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Review

Botulinum Toxin A for the Management of Post-Laryngectomy Salivary Leak and Pharyngocutaneous Fistula: A Case Series and Narrative Review

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Abstract

Post-laryngectomy salivary leak and pharyngocutaneous fistula (PCF) are recognised complications that prolong hospitalisation, delay adjuvant treatment and, in severe cases, risk major vessel exposure; current management relies on conservative measures or systemic anticholinergic agents, which carry a substantial burden of unwanted effects. We present four consecutive patients treated with a standardised regimen of botulinum toxin A (BoNT) injected into the parotid tail, parotid body and submandibular gland after failure of conservative management for post-laryngectomy salivary leak/PCF; all four achieved clinical and radiological resolution without significant local or systemic complications. We conducted a narrative review of the literature (PubMed, EMBASE, Cochrane, Google Scholar) using a structured search and screening process, screening 1198 records (701 after deduplication) and identifying 13 eligible studies (231 patients who received BoNT across 12 primary studies) evaluating BoNT for salivary leak/fistula across post-laryngectomy PCF and post-parotidectomy sialocele/fistula populations. A previous systematic review is discussed as supporting context; its patient cohort is not included in the total above, as its 27 source articles may overlap with the primary studies included in this review. Across the case series and a limited, predominantly observational literature base, BoNT was associated with rapid salivary suppression (up to ~95% reduction in one study), high fistula closure rates (54–100%), and accelerated healing, including a statistically significant reduction in healing time in one comparative study (18.5 vs. 26 days, $p = 0.008$); adverse events were reported as rare and minor, though these findings warrant cautious interpretation given the evidence base. BoNT injection is a low-risk, potentially high-yield adjunct for post-laryngectomy salivary leak and PCF, avoiding the systemic anticholinergic burden of alternative pharmacological treatments; multicentre studies with standardised dosing protocols are needed to establish its role in standard practice.

Keywords: botulinum toxin; pharyngocutaneous fistula; salivary leak; laryngectomy; sialocele; head and neck cancer

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1. Introduction

Total laryngectomy (±pharyngectomy) is a treatment option for advanced laryngeal or hypopharyngeal cancers as either a primary surgical treatment, a salvage procedure following recurrence post-chemoradiotherapy, or in a functional context to reduce aspiration after completion of organ preservation treatment.

Post-operative salivary leaks after laryngectomy are a recognised complication and can result in prolonged hospitalisation, delayed feeding, risk of wound breakdown potentially leading to pharyngocutaneous fistula (PCF), and delay in adjuvant treatments [1]. The most severe complication is major vessel blowout and death. The incidence of salivary leaks is highly variable, ranging anywhere between 5 and 60% [2–6]. A 2014 systematic review and meta-analysis reports an incidence of PCF of 14.3% in primary total laryngectomy, and 27.6% in salvage total laryngectomy [7].

There are many different variables identified in the literature that increase the risk of salivary leaks. These include medical factors such as previous radiotherapy (RT) (either previous radiation to the neck, salvage laryngectomy, or post-RT functional laryngectomy) [8], pharyngolaryngectomy (partial or total), concurrent neck dissection, positive margins, and tumour recurrence. Patient factors also play a significant role, including hypoalbuminaemia secondary to poor nutrition, gastro-oesophageal reflux disease (GORD), congestive heart failure and low haemoglobin, and other systemic comorbidities (diabetes, liver disease, and hypothyroidism) [9]. Other significant contributing factors, such as wound infections, smoking, perioperative steroid use, and preoperative IMRT, also have a substantial impact on healing [10,11].

Management of PCF and salivary leaks tends to be conservative [12]. Antibiotic therapy, packing of the fistulous opening, nasogastric feeding, and optimisation of patient factors are used in combination to promote healing [13]. Salvage surgical repair (commonly with a vascularised flap) is reserved for patients with high-output fistulae, failure of conservative management, or exposure of major vessels [14]. Conservative management tends to result in resolution in 80% of patients; however, this requires prolonged hospital admission and observation by surgical teams. Optimising this time frame allows better mortality and morbidity outcomes, well-timed adjuvant treatment, and a prompter return to a normal diet [13].

