible. Therefore, a qualitative narrative synthesis was performed. The included studies were grouped according to the type of post-parotidectomy complication and analyzed with regard to treatment effectiveness, duration of clinical benefit, recurrence rates, adverse effects, and practical clinical applicability.

3. Results

3.1. Botulinum toxin in the management of Frey syndrome

The strongest and most consistent evidence for the use of botulinum toxin in post-parotidectomy complications concerns Frey syndrome. Across the included studies, botulinum toxin was repeatedly shown to be an effective, minimally invasive, and well-tolerated treatment for gustatory sweating, with rapid symptom relief and relatively long-lasting benefit. In many of the included studies, objective assessment of Frey syndrome was performed using Minor's starch-iodine test, which allows visualization and quantification of the sweating area.

The largest and most comprehensive dataset was provided by Jansen et al., who analyzed 440 botulinum toxin treatments performed in 100 patients over a 16-year period. In this cohort, 70.5% of patients required repeated injections, with a median of four treatments per patient, reflecting the recurrent nature of Frey syndrome. The median interval between treatments was approximately 12 months and remained stable over time, indicating that the duration of clinical benefit did not decrease with repeated administration. Different formulations of botulinum toxin type A, including onabotulinumtoxinA, abobotulinumtoxinA, and incobotulinumtoxinA, were used during the study period, all demonstrating comparable clinical effectiveness.

A more recent prospective observational study by Marchese et al. expanded the clinical perspective by demonstrating that Frey syndrome may involve not only gustatory sweating and flushing, but also additional sensory symptoms such as pain, itching, and paresthesia. In their cohort, all patients reported gustatory sweating prior to treatment, while 80% experienced paresthesia, 77% flushing, and 60% pain and itching, highlighting the multidimensional nature of this condition. Following botulinum toxin type A injection, both the overall symptom burden and individual symptom scores decreased significantly at each follow-up assessment, with all symptoms except pain showing statistically significant improvement at early post-treatment evaluation ($P < 0.05$). The greatest mean reduction was observed for gustatory sweating (1.53 ± 1.81), followed by paresthesia (1.13 ± 1.55), flushing (1.00 ± 1.51), pain (0.60 ± 1.06), and itching (0.60 ± 1.06), with improvement in sweating being significantly greater compared to other symptoms ($P < 0.05$). At 6-month follow-up, gustatory sweating remained the most prominent residual symptom, whereas flushing showed the lowest severity score. The mean duration of clinical benefit was approximately 8–10 months, with the most pronounced improvement observed in gustatory sweating compared to other symptoms (Marchese et al., 2021).

This issue was also addressed by Wang and Wang, who treated 10 patients with severe Frey syndrome using intradermal botulinum toxin type A, performing a total of 16 treatment sessions. In all cases, gustatory sweating improved rapidly, with clinical response observed within 2 days after injection, and no adverse effects were reported. Recurrence of symptoms was common, occurring after the first 13 injections, which necessitated repeated treatment. The mean duration of effectiveness was 9.3 months, with a wide range from 2 to 28 months, reflecting interindividual variability in response. Notably, one patient presenting with associated gustatory flushing did not experience improvement despite three consecutive treatments (Wang et al., 2005).

Beerens and Snow analyzed 13 patients with Frey syndrome treated with botulinum toxin type A and found that after 3 months, 11 of 13 patients showed a reduction in gustatory sweating of more than 90%. During long-term follow-up, nearly all patients developed recurrent symptoms, with a mean recurrence-free period of approximately 11 months after the initial treatment and 15 months after repeated injection. The treatment was generally well tolerated, although two patients developed temporary paresis of the perioral muscles (Beerens et al., 2002).

Similarly, Eckardt and Kuettner evaluated 69 patients after superficial parotidectomy, of whom 43 reported Frey syndrome and 33 requested treatment. In this treated group, the affected skin area ranged from 16 to 81 cm^2 and the Botox dose ranged from 16 to 80 IU. All clinically relevant symptoms disappeared within one week after a single injection, and the treatment was well tolerated without reported side effects. However, nine patients required a second injection after 12 months due to recurrence of symptoms (Eckardt et al., 2003).

