Sublabial Approach Versus Modified Denker's Procedure: A Comparative Study of Pre-maxillary Tissue Clearance in Covid-Associated Mucormycosis

Shivam Sharma¹ · Anjani Kumar Sharma¹ · Amreen^{1,2} · Pawan Singhal¹ · Ashok Poonia¹ · Shubham Agrawal¹ · Kailash Singh Jat¹ · Man Prakash Sharma¹

Received: 9 October 2021 / Accepted: 27 December 2021 / Published online: 7 February 2022
© Association of Otolaryngologists of India 2022

Abstract To compare the efficacy of the sublabial and modified Denker's procedure in clearance of fungal disease from the anterior wall of maxilla and the pre-maxillary area i.e. the difficult areas of maxillary sinus. A prospective observational study was conducted over a period of 2 months (April 21–June 21) in the ENT department of Sawai Man Singh hospital, Jaipur. All the patients with clinical involvement of the premaxilla or the cheek abutting the anterior wall of maxilla were included in the study population. Cases matched in both groups were subjected to debridement either by the sublabial or the modified denker's approach. Outcomes were measured by assessing

the daily CRP values, post-operative DNE every 3 days after pack removal, and imaging at the end of 1 month. Repeat biopsies were performed in patients that still had persistent symptoms after getting operated on. 16 of the 60 patients (26.6%) operated on by the endoscopic approach showed evidence of residual disease on follow-up whereas only 5 patients (9.6%) in the other category had a similar outcome. Most of the recidivism was seen in the anterior maxilla. Lower rates of complications were found following debridement by the sublabial approach. Since the sublabial approach is the most direct approach for the key areas of fungal involvement of maxillary sinus, it is recommended over the modified Denker's procedure for disease clearance from pre maxilla and the anterior wall of maxillary sinus. This view is also supported by the lower rates of complications encountered following the former.

✉ Amreen
amreenspsingh@gmail.com
Shivam Sharma
shivam92@hotmail.com
Anjani Kumar Sharma
dranjaniasharma@gmail.com
Pawan Singhal
drps.ent@gmail.com
Ashok Poonia
ashokpoonia67@gmail.com
Shubham Agrawal
drshubz.jpr@gmail.com
Kailash Singh Jat
drkailashsms@gmail.com
Man Prakash Sharma
drmanprakash@yahoo.co.in

Keywords COVID-associated mucormycosis · Premaxilla · Caldwell-Luc · Modified Denker's procedure · Infraorbital nerve · Endoscopic clearance

Introduction

Ever since early 2019 when the novel coronavirus infection attained pandemic proportions, COVID-19 has been presenting with new features at an alarming pace [1]. One of these is COVID-associated mucormycosis that recently emerged in alarming numbers as a sequela of COVID-19 infection. Mucormycosis is a deadly fungal infection with predilection for immunocompromised individuals [2, 3]. Only rarely have ever been case reports where individuals with no clear predisposition were found to be afflicted [4]. Even though the exact incidence of this disease has never been clearly reported, traditionally, mucormycosis has

¹ Department of Otolaryngology and Head and Neck Surgery, S.M.S. Medical College and Hospital, Jaipur, Rajasthan 302004, India

² No. 115, Shastri Colony, Opposite to A. S. Sen. Sec. School, Talwara Road, Mukerian district, Hoshiarpur, Punjab, India

been considered a rare disease [5]. But the recent scenario showed mucormycosis attaining epidemic proportions. Before the era of Covid-19, computational-based approaches estimated the prevalence of mucormycosis at 140 cases per million population in India which is palpably less than the alarming surge noticed lately. An indiscriminate use of steroids, the resultant surge in diabetes mellitus and thromboembolic phenomenon due to Coronavirus after the second wave of COVID-19 rendering the recipients immunocompromised is the prime suspect [6].

Mucormycosis is classified according to the anatomical region affected and its extent. It may be rhino-orbito-cerebral, pulmonary, cutaneous or disseminated; the rhino-orbito-cerebral form being the most common (30–50%) [7].