Anticholinergic drugs (AC) are used to aid the medical management of PCF. Salivary secretion is controlled by the autonomic nervous system, which controls the parotid, submandibular, sublingual, and minor salivary glands [15]. Acetylcholine is released from postganglionic neurons and binds to the muscarinic salivary gland receptors; this is the primary stimulus for salivary secretion. Systemic anticholinergic medications antagonise these receptors and induce hyposalivation [16]. Principally, this aims to reduce salivary output, reducing fistula output and allowing better healing. However, given the pharmacology of AC, unwanted interactions with multiple other drug groups can cause wide-reaching consequences impacting the central nervous system, heart, colon, urinary bladder, respiratory tract, and basal ganglia in the brain [17]. Therapeutic effects of systemic ACs depend on target-tissue muscarinic receptors; tissues expressing the same receptors will also be affected.

Botulinum toxin A acts on acetylcholine-containing vesicles within the presynaptic membrane at cholinergic nerve terminals. It blocks acetylcholine release at the neuromuscular and neuroglandular junction, which reduces parasympathetically mediated glandular secretion. This mechanism of action allows for a targeted local mode of action on the target glands for approximately 3–6 months. This immediately reduces long-term risks of this drug, as the effects are temporary. This offers a rationale distinct from systemic anticholinergic drugs. By not affecting anti-muscarinic receptors throughout the body, and instead only affecting the targeted salivary gland, BoNT injections produce a localised reduction in salivary output at the site of the leak or fistula without the systemic anticholinergic burden described above.

To our knowledge, this case series is among the first to specifically report a retrospective series with the use of a standardised BoNT injection protocol for post-laryngectomy

and post-pharyngolaryngectomy PCF. This indication remains under-represented in the existing literature relative to post-parotidectomy sialocele/fistula. By combining our case series with a narrative review of the literature base, this study aims to identify the rationale for a future prospective, multicentre trial in this specific population.

This study aimed to identify whether botulinum toxin A (BoNT) injected directly into the salivary glands, following a post-laryngectomy salivary leak, improves recovery time and reduces prolonged hospital stay while minimising systemic complications. The null hypothesis of this study is that BoNT has no impact on recovery time or length of hospital stay (LOS).

2. Case Series

The four cases below represent original, non-overlapping clinical data collected at our institution, reported in accordance with the CARE guidelines (Supplementary File: CARE checklist), and are distinct from the studies identified in the literature review presented in Section 3. The findings from the two are considered together only in the Discussion.

Patients were recruited from the Otolaryngology, Head and Neck Surgery Department at Morriston Hospital, Swansea.

The authors collected data from a single centre, retrospectively, in a consecutive case series of patients who underwent Botulinum Toxin A (BOTOX® (onabotulinumtoxinA), Allergan, Inc., an AbbVie company, 1 N Waukegan Rd., North Chicago, IL 60064, USA) salivary gland injections after development of salivary leak and pharyngocutaneous fistula post-laryngectomy (±pharyngectomy). Injections were offered to patients who had either clinical (confirmed by drain amylase levels) or radiological evidence of salivary leak/PCF (following a water-soluble contrast swallow (CS)). Standardised water-soluble contrast swallows were organised between 7 and 14 days post-operatively. All patients remained fed via a nasogastric tube (NGT) or radiologically inserted gastrostomy (RIG) throughout the duration of the study until radiological evidence of resolution of PCF was confirmed. All patients were trialled on a period of conservative management (nil by mouth, enteral feeding, IV antibiotic therapy as per local microbiology guidance) prior to salivary gland injections. Conservative management included packing of the fistula tract with alginate dressing in all four patients, in addition to nil-by-mouth status, enteral feeding, and antibiotic therapy, prior to botulinum toxin injection.

A standardised injection regimen was used, with documented verbal consent. Each patient was administered 100 International Units (IU) of botulinum toxin in 1 mL normal saline, divided equally into 6 parts (approximately 17 units per area) and injected into:

- Tail of the parotid;
- Body of the parotid (1 cm anterior to the tragus, 1 cm inferior to the zygomatic arch);
- Submandibular gland.

All patients were kept under observation in the department until clinical and radiological resolution of salivary leak/PCF. Immediate post-injection complications (bruising, pain, wrong injection site) were documented. Patients were specifically asked about xerostomia symptoms while inpatient, in addition to a retrospective review of patient notes for other long-term symptoms (systemic side effects, facial nerve palsy). None of the four patients reported short-term or long-term xerostomia.

2.1. Patient A–56F

This patient had previous T3N0M0 laryngeal SCC (May 2017) and was treated with CRT after MDT discussion. She had a significant smoking history (30 cigarettes/day for 30 years previously, now 10/day) and previous history of radical cystectomy, total abdominal hysterectomy, and bilateral salpingo-oophorectomy for extensive bladder cancer.