Long-term clinical experience was further presented by Laskawi et al., who reported 19 patients and 22 treated sides. In all treated cases, gustatory sweating ceased completely within 2 days. Side effects were not reported, and in those with recurrence, the mean duration of effect was 17.3 months, supporting the long-lasting but not permanent benefit of treatment (Laskawi et al., 1998).

In another study, Arad-Cohen and Blitzer described seven patients with Frey syndrome treated with intradermal botulinum toxin type A injections, all of whom experienced significant clinical improvement or complete resolution of symptoms. The duration of symptom relief ranged from 5 to 24 months, with a mean duration of approximately 12 months. Only one patient developed a mild and transient weakness of the upper lip, confirming the favorable safety profile of this treatment (Arad-Cohen et al., 2000).

Dulguerov et al. evaluated the effectiveness of botulinum toxin type A in patients with Frey syndrome using objective measurements, including Minor's starch-iodine test to assess the sweating area and quantitative evaluation of sweat production. The authors demonstrated a significant reduction in both the surface area of sweating and the amount of sweat secretion following treatment, confirming the objective efficacy of botulinum toxin. However, changes in erythema and skin temperature were more difficult to assess reliably, and improvement in flushing was less consistent compared to sweating (Dulguerov et al., 2000).

One of the earlier clinical studies was published by Naumann et al., who treated 45 patients with gustatory sweating using botulinum toxin type A. The maximum therapeutic effect was observed after approximately 7 days, and the hyperhidrotic area decreased from 17.6 ± 8.6 cm² before treatment to 1.3 ± 1.6 cm² after treatment. Half of the patients reported complete abolition of symptoms, while the remainder described marked improvement, and no toxic effects were observed during the 6-month follow-up period (Naumann et al., 1997).

Although botulinum toxin type A remains the mainstay of treatment, botulinum toxin type B has also been investigated as an alternative option. Cantarella et al. treated seven patients with severe Frey syndrome using botulinum toxin type B. One month after treatment, six of seven patients reported complete resolution of sweating and flushing, while the remaining patient described substantial improvement. Subjective benefits remained stable for 6 months in four patients and for 9 months in the other three, and all patients still reported some improvement at 12 months (Cantarella et al., 2010).

3.2.Botulinum toxin in the management of sialocele

Sialocele is a common complication following parotidectomy, resulting from disruption of the salivary gland or duct and leading to the accumulation of saliva in the surrounding tissues. While many cases resolve with conservative management, persistent sialoceles may require additional therapeutic interventions (Kinberg et al., 2022; Yang et al., 2023). Several studies included in this review demonstrate that botulinum toxin is an effective treatment option for sialocele by reducing salivary secretion through inhibition of parasympathetic stimulation.

The most recent data are available from a randomized controlled trial conducted by Sheykhveisi et al., which evaluated the role of botulinum toxin in the management of post-parotidectomy sialocele. In this study, patients were randomly assigned to receive either botulinum toxin injection or conservative treatment. The botulinum toxin group demonstrated reduced salivary leakage and faster clinical resolution of the sialocele compared to the control group. Quantitative analysis demonstrated a significantly lower drainage volume in the botulinum toxin group at 48 hours (1.5 ± 12.2 vs 5.4 ± 27.2; $p = 0.003$), while differences at 24 hours were smaller (2.8 ± 19.1 vs 2.1 ± 23.9; $p = 0.021$). No serious adverse effects related to the treatment were reported (Sheykhveisi et al., 2025).

In addition to therapeutic use, botulinum toxin has also been explored as an adjunct in the early postoperative period. Lee et al. conducted a prospective pilot study evaluating the effect of intraoperative botulinum toxin injection during superficial partial parotidectomy. In this study, botulinum toxin was administered to the parotid bed at the time of surgery. Patients receiving botulinum toxin demonstrated reduced postoperative drainage volume and a lower incidence of salivary complications, including sialocele, compared to those who did not receive the injection (Lee et al., 2021).

One of the earlier reports by Chow and Kwok described the successful treatment of a persistent parotid sialocele using botulinum toxin type A after failure of conservative management. In this case, two percutaneous injections of botulinum toxin (50 and 70 units) were administered into the parotid region surrounding the sialocele at a 4-day interval. Complete resolution of the sialocele was observed shortly after the second injection. The patient had resumed oral intake after the first injection, and no recurrence or adverse effects were reported (Chow et al., 2003).

