



# African Journal of Biological Sciences



## KNOWLEDGE, AWARENESS AND PERCEPTION OF DENTAL STUDENTS ON USAGE OF BIOLOGIC AGENTS IN THE MANAGEMENT OF ORAL MUCOSAL LESIONS

**Dr. ABARNA JAWAHAR\*<sup>1</sup>**

Senior Lecturer

Department of Oral Medicine and Radiology Sree Balaji Dental College and Hospitals,  
Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, India  
Email id: drabarnajawahar@gmail.com

**Dr. P.SOWMYA<sup>2</sup>**

Undergraduate student

Department of Oral Medicine and Radiology Sree Balaji Dental College and Hospitals,  
Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, India  
Email id: psowmi279@gmail.com

**Corresponding Author**

**Dr. ABARNA JAWAHAR\***

Senior Lecturer

Department of Oral Medicine and Radiology Sree Balaji Dental College and Hospitals,  
Bharath Institute of Higher Education and Research (BIHER) Bharath University, Chennai, India  
Email id: drabarnajawahar@gmail.com

### ABSTRACT

In the recent past, there has been an increasing trend in the usage of biologic agents in systemic immune mediated diseases like rheumatoid arthritis, psoriasis, inflammatory bowel diseases and in certain types of cancers. Due to an increased understanding of disease pathogenesis, BAs are used nowadays in the management of several immune mediated oral disorders like oral lichen planus, oral pemphigus vulgaris, mucous membrane pemphigoid, Bechet's disease, Sjogren's syndrome and Orofacial granulomatosis. The aim of the study is to assess the knowledge and create awareness about usage of biologic agents in management of oral mucosal disorders among dental students. A questionnaire survey was conducted among dental students of a private dental college and hospital in Chennai. When asked about usage of biologic agents in oral mucosal disorders only 69% had responded yes. Only 51% had responded that biologic agents are used in the management of oral mucosal diseases like oral lichen planus, pemphigus vulgaris and recurrent aphthous stomatitis. When asked about whether knowledge on biologic agents is essential for dentists, 91% responded yes. Our study findings show that awareness on usage of biologic agents among dental students is not adequate. The dental professionals should be aware about the usage, directions, dosage and possible adverse effects of biologic agents in management of oral mucosal lesions.

**KEYWORDS:** Biologic agents, Biologic therapies, Immune mediated disorders, Autoimmune disease.

## INTRODUCTION

Biologic agents (BA) are a group of drugs that are produced by living organisms using recombinant biotechnology. They are also commonly known as targeted immunomodulator therapies and biological response modifiers. BAs are currently the fastest growing class of therapeutic drugs in the management of several cancers and immune mediated diseases such as rheumatoid arthritis, psoriasis and inflammatory bowel disease as its usage has resulted in high rates of efficacy and remission. They consist of humanized or chimeric monoclonal antibodies or variant fusion proteins that block specific steps in proinflammatory pathways (Eleni et al., 2013; O'Neill ID and Scully 2012; Chong and Wong 2007; Jackson JM 2007).

Biologic Agents are broadly categorized into 3 groups as Tumor Necrosis Factor - alpha (TNF-a) inhibitors, lymphocyte modulators and interleukin inhibitors. The tumor necrosis factor-alpha is an important proinflammatory cytokine, which has been identified to play a key role in the pathogenesis of immune mediated diseases, which acts by numerous pathways to promote increased leukocyte activation and recruitment to sites of tissue inflammation. TNF-a inhibitors bind and / or neutralize the soluble and membrane-bound TNF-a, thus blocking its effect on target inflammatory cells. The most commonly and widespread used TNF-a inhibitors include infliximab, adalimumab and etanercept (Chong and Wong 2007). Lymphocyte modulators include T cell and B cell modulators, which act on specific CD antigens, targeting memory T cells, natural killer cells and mature B cells respectively. Commonly used lymphocyte modulators are Alefacept, Efalizumab (T-cell modulators) and Rituximab (B-cell modulators) (Stasi 2010). Interleukin inhibitors act by binding to their receptors on T lymphocytes and natural killer cells thus preventing IL-12 and IL-23-mediated T-cell activation and cytokine production. Ustekinumab is a commonly used Interleukin inhibitor (Benson et al., 2011).

Nowadays due to an increased understanding of disease pathogenesis, BAs are used increasingly in the management of several immune mediated disorders of the oral mucosa like oral lichen planus, oral pemphigus vulgaris, mucous membrane pemphigoid, Behcet's disease, Sjogren's syndrome and Orofacial granulomatosis. Several studies have found that recalcitrant cases of Recurrent Aphthous stomatitis have also been successfully treated with BAs (Sidhu et al., 2019).

