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Salivary Amylase As A Diagnostic Tool In Dentistry

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Abstract
Pain perception is highly subjective and varies among individuals, making its precise assessment a challenge for clinicians. This article highlights the potential of non-invasive methods, specifically utilizing salivary amylase (SAA) as a biomarker, to evaluate pain intensity. The fluctuations in SAA levels have been explored across various fields of dentistry to assess stress, anxiety, and pain responses. By leveraging saliva as a diagnostic tool, clinicians can gain valuable insights into patient discomfort, aiding in the development of more effective treatment and pain management strategies.
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I. Introduction

Dental procedures are often associated with significant stress, anxiety, and pain. To assess these responses, various studies have explored the use of biomarkers present in body fluids such as blood, urine, and saliva. Among these, saliva has emerged as the most effective and practical biomarker due to its cost-effectiveness, ease of collection, and non-invasive nature (Christidis et al., 2020; Laurikainen et al., 1988; Van Stegern et al., 2006).

One of the key salivary biomarkers for assessing psychological stress and pain severity in dental treatments is salivary alpha-amylase (SAA). SAA has been extensively used to evaluate pain perception and its severity in oral and periodontal diseases (Canigur Bavbek et al., 2021; Wittwer et al., 2016). The activation of pain stimuli triggers the sympathetic nervous system (SNS), leading to the release of epinephrine and norepinephrine, which in turn elevate SAA levels. Studies indicate that SAA levels tend to increase with age, as acinar cells of the salivary glands produce this enzyme in response to autonomic nervous system inputs.

Dental treatments, being inherently stressful, activate both the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis, resulting in the release of cortisol. Additionally, immunoglobulin A (IgA), another salivary biomarker, is influenced by the SNS and HPA axis, with its levels being analyzed to assess stress responses.

The measurement of SAA levels has been explored across various dental disciplines, including oral surgery, endodontics, orthodontics, pediatric dentistry, implantology, and parafunctional habits. To validate these findings, several studies have conducted surveys among individuals undergoing dental treatments, with participants providing informed consent before taking part in the research.

Understanding salivary biomarkers in relation to dental stress and pain perception opens new avenues for improving patient management and developing strategies to mitigate dental anxiety effectively.

II. Evaluating Pain In Third Molar Surgery Using Salivary Amylase

The management of symptomatic third molars typically involves antibiotic therapy, surgical extraction, operculum excision, irrigation, and curettage, as leaving an infected tooth untreated can lead to severe complications such as deep fascial space infections, airway obstruction, and life-threatening conditions (Kunkel et al., 2004, 2007). Additionally, post-operative complications such as osteomyelitis, alveolar osteitis, and septicemia have been reported following third molar extractions (Jensen et al., 1986; Meurman et al., 1995; Mohammed-Ali et al., 2010). Due to the significant impact of post-operative pain on a patient's ability to speak, eat, and overall emotional well-being, accurate pain assessment is crucial. The Visual Analog Scale (VAS) is widely used for this purpose, where a 100mm horizontal line represents pain intensity from "no pain" to "worst pain imaginable" (Katz & Melzack, 1999).

Recent studies have explored salivary alpha-amylase (SAA) as a biomarker for assessing pain intensity in mandibular third molar surgery, showing a positive correlation between VAS scores and SAA activity. A study published by Wiley Online Library analyzed symptomatic and asymptomatic patients, assessing their pain levels and analgesic intake over two weeks. The results indicated that post-operative pain levels were higher than pre-treatment levels, reinforcing the correlation between pain intensity and SAA activity.

A separate study conducted at Chiang Mai University between October 2019 and May 2020 evaluated SAA levels in patients undergoing third molar extractions. Participants were categorized into groups based on symptoms and treatment type, with exclusions for factors that could influence salivary gland function, such as fever, salivary disease, medication use, and airway obstruction. Local anesthesia (4% articaine epinephrine solution) was administered using the inferior alveolar nerve block and buccal infiltration techniques, and the surgical procedure lasted approximately 20 minutes. Patients were advised to take paracetamol (500mg every six hours) and ibuprofen (400mg as needed for pain relief). VAS scores were recorded before treatment, after anesthesia wore off, and twice daily for one week.