After chemoradiotherapy, the patient had ongoing airway issues and swallowing dysfunction. Concerns were raised regarding recurrence of supraglottic/laryngeal malignancy and were investigated with CT and MRI, with biopsies showing fungal infiltrate with no invasive malignancy. She then presented in extremis in October 2025 with stridor and airway compromise, requiring local anaesthetic tracheostomy and biopsies. All biopsies showed fungal infiltrates on the surface with no invasive malignancy. The patient underwent a functional laryngectomy, with histology clear of malignancy. She had an initial post-surgical water-soluble contrast swallow on day 12, which showed no leak. Due to complex patient factors, peristomal breakdown occurred, causing a frank PCF, which also led to aspiration pneumonia. The patient was then fed via nasogastric (NG) tube, and a salivary bypass tube was also inserted. She was trialled on conservative management (as per Methods) for 23 days, with no resolution. A standard botulinum toxin regimen was given to the patient after verbal consent (as per Methods). The patient had resolution of leak symptoms and was able to be discharged from hospital 27 days after this. A repeat barium swallow 6 weeks post-discharge showed no leak.

2.2. Patient B–65M

This patient presented initially with T4b left hypopharyngeal carcinoma, treated with radiotherapy, completed in April 2025. MRI and PET findings were suspicious for residual disease, confirmed with biopsy. The patient then underwent a salvage pharyngolaryngectomy and ALT free flap. As an inpatient, the patient suffered a segmental pulmonary embolism on day 8. An initial barium swallow (day 12) showed no leak. The patient was initially commenced on oral intake and managed this well. The patient was then noted to have stomal edge breakdown on day 15 post-op and was commenced on oral antibiotics. Despite this, a large leak was identified on day 22 in the supraclavicular region. The leak was packed with alginate dressing, and the patient was maintained on strict nil-by-mouth and RIG feeding. A repeat water-soluble contrast swallow 3 weeks later still showed an ongoing leak. Standardised botulinum toxin was given at this point with verbal consent. The patient was noted to have significant improvement within a week of injection and was discharged with no leak 2 weeks after injection. Ongoing RIG feeding continued due to issues with propulsion of the food bolus past the free flap reconstruction.

2.3. Patient C–67M

The patient presented with a T4a N1 right-sided hypopharyngeal carcinoma (poorly differentiated) and underwent a total pharyngolaryngectomy and bilateral neck dissections, with left ALT free flap reconstruction. A salivary bypass tube was inserted intraoperatively. The day 15 contrast swallow showed a large anterior leak pooling near the right side of the laryngectomy stoma. On return to theatre, the stoma was reopened, and a cavity was identified. This was washed out and a drain inserted. Endoscopic examination showed a healthy flap with a fistulous opening at the anastomotic site. This was packed, and intraoperative BoNT was injected (standard regimen). Strict nil-by-mouth status and RIG feeding were maintained for the remainder of the hospital stay. The patient was shown to have decreased drain output within 2 weeks of BoNT and drain insertion, with the day 49 contrast swallow showing no leak.

2.4. Patient D–79M

This patient presented to clinic with airway compromise and was immediately taken to theatre for panendoscopy, biopsy, and high tracheostomy. The patient had a right-sided hypopharyngeal tumour (T4a, N3bM0, poorly differentiated SCC). He underwent a pharyngolaryngectomy with left radial forearm free flap reconstruction. A persistent leak was identified, and fluid from the leak was sent for amylase testing, identifying it

as saliva (day 6). A contrast swallow was delayed due to clinical findings of leak, and BoNT treatment was given on day 8 (verbal consent, standardised regimen). The patient then underwent RIG insertion on day 16. The leak was monitored, and the patient had significant improvement in the leak within 10–12 days of BoNT treatment. The patient remained clinically well, and a day 32 contrast swallow showed no evidence of salivary leak.

Table 1 summarises the clinical timeline for all four patients, reporting day of fistula diagnosis, duration of conservative treatment, day of BoNT injection, time to clinical improvement, and time to radiological closure.

Table 1. Clinical timeline for the four institutional patients treated with botulinum toxin A.