BAs commonly used in the management of oral diseases include Adalimumab, Etanercept, Infliximab, Alefacept, Efalizumab, Rituximab, Epratuzumab and Basiliximab. They are available

in injection preparations with different routes of administration and schedules. Infliximab and Rituximab are administered as intravenous infusions (IV) periodically. Etanercept and Adalimumab are given as subcutaneous (SC) injections (biweekly, weekly, every 2 weeks or monthly). Alefacept is given as intramuscular (IM) injections weekly (Sidhu et al., 2019).

Research papers that discuss usage of biologic agents and its application in management of several immune mediated disorders of oral mucosa have been increasing in the recent few years. However the impact on usage of biologic agents among dental students is not yet explored. Dentists and dental students should be aware of the recent trends and drugs available in order to successfully treat and manage oral mucosal diseases. Hence this study was aimed to assess the knowledge and create an awareness among the dental students on usage of biologic agents in management of oral mucosal diseases.

## **MATERIALS AND METHODS**

A cross-section online questionnaire-based survey was conducted among dental students of a private dental college and hospital in Chennai. The present study extended for a period of 3 months (March, April and May 2023). The study included undergraduate dental students (only third years, final years and house surgeons) who were willing to participate in the survey. The post-graduates, faculties were excluded from the study.

Sample size calculation was done using Epi info software keeping 50% prevalence and marginal error as 5% with a level of significance at 95%. A total of 146 dental professionals participated in the survey. The survey consisted of 11 close ended questions. The objective of the survey questions was to assess the knowledge and create an awareness about the usage of biologic agents in the management of oral mucosal disease.

- 1) What are biological agents ?
  - a) Pharmaceutical drug made from biological sources
  - b) Pharmaceutical drug made from chemicals in lab
  - c) Both
  - d) None of the above
  
- 2) What are the commonly available biologic agents ?
  - a) Etanercept
  - b) Adalimumab
  - c) Infliximab
  - d) All of the above
  
- 3) Biologic agents are commonly used in the management of ?
  - a) Rheumatoid arthritis
  - b) Psoriasis
  - c) Crohn's disease
  - d) All of the above
  
- 4) Do you think biologic agents are used in the management of oral mucosal disease ?
  - a) Yes
  - b) No
  - c) Don't know
  
- 5) In oral medicine biologic agents are commonly used in the management of ?
  - a) Recurrent aphthous stomatitis
  - b) Pemphigus vulgaris
  - c) Oral Lichen Planus
  - d) All of the above

6) Do you think biologic agents can be used as the first line of drug in the treatment of pemphigus vulgaris as replacement for corticosteroids ?

- a) Yes
- b) No
- c) Don't know

7) Do you know the preferred route of administration for biologic agents ?

- a) Intravenous (IV) route
- b) Intramuscular (IM) route
- c) Both
- d) None of the above

8) Do you think usage of biologic agents can reactivate previous viral infections such as Hepatitis B, Hepatitis C and HIV virus ?

- a) Yes
- b) No
- c) Don't know

9) What can be the possible adverse effects of usage of biologic agents ?

- a) Hypersensitivity (Anaphylaxis reaction)
- b) Development of new infection
- c) Reactivation of old infection
- d) All of the above

10) Do you think it is safe to prescribe biologic agents to pregnant patients ?

- a) Yes
- b) No
- c) Don't know

11) Do you think knowledge on usage of biologic agents is essential for dentists ?

- a) Yes
- b) No

## RESULTS AND DISCUSSION

BAs are protein-based molecules or mixtures of molecules which are manufactured from living microorganism, plant or animal complex using recombinant DNA. When the dental students were asked what biologic agents are, only 41% had chosen pharmaceutical drugs made from biological sources, about 42% had chosen both pharmaceutical drugs made from biological sources and chemicals in the lab (Figure 1.1) (Georgakopoulou et al., 2013) .

Biologic agents are targeted immune modulating agents which are increasingly used nowadays in the management of inflammatory and neoplastic diseases. When dental students were asked on usage of BAs, about 58% had chosen BAs are used in the management of rheumatoid arthritis, psoriasis and crohn's disease (Figure 1.2). Recently BAs are used in patients suffering from refractory forms of immune-mediated diseases of the oral cavity like oral lichen planus, oral pemphigus vulgaris, mucous membrane pemphigoid, recurrent aphthous stomatitis, Sjogren's syndrome and Bechet's disease (Ho DY and Subramanian 2020). When dental students were questioned on whether they were aware of usage of biologic agents in oral mucosal diseases 69% had said yes (Figure 1.3). About 52% had selected that BAs are commonly used in management of oral lichen planus, pemphigus vulgaris and recurrent aphthous stomatitis (Figure 1.4).