Non-stimulated saliva samples were collected before treatment and on days one and seven post-surgery. Samples were centrifuged, and SAA activity was analyzed using an enzymatic colorimetric assay. The results showed that while pain levels were similar between symptomatic and asymptomatic groups, patients with pericoronitis experienced increased post-operative pain. Pain levels peaked immediately after anesthesia wore off and gradually declined over the first week, with symptomatic patients reporting pain relief by Day 4 and asymptomatic patients by Day 6. However, on Day 7, pain persisted in 25% of symptomatic patients and 50% of asymptomatic patients.

SAA levels in asymptomatic patients were low before treatment, increased during surgery, and gradually returned to baseline, whereas symptomatic patients exhibited high pre-treatment SAA levels that further increased during the procedure before declining post-operatively. Medication intake patterns also varied, with symptomatic patients consuming more paracetamol and less ibuprofen due to the elimination of infection, while asymptomatic patients relied more on ibuprofen for pain relief.

Another study investigated the impact of conscious sedation on SAA levels during third molar extractions. Eighteen male patients were divided into two groups: one receiving sedation and the other undergoing extraction under local anesthesia. Saliva samples were collected at five different time points initial consultation, upon sitting in the dental chair, before local anesthesia administration, immediately after extraction, and four hours post-extraction. The study found that while conscious sedation effectively managed dental anxiety and phobia, it did not significantly impact acute stress levels during surgery.

These findings highlight the potential of SAA as an objective biomarker for pain assessment in oral surgery. As a non-invasive and cost-effective tool, SAA measurement can enhance post-operative pain management strategies, allowing clinicians to tailor treatment plans for improved patient outcomes.

III. Orthodontics

Orthodontic treatments often induce varying levels of discomfort and anxiety in patients, leading to both physiological and psychological responses. While pain management is a key consideration in orthodontics, understanding the biomarkers that correlate with pain intensity and anxiety can help improve treatment approaches. Salivary biomarkers, such as salivary alpha-amylase (SAA), have been explored for their potential in assessing stress and pain levels during dental procedures. This article examines studies on the relationship between dental anxiety, pain, and SAA levels in orthodontic treatments, highlighting the complex interplay between psychological factors and physiological responses.

A pilot study was conducted to assess the relationship between dental anxiety and intraoperative pain during orthodontic treatment, revealing a moderate but significant correlation between the two. The study utilized Corah's Dental Anxiety Scale (DAS), a questionnaire consisting of four questions, each with five response options ranging from 1 (no anxiety) to 5 (high anxiety). Conducted at Columbia University, the study found a positive correlation between dental anxiety and pain intensity. Saliva samples were collected using the swab technique from the sublingual region to measure salivary alpha-amylase (SAA) levels. However, Compos et al. reported no direct correlation between SAA levels and pain intensity during orthodontic procedures such as bracket placement, indicating that the increase in SAA levels was not linearly associated with pain.

Another study surveyed 20 male patients aged 11 to 37 years, assessing their pain levels before treatment, after bracket placement, bonding, and initial arch wire insertion. Pain was measured using the Visual Analog Scale (VAS). While this study also found no direct correlation between pain intensity and SAA levels, patients exhibited elevated SAA levels throughout the treatment period. These findings suggest that while orthodontic procedures may trigger physiological stress responses, SAA may not be a reliable biomarker for pain intensity in orthodontic treatments.

IV. Endodontic And Restorative Treatment

Endodontic and restorative treatments often require effective pain management, as patients experience varying levels of discomfort and anxiety during these procedures. Salivary biomarkers, such as salivary alpha-amylase (SAA), have been studied for their potential to correlate with pain intensity and stress levels in dental settings. Understanding these biomarkers can provide valuable insights into managing pain and improving patient care. This article explores studies on the relationship between SAA levels, pain intensity, and dental anxiety in endodontic and restorative treatments, shedding light on the complexities of pain perception and physiological responses during dental procedures.

A study involving 55 patients with mandibular molar pain and symptomatic irreversible pulpitis found a correlation between pain management and SAA levels. The patients, aged 18-55 years, were assessed using the Visual Analog Scale (VAS) for pain before and 3 hours after treatment. The results showed a decrease in SAA levels post-operatively, highlighting the potential of SAA as a marker for pain intensity and the effectiveness of pain management in endodontics. In endodontics, the focus is not only on debridement and bacteria removal but also on managing pain severity to ensure treatment success. The study confirmed a positive correlation between SAA levels and pain management effectiveness.