Patient	Day of Fistula Diagnosis	Duration of Conservative Tx	Day of BoNT Injection	Time to Clinical Improvement	Time to Radiological Closure	Prior RT	Pre-op Bloods
A (56F)	Day 16	23 days	Day 39	Discharged 27 days post-BoNT	~9 weeks post-BoNT (6 weeks post-discharge)	Yes (CRT)	Albumin 32 g/L; TSH 13.6, T4 13.1 (known hypothyroid, on levothyroxine, suboptimal control)
B (65M)	Day 22	21 days (day 22 → day 43)	Day 43	~day 50 (7 days post-injection)	~day 57 (2 weeks post-injection)	Yes	Albumin 43 g/L; thyroid function not assessed pre-op
C (67M)	Day 15	3 days	Day 18	~14 days post-BoNT (decreased drain output)	Day 49	No (primary case)	Albumin 41 g/L; TSH 1.21, T4 16.4 (euthyroid)
D (79M)	Day 6	2 days (day 6 → day 8)	Day 8	Days 18–20 (10–12 days post-BoNT)	Day 32	No (primary case)	Albumin 29 g/L; TSH 5.5, T4 12.3 (subclinical hypothyroidism)

3. Literature Synthesis and Comparative Analysis

3.1. Methodology

This review of the literature aims to address the following question: in patients with a post-laryngectomy salivary leak, pharyngocutaneous fistula, or post-parotidectomy sialocele/salivary fistula (Population), does administration of botulinum toxin A into the affected salivary glands (parotid, submandibular) (Intervention), compared with conservative management/systemic pharmacological therapy (Comparator), improve fistula/leak resolution, healing time and length of hospital stay (LOS) (Outcomes)?

This review was not prospectively registered, and no formal review protocol was prepared in advance.

Inclusion criteria:

- Post-operative use of botulinum toxin following laryngectomy, pharyngolaryngectomy, or parotidectomy.

Exclusion criteria:

- Use of a parotid surgical approach for a non-parotid procedure;
- Non-primary parotid surgery;
- Botulinum toxin use for non-surgical salivary gland conditions;
- Paediatric cases;
- Non-English-language studies or unpublished studies;
- Conference abstracts;
- Botulinum toxin used for aesthetic purposes.

Databases searched were PubMed, EMBASE/MEDLINE, and Cochrane CENTRAL, together with Google Scholar as a supplementary grey-literature source. The following

search terms were used: laryngectomy, pharyngectomy, pharyngolaryngectomy, parotidectomy, "parotid surgery", sialocele, "salivary fistula", "salivary leak", "parotid fistula", "pharyngocutaneous fistula", botox, "botulinum toxin", "botulinum neurotoxin", and onabotulinumtoxina. Full database-specific search strings are provided in Appendix B. A date filter of 2000–2026 (since the millennium) was applied to all database searches; no other filters (e.g., language) were applied at the search stage, as language and publication-status restrictions were instead applied during eligibility screening (see exclusion criteria above). Google Scholar results were sorted by relevance and screened up to a pre-specified cutoff of the first 600 of 1950 total results, consistent with recommended grey-literature search methodology.

Two independent reviewers (I.M., J.A.) screened titles and abstracts, then assessed all selected papers in full-text format. Data were independently extracted by the same two reviewers using a standardised extraction form capturing study design, population, intervention (BoNT dose, technique, injection site), comparator (where applicable), and outcomes; discrepancies were resolved by discussion between the two reviewers.

Methodological quality and risks of bias were assessed using the Cochrane Risk-of-Bias tool (RoB 2) for the included randomised controlled trial, the Newcastle–Ottawa Scale for retrospective and prospective observational studies, the JBI Critical Appraisal Checklists for case series and case reports, and AMSTAR-2 for the included systematic review. The single RCT [18] was deemed as having some concerns; the retrospective case–control study [19] was rated good quality (7/9, Newcastle–Ottawa); four further observational studies [20–23] were rated moderate quality, primarily due to the absence of a comparator group; and the remaining case reports/case series [24–29] carried the inherent high risk of bias due to their design, though they were otherwise appropriately reported.

3.2. Results

Given substantial clinical and methodological heterogeneity across the included studies (spanning one RCT, prospective and retrospective observational studies, case series, case reports, and one prior systematic review), a meta-analysis was not undertaken. Findings were instead synthesised with a narrative synthesis, grouped by outcome (salivary flow suppression, fistula/sialocele closure, healing time and length of hospital stay (LOS), and safety/adverse events).