Similarly, Pantel et al. reported the use of botulinum toxin type B in the treatment of a postoperative sialocele following unsuccessful conservative management. In this case, botulinum toxin was injected into the residual parotid tissue, resulting in a rapid reduction in salivary secretion and subsequent resolution of the sialocele. The therapeutic effect was observed shortly after injection, and no adverse effects were reported during follow-up (Pantel et al., 2013).

3.3.Botulinum toxin in the management of salivary fistulas

Salivary fistula is a clinically significant complication following parotidectomy, characterized by persistent leakage of saliva through the surgical wound or skin. In cases where conservative management fails, botulinum toxin has been increasingly used as a minimally invasive therapeutic option aimed at reducing salivary secretion and facilitating tissue healing.

Prospective data demonstrated Send et al., who analyzed the management and outcomes of salivary fistulas treated with botulinum toxin. The study included 16 patients who received a total of 27 injections of botulinum toxin. The administered doses ranged from 10 to 40 units per injection, depending on the extent of the remaining glandular tissue. In most cases, a single injection was sufficient to achieve closure of the fistula; however, five patients required two injections, and three patients required three or more injections. The average time to fistula closure was 12.7 ± 5.0 days in patients treated with a single injection and 18.5 ± 16.3 days in those requiring multiple injections. A rapid and marked reduction in salivary secretion was observed following treatment, and no adverse effects related to botulinum toxin administration were reported. In the majority of cases, fistula closure was achieved without the need for additional surgical intervention (Send et al., 2019).

Further evidence is provided by Laskawi et al., who evaluated the use of botulinum toxin in 12 patients with salivary fistulas following parotidectomy. Botulinum toxin type A was injected into the residual parotid tissue under ultrasound guidance, with doses ranging from 10 to 40 units (mean dose 23.3 units). In some cases, repeated injections were required due to persistent salivary leakage. In 9 of 12 patients, treatment with botulinum toxin alone resulted in complete closure of the fistula, with resolution observed within 2 to 5 weeks (mean 3.3 weeks) after injection. A rapid and marked reduction in salivary flow was noted following treatment, and no complications were reported. In the remaining cases, additional interventions, including surgical revision or radiotherapy, were required to achieve fistula closure (Laskawi et al., 2013).

One of the earlier reports on this topic was presented by Marchese-Ragona et al., who described the use of botulinum toxin in the treatment of salivary fistula following parotidectomy. In this study, botulinum toxin was injected into the residual parotid tissue, resulting in a marked reduction in salivary secretion and subsequent closure of the fistula. The therapeutic effect was observed shortly after treatment, and no major complications were reported (Marchese-Ragona et al., 2006).

Additional evidence is provided by Graillon et al., who evaluated the use of botulinum toxin in patients with salivary gland disorders, including four cases of salivary fistula. In these patients, botulinum toxin was administered into the affected glandular tissue, with an initial dose of 50 units. In one case, a second injection of 50 units was required due to persistent leakage. Closure of the fistula was achieved in all patients following treatment. No adverse effects related to botulinum toxin administration were reported (Graillon et al., 2019).

4. Discussion

Taken together, the available evidence demonstrates that botulinum toxin is an effective and well-tolerated therapeutic option in the management of complications following parotidectomy, particularly Frey syndrome, sialocele, and salivary fistula. Across the analyzed studies, botulinum toxin consistently provided rapid reduction of symptoms, including gustatory sweating and salivary leakage, and contributed to improved postoperative outcomes. The clinical benefits were observed shortly after injection and, in many cases, persisted for several months, although recurrence of symptoms was commonly reported, especially in Frey syndrome. Importantly, repeated administrations were generally associated with sustained effectiveness and a favorable safety profile. Despite differences in study design, patient populations, and treatment protocols, the overall findings remain consistent, supporting the growing role of botulinum toxin as a minimally invasive approach in the management of post-parotidectomy complications.