Another study conducted at Babol Dental between 2015-2016 included 99 patients who were administered infiltration injections for premolar and molar composite restorations. The study measured SAA levels at three points: initial examination, immediately before restoration, and 15 minutes post-restoration. The findings revealed that SAA levels were high before the restoration procedure and decreased rapidly afterward. However, the SAA levels remained elevated for about 15 minutes after treatment, likely due to the persistence of pain stimuli. Additionally, the study found that patients with higher MDAS (Dental Anxiety Scale) scores had higher SAA levels, suggesting that dental anxiety could influence salivary amylase activity during restorative treatments. The study also noted no positive correlation between SAA levels and MDAS scores across various age groups, genders, educational levels, and histories of traumatic dental extractions.

Further investigation into the relationship between SAA levels and pain intensity in symptomatic irreversible pulpitis revealed that for every year of age, there was an increase of 2.898 units/ml in SAA levels. This finding highlights that age may be an important factor in the physiological response to dental pain, with older patients experiencing higher SAA levels. These studies collectively demonstrate that while SAA levels can serve as a biomarker for pain and stress in endodontic and restorative treatments, the relationship between pain perception, anxiety, and biomarker levels is complex and influenced by multiple factors.

V. Periodontics

Salivary alpha-amylase (SAA) has emerged as a potential biomarker with significant implications in the progression of periodontal diseases. A study conducted at RASAI Khaimah College of Dental Sciences involved 45 participants with varying stages of periodontitis, ranging from stage 1 to stage 4. Saliva samples were collected and analyzed using the ELISA kit, which revealed a positive correlation between SAA levels and clinical indicators of periodontal disease, such as probing depth and clinical attachment loss (CAL). Higher levels of SAA were observed in individuals with more severe forms of periodontal disease, suggesting that SAA could serve as an indicator of disease severity.

The underlying physiological mechanism links periodontal disease with increased pain stimuli, which activate immune responses involving pro-inflammatory cytokines, such as TNF-alpha, interleukins, and interleukin-1 beta. These cytokines trigger the sympathetic nervous system, leading to the release of epinephrine and norepinephrine. These hormones, in turn, stimulate the beta-adrenergic receptors in the salivary glands, resulting in elevated SAA levels. The saliva samples for analysis were collected from the floor of the mouth as unstimulated saliva. The results demonstrated that moderate to severe periodontitis was associated with significantly higher SAA levels, while mild periodontitis did not show a notable difference in SAA levels compared to healthy controls. These findings suggest that elevated SAA levels are more indicative of periodontitis than gingivitis, though SAA levels alone cannot predict the progression of periodontal disease without considering other factors.

Supporting this, Harian et al. found a positive correlation between SAA levels and the severity of periodontitis, particularly in cases of chronic periodontitis. Similarly, Gbadebo et al. reported higher pain levels in individuals with apical periodontitis compared to those with symptomatic irreversible pulpitis, further strengthening the link between pain, inflammation, and elevated SAA levels.

Additionally, research has shown a connection between dental plaque and SAA levels. Alpha-amylase, which helps break down complex carbohydrates into simpler sugars, may play an important role in plaque and caries formation. As SAA levels increase, so does the availability of fermentable carbohydrates for cariogenic bacteria, which can lead to acid production and contribute to dental decay. Therefore, elevated SAA levels could be a contributing factor to an increased risk of caries, further highlighting the importance of SAA in oral health. In conclusion, while SAA levels are strongly associated with periodontal disease severity and stress, they should be considered alongside other clinical factors to provide a more comprehensive understanding of disease progression and risk.

VI. Dental Implant Surgery

Dental implant surgery involves complex procedures, such as bone augmentation, soft tissue management, and the placement of healing abutments, all of which can cause heightened levels of stress and anxiety in patients. This anxiety is primarily linked to elevated cortisol levels, which in turn can lead to increased blood pressure due to activation of the sympathetic and parasympathetic nervous systems. As a result, salivary amylase levels also rise.