BAs should be considered in patients with no other treatment alternatives, considering their safety profile because of its potential side effects including life threatening serious infections and high economic costs. When dental students were asked whether BAs could be used as a first line of drug in management of pemphigus vulgaris as replacement of corticosteroids, about 47% had responded yes (Figure 1.5), but according to literature the first line of drug for management of pemphigus is systemic corticosteroids (Gniadecki 2006, Camacho-Alonso et al., 2005; Martin 2009).

BAs are also known to have a wide range of adverse effects including headaches, malaise, nausea to development of new infections affecting the urinary tract, causing pneumonia and even death due to sepsis. Studies have found that usage of BAs can reactivate old viral infections like Hepatitis B and C, Human immunodeficiency virus (HIV) and tuberculosis. Hence for this

reason prior to commencing biologic therapy, all the patients should be screened for occult infections including hepatitis B and C, Human immunodeficiency virus (HIV) and tuberculosis (Healy and Galvin 2024). When dental students were asked what can be the possible adverse effect of a biologic agent 52% had chosen hypersensitivity, reactivation of old infection and development of new infection (Figure 1.6) and when asked if usage of biologic agents can reactivate previous viral infections like Hepatitis B and C, HIV infection about 48% had responded yes and 33% had responded don't know (Figure 1.7). This shows that the awareness on adverse effects of usage of biologic agents among the dental students are not sufficient.

Biologic therapy is contraindicated in patients who are hypersensitive, currently have any active infections, cardiac disorders, malignancy, pregnancy and lactating mothers. When the dental students were asked is it safe to use biologic agents in pregnant patients only 36% had responded no, about 33% had responded yes and 31% had responded don't know (Figure 1.8) (Sidhu et al., 2019).

Immune mediated oral diseases are becoming more resistant to conventional therapies in recent years and hence the line of treatment is shifting towards usage of biologic agents. Hence it is important for the dentists and dental students to be aware of the recently evolving group of drugs for successful management of oral mucosal lesions (Healy and Galvin 2024) . When dental students were asked if knowledge on usage of biologic agents is essential for dentists, about 91% had responded yes (Figure 1.9).

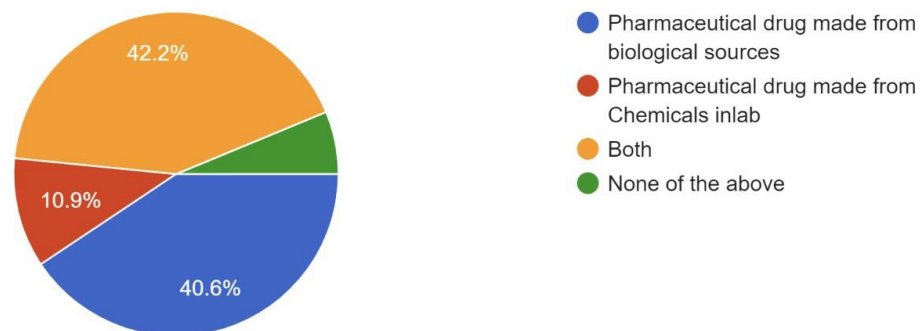


Figure 1.1 showing response to what biologic agents are.

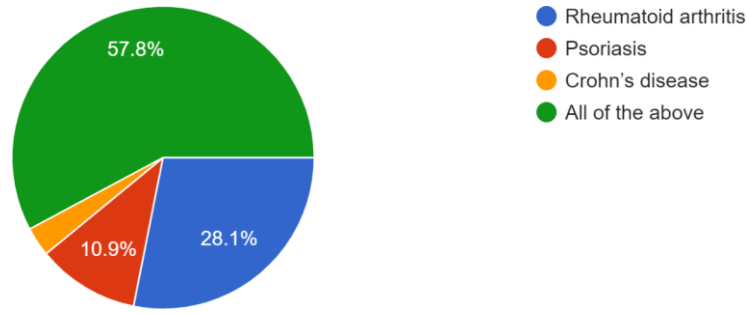


Figure 1.2 showing response to usage of biologic agents

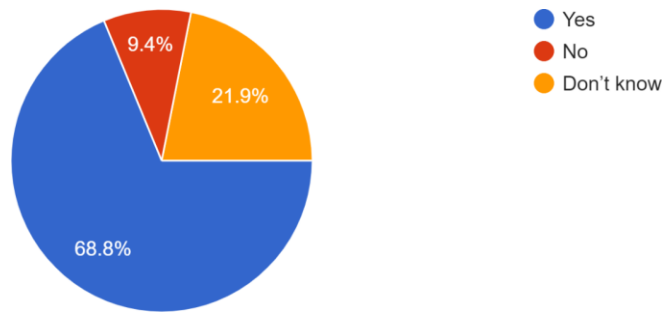


Figure 1.3 showing response on awareness of usage of biologic agents in oral mucosal diseases