Mucormycosis is an angioinvasive disease [8]. It causes thrombus formation and necrosis of the involved region at an alarming pace. The involved tissue becomes functionally dead and also acts a cesspool for further spread of the disease. Debridement and removal of the affected tissue, hence plays an important role in management. Maxillary sinus is one of the structures to be involved in the early stages of this disease in a vast majority of the cases [9]. Spread of disease to the entire antrum of Highmore encompassing all the walls is seen. This warrants the need for a surgical strategy that can enable the assessment of all the limits of the sinus equally well while at the same time providing a route of access to the adjacent suspected areas.

With the advancements in instrumentation, various approaches are available in the armamentarium of a modern-day ENT surgeon. These include exclusively-endoscopic approaches and open surgical approaches. Both these techniques have their pros and cons. While it is widely considered that open approaches cause much more extensive tissue damage and have significantly longer recovery periods for mucosa, they are still not out of date [10]. The corresponding values for endoscopic approaches are less but they have their limitations especially in terms of exposure and consequently the need for revision surgeries [9, 11].

In surgeries of the maxillary antrum, five zones are defined: zone 1, nasal cavity; zone 2, medial to infraorbital nerve (ION); zone 3, lateral to ION; zone 4, anterior maxilla; and zone 5, premaxillary tissue [12]. Zones 4 and 5 are especially difficult to tackle endoscopically though several modifications have been suggested.

Various modifications have been suggested from time to time to overcome the limitations of endoscopic approach from time to time. Modified endoscopic medial maxillectomy, total endoscopic medial maxillectomy, trans-septal approach, septal dislocation and modified Denker's approach are some of the approaches that have been suggested to counter the shortcoming of the technique [11, 13].

The most widely accepted endoscopic approach for a disease as rapidly progressive and as invasive as mucormycosis is the modified Denker's approach. An amalgamation of the techniques originally proposed by Denker and the endoscopic approach proposed by Sturmman and Canfield [11], the modified Denker's approach is a viable alternative to the classical open Sublabial approach.

As opposed to this, the open Caldwell-Luc approach via the sublabial incision has stood the test of time. Proposed more than a century ago in 1893, [9] it is still the first-line procedure in a considerable number of cases. Owing to the excellent access to any disease process that might be propagating at the anterior wall, this technique has not lost its significance [9, 14]. On the other hand, the curved endoscopic instruments are difficult to manipulate and lose precision as far as the difficult areas are concerned [13].

We compared the open Caldwell-Luc approach with pertinent modifications and the endoscopic approaches for the clearance of disease from Harvey zones 4 and 5 i.e., the anterior and the pre-maxilla (Fig. 1). Cases matched in both groups for overall extents of the disease were selected and the procedures were then performed by surgeons with comparable skill and experience.

Materials and Methods

A prospective observational study was undertaken in the Department of Otorhinolaryngology and Head and Neck Surgery at Sawai Man Singh Medical College and Hospital, Jaipur, India over a period of 2 months, from the 21st of April 2021 till 20th June 2021 with the aim to compare the sublabial and the modified Denker's approach in clearance of anterior and pre-maxillary area disease in cases of Sino-nasal Mucormycosis. All patients with invasive mucormycosis of the pre-maxillary area presenting to the ENT department were included in the study population. The involvement of the following qualified for inclusion: a visible swelling or abscess in the pre-maxillary area or the adjoining cheek, loosening of teeth, overt or gross ulcerative skin involvement in the region. The patients' presentation details, imaging findings, associated co-morbidities, clinical examination and management details were obtained and recorded. The cases were surgically debrided by the Sub-labial approach or the modified Denker's approach. Since the operating surgeon was unbiased to both approaches and the existent literature did not support one over the other to the best of our knowledge, it was decided that alternate patients will be allocated to the two different groups. To ensure comparability and to eliminate chances of bias, matching was done with respect to the likely confounding factors viz. age, gender and extent of the disease i.e. exclusively sinonasal/extending

Fig. 1 MRI showing involvement of the anterior and pre-maxillary area by Mucormycosis (Marked by black star in the upper row and white arrow in the bottom row)

into pterygopalatine fossa/extending into infratemporal fossa/intra-orbital disease/intra-cranial disease (Table 1).