Frey syndrome represents the most extensively studied and best-documented indication for botulinum toxin therapy among post-parotidectomy complications. The findings of this review consistently confirm its high clinical effectiveness in reducing gustatory sweating, with most studies reporting substantial or complete symptom resolution following treatment. The therapeutic effect is typically observed within a few days after injection and may persist for several months, most commonly ranging between 6 and 12 months. However,

recurrence of symptoms over time appears to be a frequent finding, reflecting the temporary nature of botulinum toxin action. Despite this, repeated injections have been shown to maintain clinical efficacy without evidence of reduced response, supporting the long-term applicability of this treatment approach.

In addition to its well-established effect on gustatory sweating, botulinum toxin has also been shown to influence other symptoms associated with Frey syndrome, although with varying degrees of effectiveness. While sweating is consistently the most responsive symptom, flushing appears to respond less predictably to treatment, as demonstrated in several studies (Marchese et al., 2021; Wang et al., 2005)]. This observation is further supported by objective assessments, which indicate that botulinum toxin more effectively reduces sweat production and the affected surface area than erythema or skin temperature changes (Dulguerov et al., 2000). Moreover, Frey syndrome has been increasingly recognized as a multidimensional condition involving not only sweating and flushing but also sensory symptoms such as pain, itching, and paresthesia (Marchese et al., 2021). Treatment with botulinum toxin has been associated with significant improvement across these domains, although the magnitude of response is greatest for sweating, suggesting differential sensitivity of symptoms to neuromodulation (Marchese et al., 2021). These findings highlight the complexity of Frey syndrome and suggest that, while botulinum toxin provides broad symptomatic relief, its effects may vary depending on the underlying mechanisms of individual symptoms.

Another important aspect of botulinum toxin therapy in Frey syndrome is its reproducibility and applicability across different formulations of the toxin. Although botulinum toxin type A is the most commonly used and best-studied preparation, alternative formulations such as botulinum toxin type B have also demonstrated clinical effectiveness in selected patients (Cantarella et al., 2010). This may be particularly relevant in cases of reduced response or when repeated treatments are required. Long-term data further indicate that repeated injections remain effective over time, with stable treatment intervals and consistent clinical outcomes reported across multiple treatment sessions (Jansen et al., 2017). These observations suggest that botulinum toxin therapy can be safely repeated without a loss of efficacy, making it a practical long-term management strategy for patients with recurrent symptoms.

In contrast to Frey syndrome, the available evidence on the use of botulinum toxin in the management of post-parotidectomy sialocele is more limited, although the overall findings remain consistently favorable. The reviewed studies indicate that botulinum toxin effectively reduces salivary secretion, leading to resolution of sialocele in a relatively short period of time. Clinical improvement is often observed rapidly after injection, and in many cases, a single administration is sufficient to achieve complete resolution of the lesion (Chow et al., 2003). These observations are supported by randomized data, which demonstrate reduced salivary leakage and faster clinical improvement in patients treated with botulinum toxin compared to conservative management (Sheykhveisi et al., 2025). The effectiveness of botulinum toxin in sialocele management is primarily associated with its ability to reduce salivary secretion, which facilitates spontaneous healing of the disrupted glandular tissue. This may explain the rapid decrease in fluid accumulation observed after injection and the relatively short time to clinical resolution reported in several studies (Chow et al., 2003; Sheykhveisi et al., 2025). Importantly, the minimally invasive nature of botulinum toxin administration makes it an attractive alternative to more aggressive interventions, particularly in cases where conservative treatment has failed. In addition to its therapeutic application, botulinum toxin has also been investigated as a preventive strategy. Intraoperative administration during parotidectomy has been associated with reduced postoperative drainage and a lower incidence of salivary complications, including sialocele (Lee et al., 2021). These findings suggest that early modulation of salivary secretion may influence postoperative healing and reduce the risk of fluid accumulation. However, the available evidence in this area remains limited, and further studies are required to determine the optimal timing, dosage, and patient selection for preventive use of botulinum toxin.