A study conducted by Tokyo Medical and Dental University with 44 patients (mean age 62 years) explored the relationship between dental implant surgery and salivary amylase activity. The study measured SAA levels using a SA monitor and a dry chemical system. A testing tip was placed under the patient's tongue for 30 seconds to assess the levels. The findings indicated that SAA activity remained elevated post-surgery, even though other vital signs returned to normal shortly after the procedure. This suggests that SAA levels can be an effective indicator of mental and physical stress during surgical procedures.

The results further revealed that the SAA levels were higher after surgery than before, with a significant increase following prolonged surgical hours and patient fatigue. Additionally, the use of intravenous anesthesia was associated with elevated SAA levels, highlighting the impact of both the procedure itself and anesthesia on stress and anxiety. Overall, this study demonstrates the potential of SAA as a reliable marker for assessing stress during dental implant surgeries.

VII. Salivary Cortisol And SAA Levels In Pedodontics

A study conducted on children aged 6-9 years and 3 months to 1 year aimed to assess the relationship between salivary cortisol, SAA levels, and stress in pediatric dental patients. A total of 1,567 children were screened, and 703 caries-free children were selected for further analysis, with a follow-up period of 3 months. The participants were divided into three groups: phobic, anxious, and control, based on their behavioral response to dental visits. Out of the initial 703 children, 183 met the criteria, and 151 completed the study.

The findings indicated that SAA levels serve as an indicator of acute stress and can effectively differentiate between anxiety and fear. On the other hand, cortisol levels appeared to reflect long-term stress, lacking sensitivity to distinguish between anxiety and fear in children. Saliva samples were collected using the passive drool method, and heart rate measurements were taken with a pulse oximeter at 5-minute intervals. The study revealed that the anxious group had the highest heart rate, even when not seated in the dental chair. In contrast, the phobic group showed no increase in heart rate but exhibited elevated levels of both SAA and cortisol. The anxious and control groups demonstrated lower SAA levels, suggesting a relationship between dental fear and increased salivary cortisol and SAA levels.

This study underscores the potential of salivary cortisol as an assay for dental fear but suggests that it does not effectively differentiate between anxious and phobic groups. These insights are valuable for clinicians and researchers in determining the most appropriate behavioral management techniques for pediatric patients. Additionally, a survey conducted at Osaka Dental University Hospital revealed a significant decrease of 83% in IgA levels following dental treatment, with IgA levels being higher than cortisol levels, further emphasizing the role of stress in pediatric dental care.

These findings highlight the potential for salivary biomarkers such as SAA and cortisol to guide clinicians in understanding the stress responses of pediatric patients during dental procedures and tailoring their approach to individual needs.

VIII. Oral Parafunctional Activity And Salivary Amylase Levels

The relationship between salivary amylase (SAA) levels and oral parafunctional habits, such as bruxism, TMJ (Temporomandibular joint) joint noise, and attrition, has been explored in recent studies. To measure SAA levels, a specialized chip was placed under the tongue to absorb saliva, which was then monitored for changes in SAA concentration. The results revealed that individuals with higher levels of TMJ joint noise and attrition showed significantly elevated SAA levels, while bruxism was associated with lower SAA concentrations.

Interestingly, stress was found to be more strongly correlated with TMJ joint noise and attrition, while bruxism was noted as an activity primarily linked to stress relief. In children undergoing long-term psychostimulant therapy, SAA levels were notably lower compared to healthy children, indicating the potential impact of stress and medication on salivary biomarkers. The study also found a negative correlation between SAA levels and bruxism, suggesting that bruxism may act as a coping mechanism to manage stress, ultimately affecting salivary amylase levels.

These findings emphasize the complex relationship between stress, oral parafunctional activities, and salivary amylase, highlighting the potential of SAA as a marker for stress-related oral behaviors and the need for further exploration of its role in managing dental health.

IX. Conclusion

Salivary amylase has emerged as a valuable biomarker for assessing dental-related anxiety, pain, and stress. Its utilization before dental procedures can aid clinicians in tailoring treatment protocols and optimizing pain management strategies. Studies have demonstrated a positive correlation between salivary amylase levels and stress, anxiety, and pain experienced during dental treatments. Although some variations exist among different surveys, the majority support its relevance in evaluating psychological and physiological responses to dental procedures. Given the non-invasive and easily accessible nature of saliva sampling, salivary amylase presents a promising tool for clinicians to enhance patient care and improve treatment outcomes.

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