



# First Bite Syndrome: Definition, Etiopathogenesis, diagnosis and Management



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## Abstract

First bite syndrome is a clinical term that represents the development of a severe, excruciating pain in the parotid region characteristically at the initial bite of a meal, then decrease in intensity with the following bites of each meal, it is believed that this syndrome is a postoperative complication of parapharyngeal space surgery.

**Methodology:** Based on the indexed previous articles, published reviews (pubmed) and Google scholar, we go through the diagnosis, incidence, pathophysiology and treatment modalities of first bite syndrome.

**Keywords:** First bite syndrome; Parapharyngeal space; Horner syndrome; Parotid gland; External carotid artery; Botulinum toxin type A

**Abbreviations:** FBS: First Bite Syndrome; PPS: Parapharyngeal Space; NSAID: Non-Steroidal Anti-Inflammatory Drug; GABA: Gamma-Aminobutyric Acid; BTA: Botulinum Toxin Type-A

## Main Text

Head and neck surgery is one of the most complex and adverse scopes of surgery, involving complicated anatomical structures that directly correlates with patients quality of life, and any interruption of these structures could result in a devastating outcomes, one of the various clinical postoperative complications of upper neck surgery is first bite syndrome (FBS), which remains a vague, frequently missed and unpredicted complication despite the characteristic clinical picture that distinguish it. In this article we will explore step by step the definition, postulated hypothesis of pathophysiology, how it is diagnosed and the recent modalities of treatment for this not uncommon but often challenging to diagnose syndrome. As documented in literature, first bite syndrome reflects the onset of an intense pain in the parotid region accompanying the first bite of each meal, which then decline and subsides with the following meal [1-4]. Since its first documentation in literature it was considered as a postoperative complication of cervical surgery [2-6], several modalities of treatment proposed with varying degrees of efficiency and compliance, with the main goal being the improvement of the patients quality of life. As clear as it's named, first bite syndrome (FBS) is defined as the onset of an intense, shock-like, excruciating pain in the parotid region that sometimes extends into the ear, which characteristically begins with the patient's first bite at each meal then weakening in intensity with following bites [1], FBS is

considered as a complication of parapharyngeal space surgery (PPS). The pain in FBS is so severe that is inversely correlates with the patient's quality of life and nutritional intake, with them willingly avoid and skip meals to prevent themselves from this painful experience [6]. Interestingly, this episode of pain repeats itself with every meal [1-4].

## Etiopathogenesis

Since its recognition, FBS has been considered as a postoperative complication of parapharyngeal space surgery, with the clinical features manifesting itself 4-7 days or even weeks postoperatively [4]. PPS is an inverted pyramidal shaped space extending from the skull base superiorly to the greater cornea of the hyoid bone inferiorly, with the styloid process dividing it into anteromedial and posteriolateral compartments. Any upper neck surgery or surgery involving structures contained in PPS namely, deep lobe of parotid gland, lower four cranial nerves, carotid sheath and its content, sympathetic chain and lymph nodes carry the risk of developing FBS. The postulated hypothesis of the pathophysiology of FBS is that it is developed as a result of injury and excision of the sympathetic innervation of the parotid gland myoepithelial cells, which leads to sympathetic denervation of these cells resulting in hypersensitivity and over stimulation of the parasympathetic secretion to the myoepithelial cells, leading to

this tremendously painful contraction of the parotid myoepithelial cells [1-3].

### Incidence

Up to date there is no universally accepted incidence rate concerning FBS due to lack of sufficient studies about it, however, in 2016, Mehmet Özgür Avingçal et al. [4] reported an incidence rate of 30% after studying 53 patients underwent upper neck surgery between 2002 and 2013. Moreover, Abdeldoui A et al. [6] in 2013 documented an incidence rate of 9.6% of all patient undergoing upper cervical surgery between 1999 and 2010, same ratio was reported by Linkov et al. [5] in 2012.

### Clinical features

Patient with FBS present a characteristic clinical features, an excruciating pain in the ipsilateral parotid region following surgery in PPS that start with the first bite of each meal, then subsides with subsequent masticatory cycle, with this episode of pain being at its highest with the first meal of the day, even the subjective thinking of dietary intake can initiate these symptoms in some patients [1-4].

### Differential diagnosis

As FBS is considered a post-operative complication of parapharyngeal space surgery, other complications should be mentioned also, these include the following [7]:

- i. Lower cranial nerves injury, particularly the vagus nerve.
- ii. Horner's syndrome.
- iii. Palatal insufficiency.
- iv. Frey's syndrome.
- v. Shoulder weakness.
- vi. Vascular injury.
- vii. Dysphonia.
- viii. Vascular injury and hematoma.

However, the clinical picture of FBS along with the characteristic pattern of pain, will aid the clinicians to distinguish FBS from other complications, particularly Temporomandibular joint dislocation pain and postoperative neuralgia.

### Investigations

It is generally agreed that FBS is diagnosed clinically with no specific investigation to confirm the diagnosis of FBS until recently. The characteristic symptoms along with the history of parapharyngeal space surgery should point out FBS from the state of suspicious into state of confirmation. More researches combined with animal and clinical trials can lead to an easy and accurate methods to aid clinicians investigate for FBS in the future.