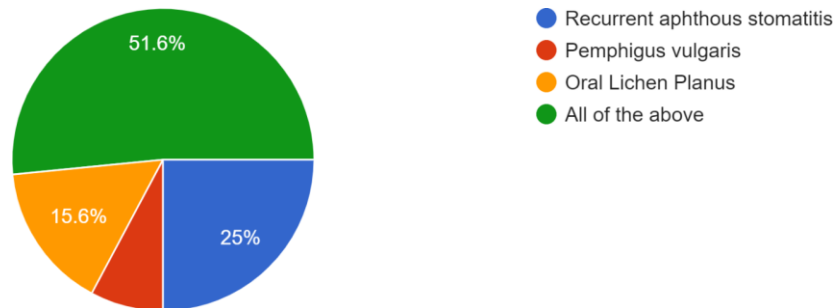


Figure 1.4 showing response to usage of biologic agents in management of oral mucosal diseases



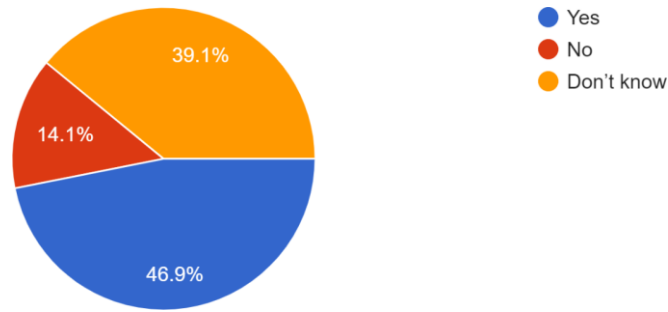


Figure 1.5 showing response to usage of biologic agents as first line of drug in treatment of pemphigus vulgaris

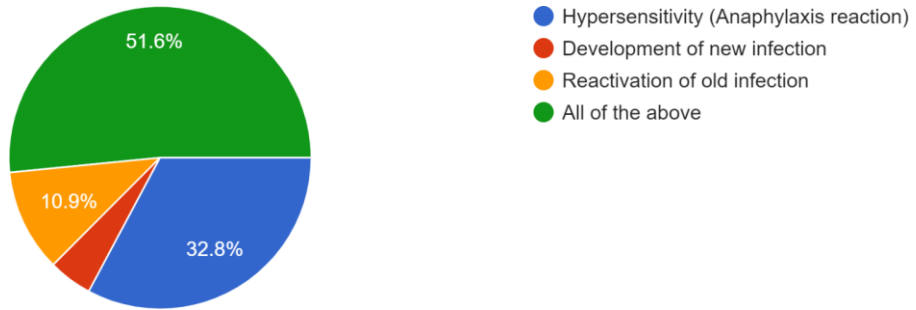


Figure 1.6 showing response to possible adverse effects on usage of Biologic agents

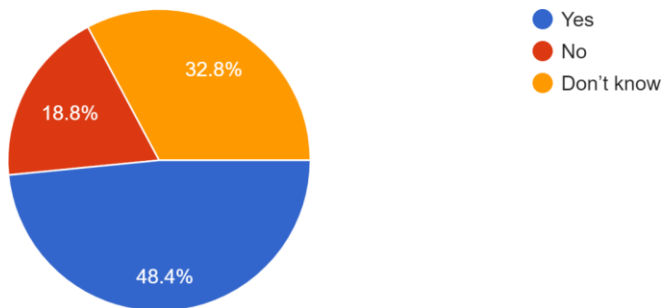


Figure 1.7 showing response to possibility of reactivation of old viral infections