The literature search was performed across PubMed (n = 139), EMBASE/MEDLINE (n = 459), and Cochrane CENTRAL (n = 0), together with Google Scholar as a supplementary grey-literature source, screened by relevance ranking up to a pre-specified cutoff of the first 600 of 1950 total results [30]. This yielded 1198 records in total, of which 497 duplicates were removed, leaving 701 unique records. All 701 were screened by title and abstract, of which 659 were excluded as not meeting the inclusion criteria. The remaining 42 articles were independently assessed in full-text format; 29 were excluded because they did not specify botulinum toxin as a post-operative treatment modality. This left a total of 13 articles (Figure 1).

The included primary studies (RCT, prospective, retrospective, case series) covered 231 patients worldwide who received BoNT undergoing this treatment modality. A previous systematic review (Maharaj et al., 2020) [31] is discussed separately as supporting evidence only, and its patient cohort is not included in this total, as its 27 source articles may overlap with the primary studies included in this review. The large majority of evidence relates to post-parotidectomy surgery and sialoceles. Although the articles did not all document the same outcome measures, specific themes could be identified from the literature.

The complete study-level data are available in Appendix A, Table A1.

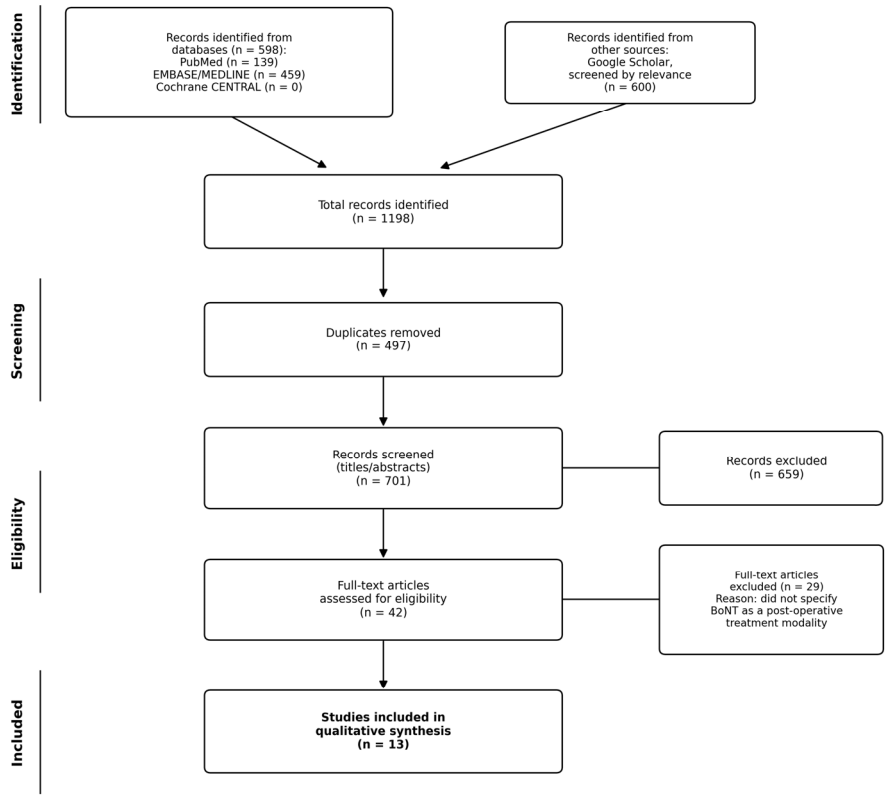


Figure 1. Flow diagram of the literature search and study selection process (identification, screening, eligibility, and included studies) for this narrative review.

Rapid salivary suppression. Four articles (n = 158) identified a significant reduction in salivary flow, though none used objective instrumental measurement (e.g., sialometry); all reported reductions were based on clinical or patient-reported assessment. A prospective study reported a subjectively assessed ~95% reduction in saliva; the largest study describing salivary flow (retrospective study, 2004, n = 33) reported a 79% clinician-assessed improvement. The remaining studies varied in the degree of reduction reported, but none provided quantitative, instrument-based measurement of salivary flow.

High closure rates. All articles demonstrated high closure rates associated with BoNT treatment. A 2020 systematic review describes 70–100% success rates in closure. The oldest paper (2000 prospective study, n = 4) identified a 100% closure rate, whilst the lowest rate of closure was 54% in a 2022 prospective study (n = 13).