Initially, a total of 130 patients were recruited; 65 in each group. However, 18 patients were lost to follow-up for various reasons. Of these, 5 had undergone the endoscopic modified Denker's procedure and the rest had undergone the procedure by sublabial approach. As 'per protocol' analysis approach was adopted, data of the 60 patients from the endoscopic approach group and 52 patients from the sublabial approach group was analysed and presented. Group comparability was again ensured after the drop-outs.

Recurrence was assessed by assessing the daily CRP values, post-operative DNE every 3 days after pack removal, and imaging at the end of 1 month. Repeat

biopsies were performed in patients that still had persistent symptoms after getting operated on.

Results

In our study, 112 cases of CAM with pre-maxillary involvement were operated on. 60 of these underwent debridement by the modified Denker's approach and the other 52, by the Sub-labial approach. 16 of the 60 patients (26.6%) operated on by the endoscopic approach showed evidence of residual disease on follow-up whereas only 5 patients (9.6%) in the other category had a similar outcome.

Also, we observed that those operated on by the Sub-labial approach had local ill-effects of crusting, atrophic

Table 1 The likely factors affecting surgical outcome

Variables	Group A	Group B	'p' Value*
Age (Years)	53.17 ± 7.52	54.68 ± 6.48	0.223**
Male gender (%)	43 (66.15)	45 (69.23)	0.851
Extent of disease			
Sinonasal (%)	65 (100.00)	65 (100.00)	NA
Pterygopalatine fossa (%)	22 (33.85)	21 (32.31)	1.000
ITF (%)	7 (10.77)	7 (10.77)	0.777
Intra-orbital (%)	3 (4.62)	3 (4.62)	0.676
Intra-cranial (%)	0 (0.00)	1 (1.54)	1.000

*Chi Square test, **Unpaired 't' test

rhinitis and occasional epiphora less commonly (Table 2). The number of patients operated on by the Sublabial approach that presented with such complaints or findings post-operatively were significantly less. However, 4 of the patients operated on by the same approach developed an oro-antral fistula.

Another observation made was that a sizable proportion of the residual/recurrent cases presented with tissue involvement in the form of abscesses most of which were anterior gingival rather than posterior along with adjacent bony erosion of the palate (Figs. 2 and 3) (Table 3).

Discussion

Mucormycosis presents most commonly in the form of rhino-orbito-cerebral disease [15], the initial clinical features of which are ethmoid and maxillary sinusitis, with facial soft tissue oedema and periorbital cellulitis in a majority of cases [16].

Mucor leads to a deadly infection in the sinuses leading to obstruction of blood vessels by its proliferating hyphae which have high affinity to the internal elastic lumina of arterial blood vessels and are highly angio-invasive causing thrombosis and thromboembolism ultimately leading to necrosis and infarction [17]. A hypothesis for spread is that along the infraorbital foramina and the nerve leading to involvement of the bone and soft tissue adjoining the anterior wall of maxillary sinus. During the period of our study, infraorbital nerve was sectioned and subjected to biopsy and fungal cultures in cases where its involvement was suspected or grossly noticed. The results supported the hypothesis (Fig. 4). Owing to its invasive nature, it can invade and spread from the nose and sinuses to several adjacent critical structures such the orbit, brain, palate and gingiva and spread far away also via the pterygopalatine and infratemporal fossae leading to various complications such as loss of vision, palatal ulceration, facial pain and swelling, orbital cellulitis and brain infarction [18]. All these complications can result very quickly and may happen in a matter of days and may require multidisciplinary management from the very beginning [19]. Management

includes prompt diagnosis based on imaging and fungal staining followed by surgical debridement and appropriate antifungal therapy [20]. Surgical debridement of the involved tissue is an integral part of the management protocol.

A comprehensive removal of the diseased mucosa and any other foci of infection is warranted for a successful therapy. In our study, we compared the two approaches most widely accepted for dealing with the disseminated diseases of the paranasal sinuses, the Sublabial approach and the modified Denker's approach which eliminates the need for a separate sublabial incision.

The Caldwell-Luc procedure was first described back in 1893 by two independent workers with slightly different techniques. This procedure employs a gingiva-labial incision to expose the anterior wall of maxilla. Drainage of the sinus into inferior meatus via creation of a window is established [21].