### Treatment

Until recently there is no definitive management of FBS despite the fact that it's not an uncommon complication of PPS surgery, and this can be attributed to lack of animal trials and shortage of studies concerning FBS. Generally, some patient with FBS improve with time but the debilitating nature of FBS requires urgent intervention to improve quality of life [4]. Several methods have been used with varying degree of efficiency, starting with dietary modification [1], as patients report that the episodes of pain magnify with acidic food, however, this line of treatment showed absolutely no improvement. Another line of treatment is medical prescriptions, with non-steroidal anti-inflammatory drugs (NSAID) being used but proved to be not effective, anticonvulsants particularly carbamazepine and tricyclic antidepressants like amitriptyline have also been used, with some patients reporting a decrease in intensity but same duration of pain, but a close monitoring and follow up should be commenced as these drugs have a serious complications and side effects. GABA analogues (gabapentin) have been used and resulted in a decrease in magnitude and duration of pain, however medical treatment nowadays is not considered a preferable mood of treatment due to its side effects and little efficiency [8].

There have been several modalities of surgical treatment of FBS including auriculotemporal nerve resection, tympanic neuroectomy and total parotidectomy, all of which have shown to be beneficial in management of FBS [6], but on the other side all of those modalities carry its own risk postoperative and immense care should be taken when planning each of these methods. More recently, intraparotid injections of botulinum toxin type A (BTA) which prevents the release of acetylcholine in synapses have shown great results in relieving the pain, with reports of complete resolution following injections [9]. In 2008, Ali et al. [10] Documented a case report of a patient suffering from FBS following several parapharyngeal space surgeries, the patient was injected with a 75 units of BTA, under ultrasound guidance, the patient reported a dramatic decrease in intensity of pain in less than 48 hours, with no painful symptoms for a 10-weeks follow-up, same dose has been used by Sims et al. [11]. In his case report involving 3 patients, with 2 out of the three patients reported being symptoms free for almost 4-months follow up. In 2017, Costales-Marcus et al. [12] Managed five patients with FBS with 30 units of BTA injections, 4 patients reported a decrease in intensity of pain, and one patient experienced no change in pain severity, all of them needed a repetitive injection of BTA. Since the effects of BTA are temporary, most patient will need another dose of BTA injection after 4 to 6 months follow up. Most reports from literature show a promising result with BTA injections as it is generally safe, non-invasive and highly effective in relieving the pain [9].

### Prognosis

FBS has an unpredictable prognosis, as it may resolve spontaneously or it may continue with the same intensity and magnitude, however, documents have reported a substantial

relief of pain after different periods of follow-up depending on the modality of treatment used, while oral medications in the form of anticonvulsants and/or GABA analogue showed mild to moderate decrease in the intensity of pain, intraparotid injections of botulinum toxin type A showed a substantial relieve of pain in 4 to 6 months of follow up, with some patient reporting complete resolution of pain during a period of 4 months of follow up [9-12].

### Discussion

The term first bite syndrome was firstly reported by Netterville in 1998, who documented a review of 46 patients of vagal paragangliomas treated during a 20-year period, 9 of them developed a characteristic postoperative complication, severe pain in the ipsilateral parotid region that is associated with the first bite of each meal then diminishes with the subsequent bites. 8 out of the 9 patients had their sympathetic chain resected and the ninth patient experienced Horner syndrome as a result of loss of sympathetic function. These findings led to the hypothesis of sympathetic denervation of parotid myoepithelial cells as a suggested pathophysiology for FBS [1]. In 2002, Chiu et al. [2] in their retrospective review of 12 patients with FBS following surgery involving parapharyngeal space, documented that half of patients developed Horner syndrome caused by sympathetic trunk injury, while the other 6 had an external carotid artery ligation just after the origin of facial artery, all of the 12 patients had some residual parotid gland tissue after surgery. These findings have supported the theory of sympathetic denervation and subsequent super sensitivity of parasympathetic receptors as a leading cause of FBS [2]. Kawashima et al. [3] in 2007 reviewed a retrospective study of 29 patients with parapharyngeal space tumor treated surgically. In this study 9 cases of FBS developed, all of which had surgical resection of their superior cervical sympathetic ganglion. Surprisingly, 2 of the patients who did not develop FBS had their sympathetic trunk ligated with preservation of the superior cervical sympathetic ganglion, which suggested that the residual or autonomous activity of superior cervical sympathetic ganglion can prevent the development of FBS [3]. The correlation between FBS and surgery involving parapharyngeal space is well established. In 2017, Elimairi I et al. [13] documented a retrospective study of a 17 patients who developed FBS as a complication of upper neck surgery, 14 of those patients had parotid surgery, 2 patients developed the syndrome after resection of carotid body tumour, and the last patient had surgical resection of the styloid process because of Eagle syndrome, all these patient were treated with GABA analogue then cryoablation with moderate improvement [8]. In 2007, Claudia R Cernea et al. [14] documented a case report of a patient developing FBS following surgical resection of styloid process, which further confirms the relation between FBS and parapharyngeal space surgery [8]. Although all these review strongly agree with the postulated hypothesis that FBS develop as a complication of upper neck surgery particularly involving parapharyngeal space, there have been some reports of FBS as a presenting symptom rather than an outcome, as Maheer M

Masood et al. [15] documented in 2017 a case report of a patient with no surgical history and no clinical symptoms other than a 9 years history of FBS, after a thorough clinical and radiographic examinations the patient diagnosed with a primary squamous cell carcinoma of the parotid, the patient treated surgically with complete resolution of FBS after treatment [16].

### Conclusion

Despite the increased availability of data and understanding of this complication, FBS remains a challenging clinical entity that requires a special attention from the operating surgeons to prevent its occurrence following parapharyngeal space surgery. Due to its debilitating nature and the unpredictability of treatment, surgeons should counsel their patients thoroughly about these postoperative complications.

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