Accelerated healing. All articles inferred accelerated healing rates. The largest study (2025 retrospective case–control, n = 135) showed that BoNT treatment leads to faster healing compared with control (18.5 vs. 26 days, $p = 0.008$) when assessing improvements in PCF/OCF outcomes. A small case series assessing parotid sialocele following buccal squamous cell carcinoma (SCC) (n = 3) identified that all patients recovered with no delay in adjuvant radiotherapy. Similarly, in a 2021 case series (n = 5), it was identified that healing of parotid injury (including parotid duct injury) was accelerated by BoNT treatment (leak improved by day 3, full recovery in all patients). This was despite administration of BoNT at different times (three post-op, one pre-op, and one intraoperative).

Safety profile. Across all patients studied (n = 231), no long-term adverse outcomes were reported in the identified literature. One patient suffered a small peri-procedure adverse event (localised skin swelling), and one patient developed transient xerostomia. There was no significant systemic toxicity or facial nerve injury.

4. Discussion

Post-laryngectomy salivary leakage (and subsequent PCF) is a complex and difficult condition to treat. This is combined with significant comorbidities in the patient cohort (elderly, long-standing nutritional deficits, previous RT) that make treatment plans complex and multifactorial [32]. There is no single treatment modality best suited for this cohort of patients, with the best outcomes coming from conservative management [13]. This involves watchful waiting, strict enteral feeding, and antibiotic cover. Unfortunately, this requires prolonged hospital stays for patients, leading to increased healthcare costs, risk of hospital-acquired infections, and further deconditioning of the patient. Systemic pharmacological treatments such as anticholinergics are effective at reducing salivary flow, but can have significant unintended side effects. Given their mechanism of action (blocking postganglionic acetylcholine binding with muscarinic receptors in salivary glands), this can also affect other organ systems [17]. Anticholinergic burden is caused by the cumulative effect of multiple drug classes with anticholinergic properties, leading to increased risk of cognitive impairment, falls, delirium, and mortality in patients over 65. This can have both short- and long-term complications for the patient, requiring further medical intervention and hospital stays [33].

The above case series highlights the benefits of a standardised BoNT regimen for these patients. Avoiding systemic drug therapy and instead focusing on targeted, organ-specific treatment (namely the salivary glands) reduces the risk of anticholinergic burden and other medical issues. BoNT therapy is safe; there were no significant local or systemic complications secondary to administration. Small 30G needles (in combination with insulin syringes) were able to deliver specifically dosed BoNT with minimal pain on administration [34]. Readily available landmarks (1 cm anteroinferior to the tragus, 1 cm beneath the ear lobule, and palpation of the submandibular gland) allowed for quick and easy administration to good effect. In this consecutive case series, all patients were trialled on prolonged conservative management of salivary leaks/PCF. This included strict nil-by-mouth, nasogastric/RIG feeding, and antibiotic therapy [13]. Despite this, there was no resolution of symptoms. After administration of BoNT, all patients had resolution of their pathology.

The above narrative review of the literature supports the conclusions of the case series. The search for BoNT therapy as a treatment specifically for PCF returned few articles, indicating a scarcity of studies in the literature. Given the pathophysiology (and mechanism of action of BoNT), the authors decided to broaden the search terms to include post-parotidectomy sialoceles/fistulae. Across the articles that met the inclusion criteria, a number of themes emerged supporting the use of BoNT therapy.

A large number of patients described a reduction in salivary flow from the salivary glands addressed, with a prospective study identifying reductions of up to 95% [26]. Despite this, there were no reports of an increased incidence of intraoral infections prior to adjuvant radiation. For those papers which described fistulae, a high rate of closure was identified across the reviewed literature, including a 70–80% closure rate reported by a prior systematic review and a retrospective cohort study [20,31]. Although this may have been in part due to prolonged conservative management, a retrospective case–control study did indicate a statistically significant ($p = 0.008$) improvement in healing time (18.5 vs. 26 days) [19]. Faster healing may in turn shorten inpatient admission and reduce the risk of hospital-acquired infections/complications in this complex and comorbid patient cohort, though this was not directly measured across the wider literature and should be interpreted cautiously. Across all patients, there were no significant, long-lasting complications from BoNT administration; of the 231 patients, only one suffered short-lived skin swelling, and one patient had transient xerostomia [18]. Neither condition affected patient morbidity or mortality, and both were well tolerated.