It is considered to be an exceptional procedure, through which the sinus mucosa is completely removed [9]. The most common postoperative complications in the Caldwell-Luc approach are represented by facial swelling or numbness (62–90%) and facial or cheek discomfort (in up to 33% of cases) [22, 23]. Facial and cheek swellings can occur as a result of anaesthetic infiltration, of the tamponade of the sinus cavity or of the violent traction exerted by the retractors during the surgery. Other complications include facial asymmetry, facial paraesthesia in the sub-orbital region paraesthesia (by injuring the infraorbital nerve), haemorrhage, persistent suborbital neuralgias, oro-antral fistulas, gingivo-labial fistulas, dental devitalisation, dacryocystitis (stenosis of the lacrimal ducts by injury of the nasolacrimal duct), or recurrence of rhinosinusitis [9, 13].

In most cases, these complications are temporary; their persistence being reported in 15–20% of cases. Rare complications such as epistaxis (0.4%), oro-antral fistula (0.4%) and epiphora (0.44%) represented a small percentage [24].

The modified Denker's approach is an amalgamation of the classical Denker's approach described in 1906 by Alfred Denker [25] and the endonasal procedure described in 1908 by Strumann and canfield [26, 27]. Also known by the acronym TEAMM: total endoscopic anterior medial maxillectomy, this is a widely used approach for extensive diseases of the maxillary antrum. Through mucosal cuts in the nasal cavity along the floor and anterior to the middle turbinate, subperiosteal flaps are elevated to expose the anterior maxilla, the infraorbital foramen, and its neurovascular bundle as well as the lateral nasal wall. A bony window is created in the anterior wall and connected to the medial maxillectomy incisions made beforehand. This

Table 2 Post-operative complication comparison of both the approaches

S. no	Local ill-effects	Sub-labial	Modified Denker's
1	Crusting in nasal cavities	07	40
2	Atrophic rhinitis	01	06
3	Occasional epiphora	03	37
4	Oro-antral fistula	04	–

Fig. 2 Clinical image showing residual disease presenting in the form of gingival abscess (marked by black arrows)

Fig. 3 A Contrast CT Scan of the PNS showing palatal erosion due to Mucormycosis (Encircled) (Coronal cuts in upper row and axial cuts in bottom row)

Table 3 Sites of residual disease presenting as gingival abscess

S. no	Location	No. of cases
1	Incisors	90/112
2	Canines	105/112
3	Premolars	40/112
4	Molars	12/112

provides a number of advantages over other endoscopic procedures [11].

The entire anterior maxilla and pre-lacrimal, anterior, inferior, and lateral recesses of the maxillary sinus can be directly accessed without the need for a sublabial or trans-septal incision. Posterior wall can be accessed in its entirety [28]. This procedure is not limited by the concavity

of the anterior maxilla nor is it dependent on the use of angled scopes. The anterosuperior alveolar and infraorbital nerves are better visualized, facilitating preservation of these neural structures. Higher maxillotomy placement also reduces potential injury to the alveolar plexus. The absence of a gingiva-buccal sulcus incision prevents potential contamination of the sinus cavity with oral flora and possible development of an oroantral fistula. Cheek pain and swelling may occur, similar to sublabial maxillotomy [11]. The infraorbital and antero-superior alveolar nerves can be cautiously protected during creation of the antral window [11]. Alar collapse secondary to loss of the pyriform ridge has also been reported [23]. Nasolacrimal duct stenosis may ensue, requiring possible dacryocystorhinostomy.

In our study, 112 cases of CAM with pre-maxillary involvement were operated on. 60 of these underwent debridement by the modified Denker's approach and the other 52, by the Sub-labial approach. 16 of the 60 patients

Fig. 4 Intra-operative picture showing infra-orbital nerve involvement by Mucormycosis (Encircled) in **a** Open approach and **b** Endoscopic approach (Black star marks the pyriform aperture)

(26.6%) operated on by the endoscopic approach showed evidence of recurrence on follow-up whereas only 5 patients (9.6%) in the other category had a similar outcome.

Also, we observed that those operated on by the Sublabial approach had less local ill-effects of crusting, atrophic rhinitis and occasional epiphora.