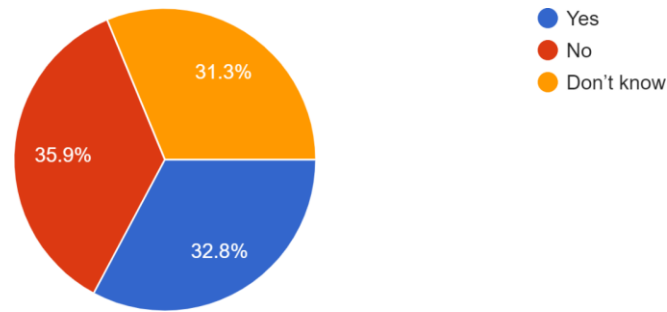


Figure 1.8 showing response on safety of usage of BAs in pregnant patients

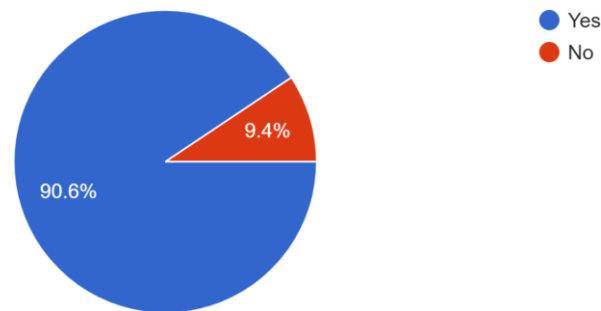


Figure 1.9 showing response whether knowledge on BAs are essential for dentists

## CONCLUSION

Biologic agents are a group of drugs that are increasingly used in the management of systemic immune mediated diseases like Rheumatoid arthritis, Psoriasis, Crohn's disease and also in certain malignancies. Most of the immune mediated oral diseases are successfully managed by optimal use of topical and conventional systemic corticosteroids, supplemented with anti-inflammatory and analgesic mouthwashes with good oral hygiene as important adjuncts. In severe and refractory cases, not responding to conventional treatment, biologic agents are used increasingly nowadays.

Even though BAs have shown improved efficacy and remission in management of several immune mediated diseases, considerable side effects have also been found with usage of BAs. It is important for the dental professionals to have sufficient knowledge and awareness on usage of BAs in management of oral mucosal lesions.

**ACKNOWLEDGMENT:**

The authors would like to thank the college management for extending their support.

**FUNDING:**

Nil

**CONFLICT OF INTEREST:**

Nil

**REFERENCES**

1. Benson J M, Peritt D, Scallon B J *et al.* Discovery and mechanism of ustekinumab: a human monoclonal antibody targeting interleukin-12 and interleukin-23 for treatment of immune-mediated disorders. *MAbs* 2011; 3: 535-545.
2. Camacho-Alonso F, Lopez-Jornet P, Bermejo-Fenoll A. Pemphigus vulgaris. A presentation of 14 cases and review of the literature. *Med Oral Patol Oral Cir Bucal* 2005;10:282-8.
3. Chong BF, Wong HK. Immunobiologics in the treatment of psoriasis. *Clin Immunol* 2007; 123: 129–138.
4. Eleni A. Georgakopoulou, Dimitrios Andreadis, Efthymios Arvanitidis, Panagiota Loumou. Biologic Agents and Oral Diseases – An Update on Clinical Applications. *Acta Dermatovenerol Croat* 2013;21(1):24-34
5. Georgakopoulou EA, Andreadis D, Arvanitidis E, Loumou P. Biologic agents and oral diseases -- an update on clinical applications. *Acta Dermatovenerol Croat.* 2013;21(1):24-34. PMID: 23683483.
6. Gniadecki R. Desmoglein autoimmunity in the pathogenesis of pemphigus. *Autoimmunity* 2006;39:541-7.
7. Healy, C., Galvin, S. Biological therapies and management of oral mucosal disease. *Br Dent J* 236, 317–321 (2024). <https://doi.org/10.1038/s41415-024-7065-9>
8. Ho DY, Subramanian AK. Infections related to biologics. *Infect Dis Clin N Am* 2020;34:xiii–xvi.

9. Jackson JM. TNF-alpha inhibitors. *Dermatol Ther* 2007;20:251-64.
10. Martin LK, Werth V, Villanueva E, Segall J, Murrell DF. Interventions for pemphigus vulgaris and Rev 2009.
11. O'Neill ID, Scully C. Biologics in oral medicine: principles of use and practical considerations. *Oral Dis* 2012;18:525-36.
12. Sidhu R, Veerabhadrapa RS, Shergill NK. Role of biologics in oral diseases-A therapeutic intervention. *International Dental Journal of Students' Research*. 2019 Apr 1;7(2).
13. Stasi R (2010). Rituximab in autoimmune hematologic diseases: not just a matter of B cells. *Semin Hematol* 47: 170–179.