There are, however, significant limitations to this narrative review. There were no unified dosing regimens, locations, or techniques across the studies described. The heterogeneity of this treatment methodology does not allow for assessment of a specific and optimal BoNT treatment protocol. Although 231 patients were assessed across the studies included in this narrative review, 100 were part of a randomised controlled trial [18]. That trial itself looked at post-parotidectomy leaks; although an excellent dataset as a proof of concept for BoNT treatment, it is unclear how directly comparable this data is to salivary leaks in post-laryngectomy patients and PCF. In combination with limited RCT (Level 2) evidence, many of the other studies were small case series and case reports (Level 4) [25,27–29]. This significantly increases reporting bias in the dataset and can therefore obscure the efficacy/limitations of the treatment. Most of the studies also had limited long-term follow-up. Although not necessarily critical (as the treatment modality reduces immediate post-operative complications), this still does not identify any longer-term consequences of BoNT treatment, which would include long-term xerostomia, late-onset leaks/PCF, or delayed facial palsy/local neuromuscular blockade. Higher-level studies are required to provide better Level 1 or 2 evidence to inform practice.

The majority of the included evidence derives from case reports and small case series (Level 4 evidence), with only one randomised controlled trial (conducted in a post-parotidectomy, not post-laryngectomy, population, and with some methodological inconsistencies as assessed by RoB 2). The consistency of direction of effect across study designs and the wider literature is reassuring, but the overall certainty of evidence for BoNT in this specific indication remains low. The aim of this review is to draw preliminary conclusions from the existing literature and our own case series to justify and inform a future multicentre trial with a strict, standardised protocol to formally assess the impact of BoNT on length of hospital stay (LOS) in this patient group, rather than to establish definitive practice-changing evidence at this stage. Given the low morbidity associated with BoNT injection, this intervention appears safe, and its addition to standardised practice may be considered by the reader.

A further limitation is the population distribution of the included evidence: only four of the 13 included studies [19,22,27,29] specifically concern post-laryngectomy or post-pharyngolaryngectomy PCF, the population most relevant to our own case series. The limitations in the research would not allow for conclusions to be drawn about the efficacy of BoNT treatment. The authors decided to broaden the scope of the literature search to evaluate efficacy of BoNT therapy in other post-operative salivary fistulae to assess outcomes. Therefore, the remaining evidence derives predominantly from post-parotidectomy sialocele and salivary fistula, a related but anatomically and physiologically distinct clinical scenario. There are limitations and caveats associated with this approach. Parotidectomy-related salivary leaks often arise from the surgical approach, the location of the parotid lesion and the remaining exposed parotid tissue post-operatively. Post-laryngectomy PCF arises in the context of a pharyngeal mucosal breakdown with multifactorial contributions from wound healing, prior radiotherapy, and nutritional status, as detailed in the introduction. The consistency of BoNT's effect across both contexts is reassuring and biologically plausible, given the shared mechanism of action (reduction in glandular salivary output reducing flow through the fistula tract), but extrapolation from the parotidectomy literature to the post-laryngectomy population is made cautiously. The post-operative benefit in laryngectomy and pharyngolaryngectomy is hypothesised, and serves as the foundation for standardised protocol-driven cohort/multicentre prospective studies.

Fistula tract packing, although used as part of the standard conservative management in all four institutional patients, was not consistently reported across the literature. The authors decided that this could not be extracted as a comparable data point. This is a further

consequence of the population imbalance described above, as tract packing is not standard practice for the post-parotidectomy sialocele/fistula management, which comprises the majority of the reviewed literature.

5. Conclusions

BoNT administration for long-term, post-operative management in higher-risk laryngectomy and pharyngolaryngectomy patients is a low-risk, potentially high-yield treatment. Patients undergoing this treatment had no significant additional morbidity, and all symptoms resolved after treatment. It is unclear whether earlier treatment, or indeed prophylactic injections, would decrease the risk of leak formation. Our case series suggests BoNT administration may accelerate clinical and radiological resolution of leaks/PCF once identified and therefore may reduce hospital LOS. We hypothesise that this would reduce conservative management time post-leak, and reduce the variability of admission data. However, no controlled comparison of length of hospital stay was performed in our series, and the wider literature's strongest comparative evidence (Chettuvatti et al.) reports healing time rather than LOS directly. The authors plan to run a multi-centre study to evaluate LOS improvements as a direct result of BoNT salivary suppression.

Further, multicentre studies should be undertaken with strict protocols to assess whether this should be standardised practice in these procedures.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/ohbm7020037/s1, Supplementary File: CARE Checklist—Completed for: "Botulinum Toxin A for the Management of Post-Laryngectomy Salivary Leak and Pharyngocutaneous Fistula: A Case Series and Systematic Review".