These observations are supported by a number of studies. Lee in 2019 concluded that despite recent advances in endoscopic techniques, the anterior maxilla remains difficult to be reached through a purely endonasal approach and that sub-labial incisions with canine fossa puncture or a Sub-labial approach are often still necessary for surgical removal of anteriorly based maxillary pathology [11, 29, 30]. Even in terms of long-term post-operative results, Bajan et al. observed that the Sub-labial surgical technique may be superior to the endoscopic technique. [9] Barzilai inferred that the use of Caldwell-Luc approach is rational in cases of fungal disease to obtain a wider exposure for total clearance [14].

Thus in all, as the time is passing, we are discovering more and more new complications of this Coronavirus pandemic. Sino-nasal mucormycosis is one such fatal outbreak, making it a fungal epidemic within a viral pandemic [31, 32]. Prompt diagnosis with complete and radical clearance of all the involved areas along with medical management is the key to managing this deadly fungal infection. Surgical clearance by the sub-labial approach offers a head on view of the anterior and pre-maxillary area with a wide access for instrumentation and offers a better chance for providing a complete cure.

Conclusion

Mucormycosis is a fulminant infection that warrants prompt diagnosis and management. An early and comprehensive surgical disease removal can significantly improve the prognosis. For a better access to the difficult to approach but commonly involved anterior areas of the maxilla, we recommend debridement via a sublabial incision as opposed to the total endoscopic approach to ensure better disease removal.

Funding This research did not receive any specific grant from funding agencies in the public, commercial, or not for profit sectors.

Declarations

Conflict of interest All Authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

References

1. Wuhan City Health Committee (WCHC) Wuhan Municipal Health and Health Commission's briefing on the current pneumonia epidemic situation in our city 2019. [Accessed 14 Jan 2020]. Available from: <http://wjw.wuhan.gov.cn/front/web/showDetail/2019123108989>