The available evidence indicates that botulinum toxin is a clinically beneficial option in the management of salivary fistula following parotidectomy, particularly in cases refractory to conservative treatment. The analyzed studies demonstrate that reduction of salivary secretion after botulinum toxin injection promotes spontaneous closure of the fistula, often within a relatively short period of time. In clinical series, fistula closure was achieved in the majority of patients, with reported success rates reaching 75% to 90% depending on the study population and timing of treatment (Send et al., 2019; Laskawi et al., 2013). In addition, treatment was associated with a rapid decrease in salivary leakage and a low incidence of complications, supporting its safety and tolerability (Send et al., 2019; Graillon et al., 2019; Laskawi et al., 2013). An important factor influencing treatment outcomes appears to be the timing of botulinum toxin administration. Studies suggest that earlier intervention, particularly in the initial stages of fistula development, is associated with higher rates of successful closure, whereas delayed treatment may require additional interventions such as surgical revision

or radiotherapy (Laskawi et al., 2013). This observation highlights the potential benefit of early therapeutic intervention in preventing chronic or persistent fistulas. Furthermore, similar to sialocele, botulinum toxin offers a minimally invasive alternative to surgical management, reducing the need for repeat procedures and lowering the risk of complications, including facial nerve injury. Despite these promising findings, the available evidence remains limited by relatively small sample sizes and the predominance of case series and retrospective analyses. Although the results are consistent across studies, further prospective and randomized trials are needed to establish standardized treatment protocols, including optimal dosing strategies and timing of administration.

An important advantage of botulinum toxin therapy in the management of post-parotidectomy complications is its minimally invasive nature combined with a favorable safety profile. Across the analyzed studies, treatment was consistently well tolerated, with only rare and transient adverse effects reported (Send et al., 2019; Jansen et al., 2017; Laskawi et al., 2013). In contrast to surgical interventions, botulinum toxin injection does not carry a risk of additional tissue damage or facial nerve injury, making it a particularly attractive option in patients requiring repeated treatment. Another significant benefit is the rapid onset of action, with clinical improvement often observed within a few days after administration, as demonstrated in patients with Frey syndrome and salivary complications (Chow et al., 2003; Eckardt et al., 2003; Naumann et al., 1997). Furthermore, the procedure can be repeated if necessary, with studies showing sustained effectiveness over time without a decrease in therapeutic response (Jansen et al., 2017). These features make botulinum toxin a flexible and practical tool in both the treatment and, potentially, prevention of postoperative complications.

Despite the overall consistency of findings, several limitations of the available evidence should be considered. Most of the included studies are based on small patient cohorts, case reports, or retrospective analyses, which limits the strength of the conclusions. Only a limited number of prospective studies and randomized trials are available, particularly in the context of sialocele and salivary fistula management (Sheykhveisi et al., 2025). In addition, there is considerable heterogeneity among studies in terms of treatment protocols, including differences in toxin type, dosage, injection technique, and timing of administration. This variability makes direct comparison of results challenging and limits the ability to establish standardized clinical guidelines. Furthermore, follow-up periods differ across studies, and long-term outcomes are not consistently reported, particularly with regard to recurrence rates and optimal retreatment strategies. These limitations highlight the need for further well-designed prospective studies to better define the role of botulinum toxin in this clinical setting.

5. Conclusions

Current evidence suggests that botulinum toxin represents an effective, safe and minimally invasive therapeutic strategy for the management of major complications following parotidectomy, particularly Frey syndrome, sialocele and salivary fistula. The findings of this review indicate that its use is associated with consistent reduction of symptoms and facilitation of postoperative healing across different clinical scenarios. In particular, botulinum toxin appears to provide reliable control of gustatory sweating and effective reduction of salivary leakage, contributing to improved patient outcomes.

Although the therapeutic effect is temporary and repeated administration is often required, the available evidence suggests that treatment remains effective over time and can be safely applied in a long-term management strategy. Moreover, the potential role of botulinum toxin in the early postoperative period may further contribute to reducing the incidence of complications. An important limitation is the predominance of low-level evidence among the available studies. Most published reports consist of retrospective analyses, small case series, or individual case reports, while high-quality randomized controlled trials remain scarce. In addition, publication bias cannot be excluded, as studies reporting favorable outcomes are more likely to be published. Considerable heterogeneity regarding toxin formulation, dosage, injection technique, follow-up duration, and outcome assessment further complicates direct comparison between studies. Therefore, further well-designed prospective and randomized studies are needed to establish standardized approaches and to better define the long-term effectiveness of botulinum toxin in this clinical setting. Future research should focus on prospective multicenter studies with standardized treatment protocols in order to determine optimal dosing strategies, timing of administration and long-therm effectiveness of botulinum toxin therapy in post-parotidectomy complications.

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