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Conflicts of Interest: The authors declare no conflicts of interest.

Appendix A

Complete Dataset of Included Studies (Table A1).

Table A1. Results of the literature review.

Study	Design	Patients	Condition	Dose	Outcomes	Ref.
Post-Parotidectomy Sialocele/Fistula						
Maharaj 2020	Systematic review	47 (27 articles)	Parotid sialocele/fistula	10–200 U	70–100% success	[31]
Vargas 2000	Prospective pilot study	4	Post-parotidectomy sialocele	30–50 U	100% closure <1 mo; no recurrence	[24]
Sheykhveisi 2025	Randomised controlled trial	100	Post-parotidectomy	Via surgery	Reduced drainage; fewer sialoceles	[18]

Table A1. *Cont.*

Study	Design	Patients	Condition	Dose	Outcomes	Ref.
Ellies 2004	Retrospective cohort study	33	Salivary disorders incl. fistulas	20–65 U	79% improvement	[20]
Steffen 2014	Retrospective cohort study	25	H&N cancer salivary issues	NS	4/6 fistulas improved	[21]
Marchese 2022	Prospective cohort study	13	PCF post-salvage surgery	40 U per parotid	54% closure; major flow ↓ correlates with healing	[22]
Melville 2016	Prospective case series	3	Parotid Sialocele	50–70 U	Complete recovery in all patients, no delay in adjuvant RT	[28]
Laskawi 2013	Retrospective case series	12	Post-parotidectomy salivary fistula	NS (injected into residual parotid tissue)	9/10 early-treated (<6 weeks) fistulas resolved with BoNT alone; 1 late-presenting permanent fistula (day 420) unsuccessful; no adverse effects	[23]
Post-Laryngectomy/Pharyngolaryngectomy PCF						
Toong 2024	Case series	2	PCF after laryngectomy	20 US-guided, B/L SMG and parotid	Closure in 1–4 weeks	[27]
Chettuvatti 2025	Retrospective case–control study	135 (31 BTX)	PCF/OCF	40–100 U (mean 59.2 U)	Healing faster vs. control (18.5 vs. 26 days, $p = 0.008$)	[19]
Ferri 2008	Case report	1	Post-laryngectomy pharyngocutaneous fistula	50 U	Improved in 4 days, BS confirmed in 7 days	[29]
Other/Parotid Duct Injury						
Jeong 2021	Retrospective case series	5	Parotid duct injury	30–40 U—3 post, 1 pre, 1 intra	Leak ↓ by day 3; full healing	[25]
Schwalje 2019	Mixed prospective/retrospective case series	2	Parotid-cutaneous fistula	Intraductal infusion	~95% reduction	[26]

Appendix B

Full database-specific search strategies (Table A2).

Table A2. Full search strategies for each database/source searched, including filters applied and the number of records returned. Deduplication (1198 → 701 unique records) was performed automatically using Mendeley, followed by manual review of all flagged duplicate pairs.

Database	Search String	Filters	Records
PubMed	(laryngectomy[tiab] OR pharyngectomy[tiab] OR pharyngolaryngectomy[tiab] OR parotidectomy[tiab] OR “parotid surgery”[tiab] OR sialocele[tiab] OR “salivary fistula”[tiab] OR “salivary leak”[tiab] OR “parotid fistula”[tiab] OR “pharyngocutaneous fistula”[tiab]) AND (botox[tiab] OR “botulinum toxin”[tiab] OR “botulinum neurotoxin”[tiab] OR onabotulinumtoxina[tiab])	Publication date 2006–2026; no other filters	139

Table A2. *Cont.*

Database	Search String	Filters	Records
EMBASE/MEDLINE (Ovid)	(laryngectomy.mp. or pharyngectomy.mp. or pharyngolaryngectomy.mp. or parotidectomy.mp. or "parotid surgery".mp. or sialocele.mp. or "salivary fistula".mp. or "salivary leak".mp. or "parotid fistula".mp. or "pharyngocutaneous fistula".mp.) and (botox.mp. or "botulinum toxin".mp. or "botulinum neurotoxin".mp. or exp Botulinum Toxin Type A/)	Publication date 2006–2026; no other filters	459
Cochrane CENTRAL	Same term set, Title/Abstract/Keyword field	Publication date 2006–2026; no other filters	0
Google Scholar	Flattened phrase version of the same term set, sorted by relevance	Screened to a pre-specified cutoff of the first 600 of 1950 total results, per Haddaway et al. (2015) [30]	600

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