2. Spellberg B, Edwards J Jr, Ibrahim A (2005) Novel perspectives on mucormycosis: pathophysiology, presentation, and management. *Clin Microbiol Rev* 18(3):556–569
3. Munir N, Jones NS (2007) Rhinocerebral mucormycosis with orbital and intracranial extension: a case report and review of optimum management. *J Laryngol Otol* 121(2):192
4. Mignogna MD, Fortuna G, Leuci S, Adamo D, Ruoppo E, Siano M, Mariani U (2011) Mucormycosis in immunocompetent patients: a case-series of patients with maxillary sinus involvement and a critical review of the literature. *Int J Infect Dis* 15(8):e533–e540
5. Prakash H, Chakrabarti A (2019) Global epidemiology of mucormycosis. *J Fungi* 5(1):26
6. Mahalaxmi I, Jayaramayya K, Venkatesan D, Subramaniam MD, Renu K, Vijayakumar P, Narayanasamy A, Gopalakrishnan AV, Kumar NS, Sivaprakash P, Rao KR (2021) Mucormycosis: an opportunistic pathogen during COVID-19. *Environ Res* 6:111643.
7. Mane R, Patil B, Mohite A, Mohanty R (2019) Facial nerve palsy: an unusual presentation in patients with rhino cerebral mucormycosis. *Indian J Otolaryngol Head Neck Surg* 71(3):2110–2113
8. Morales-Del Ángel JA, Morales-Chávez OD, Méndez-Sáenz MA, Montemayor-Alatorre A, Jasso-Ramírez NG, Treviño-González JL (2020) Clinical implications of facial edema in chronic mucormycosis: a report of 5 cases. *Arch Clin Med Case Reports* 4(5):836–844
9. Bajan A, Sarafoleanu C, Melinte VG, Decuseara R (2020) Indications of the Caldwell-Luc procedure in the era of endoscopic sinus surgery. *Roman J Rhinol* 10(39):78–84
10. Datta RK, Viswanatha B, Harsha MS (2016) Caldwell Luc surgery: revisited. *Indian J Otolaryngol Head Neck Surg* 68(1):90–93
11. Lee JT, Chiu AG (2019) Endoscopic Denker approach for anterior maxilla tumors. In: *Atlas of endoscopic sinus and skull base surgery* 2019 Jan 1, pp 183–190. Content Repository Only!.
12. Harvey RJ, Sheehan PO, Debnath NI, Schlosser RJ (2009) Transseptal approach for extended endoscopic resections of the maxilla and infratemporal fossa. *Am J Rhinol Allergy* 23(4):426–432
13. Lee JT, Suh JD, Carrau RL, Chu MW, Chiu AG (2017) Endoscopic Denker's approach for resection of lesions involving the anteroinferior maxillary sinus and infratemporal fossa. *Laryngoscope* 127(3):556–560
14. Barzilai G, Greenberg E, Uri N (2005) Indications for the Caldwell-Luc approach in the endoscopic era. *Otolaryngol Head Neck Surg* 132(2):219–220.
15. Bakshi SS (2016) An unusual cause for facial nerve palsy: mucormycosis. *Int J Diab Developing Countries* 36(4):385–388
16. Dusart A, Duprez T, Van Snick S et al (2013) Fatal rhinocerebral mucormycosis with intracavernous carotid aneurysm and thrombosis: a late complication of transsphenoidal surgery? *Acta Neurol Belg* 113:179–184
17. Damodaran O, Rizk E, Rodriguez J, Lee G (2014) Cranial nerve assessment: a concise guide to clinical examination. *Clin Anat* 27(1):25–30
18. Hosseini SM, Borghei P (2005) Rhinocerebral mucormycosis: pathways of spread. *Euro Arch Oto-Rhino-Laryngol Head Neck* 262(11):932–938
19. Gupta S, Sharma S (2019) Orbital cellulitis: defining multidisciplinary approach as the need of the hour. *Indian J Otolaryngol Head Neck Surg* 71(4):464–469
20. Nagendra V, Thakkar KD, Hrishi AP, Prathapadas U (2020) A rare case of rhinocerebral mucormycosis presenting as garcin syndrome and acute ischemic stroke. *Indian J Critical Care Med Peer-Rev Official Publ Indian Soc Critical Care Med* 24(11):1137
21. Gleeson M, Browning GG, Burton MJ, Clarke R, John H, Jones NC et al (2008) *Scott-Brown's otorhinolaryngology, head and neck surgery*, 7th edn. Hodder Arnold, London
22. Robinson S, Baird R, Le T et al (2005) The incidence of complications after canine fossa puncture performed during endoscopic sinus surgery. *Am J Rhinol* 19:203–206
23. Prosser JD, Figueroa R, Carrau RI et al (2011) Quantitative analysis of endoscopic endonasal approaches to the infratemporal fossa. *Laryngoscope* 121:1601–1605
24. Low WK (1995) Complications of the Caldwell-Luc operation and how to avoid them. *Aust N Z J Surg* 65(8):582–584. <https://doi.org/10.1111/j.1445-2197.1995.tb01700.x>
25. Denker A (1906) Ein neuer weg für die operation der malignen nasentumoren. *Munch Med Wochenschr* 20:953–956
26. Sturmman D (1908) Die Intransasale Eröffnung der Kieferhöhle. *Berl klin Wochenschr* 45:1272–1274
27. Canfield RB (1908) The submucous resection of the lateral nasal wall in chronic empyema of the antrum, ethmoid, and sphenoid. *JAMA* 14:1136–1141
28. Lee JT, Suh JD, Carrau R et al (2017) Endoscopic Denker's approach for resection of lesions involving the anteroinferior maxillary sinus and infratemporal fossa. *Laryngoscope* 127:556–560
29. Robinson S, Patel N, Wormald PJ (2005) Endoscopic management of benign tumors extending into the infratemporal fossa: a two-surgeon transnasal approach. *Laryngoscope* 115:1818–1822
30. Singhal D, Douglas R, Robinson S et al (2007) The incidence of complications using new landmarks and a modified technique of canine fossa puncture. *Am J Rhinol Allergy* 21:316–319
31. Chouhan M, Solanki B, Shakrawal N (2021) Rhino-orbital-cerebral mucormycosis: fungal epidemic in a viral pandemic. *J Laryngol Otol* 2:1–6
32. Sharma S, Grover M, Bhargava S, Samdani S, Kataria T (2021) Post coronavirus disease mucormycosis: a deadly addition to the pandemic spectrum. *J Laryngol Otol* 135(5):442–447

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.