INTERNATIONAL JOURNAL OF
INTEGRATIVE AND
MODERN MEDICINE

Analysis of Mixed Saliva Parameters in Patients with Gastrointestinal Diseases

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Annotation: Gastrointestinal tract (GIT) diseases rank among the leading pathologies of internal organs, exerting a significant impact on the general condition of the body and the quality of life of patients. In recent years, there has been growing interest in non-invasive methods of diagnosis and monitoring of such diseases, one of which is the study of the composition and properties of mixed saliva. Saliva reflects a number of physiological and pathological processes occurring in the body and can serve as an informative biological material for detecting changes associated with various GIT pathologies.

Keywords: GIT diseases, mixed saliva, enzymes, lactoferrin.

Introduction: Analysis of mixed saliva parameters allows for the assessment of not only the condition of the oral cavity but also provides data on metabolic, immunological, and inflammatory changes characteristic of digestive system diseases. In this regard, the study of mixed saliva indicators in patients with GIT diseases is of particular relevance and can contribute to the improvement of diagnostic and therapeutic approaches in gastroenterology. Recently, dentists have become increasingly concerned about comorbidities in patients seeking dental care, as it was long believed that the development of dental pathologies is of a local nature (Kaysina T.K., 2017). Currently, evidence has emerged indicating a clear relationship between oral health and the general health of the body (Mikhalchenko D.V. et al., 2013; Gazhva S.I., Igolkina N.A., 2013; Naumova V.N. et al., 2016). Researchers have found that comorbidities are associated with structural changes in the tissues of teeth, periodontium, oral mucosa, and salivary glands (Yanushevich O.O., Syrbu O.N., 2013; Kurmanalina M.A., Uraz R.M., 2015; Mitronin A.V. et al., 2016; Romanenko I.G. et al., 2017; Kilmukhametova Yu.Kh. et al., 2017; Orlova E.S., 2017; Vavilova T.P. et al., 2017).

As indicated in the studies by Tsymbalistov A.V. et al. (2013), changes in the oral cavity may cause such nosological forms of GIT diseases as celiac disease, gastroesophageal reflux, or intestinal inflammation. At the same time, the macroscopic and histological characteristics of manifestations in the oral cavity are similar to those found in the tissues of the gastrointestinal tract (Kvetnoy I.M. et al., 2009; Tytyuk S.Yu. et al., 2016; Lankarani K.B., et al., 2013). Studies by Tytyuk S.Yu. et al., 2019; Tytyuk S.Yu., Iordanishvili A.K., 2019; Mulic A., et al., 2013; Bartlett D.W., et al., 2013 have shown that in inflammatory bowel diseases, the incidence of caries and non-carious lesions of the teeth increases in 50% of young and middle-aged people aged 18 to 35 years.

According to Glavnova P.V. et al. (2015), Crippa R., et al. (2016), Raykova B.S. (2018), the prevalence of Crohn's disease is 150 people per 100,000 inhabitants in Europe and America. At the same time, pathological processes in the oral cavity in Crohn's disease are the result of decreased levels of microelements and macronutrients in the blood serum due to impaired absorption in the intestine, or local immune reactions to oral antigens. These changes are accompanied by dry mouth and halitosis, and externally manifest as typical and pathognomonic changes such as "cobblestone" hyperplasia of the oral mucosa, stomatitis, gingivitis, periodontitis, cheilitis, and geographic glossitis. Among all gastrointestinal diseases, chronic gastritis accounts for 70 to 80% (Sipponen P., Maaroos H.-I., 2015; Afanasenkova T.E. et al., 2018).

According to (Pogurets Yu.K. et al., 2017; Kaysina T.N. et al., 2017; Abakumova M.A., Konysheva A.K., 2017; Kulumbegova I.R., Khubulov S.A., 2019), in hypoacid gastritis, the rate of saliva

secretion decreases, which coincides with the formation of angular cheilitis and a white-yellow coating on the dorsal surface of the tongue.

G.I. Lukina (2011) in her study showed that in pathologies of the esophagogastroduodenal section of the intestine, the most common clinical signs of the oral mucosa are pastosity (in 58.6% of cases), dryness (in 43% of cases), and coating on the dorsal surface of the tongue (in 50.9% of cases). These patients complain of bad breath, a feeling of bitterness, sourness, and burning, and the incidence of gingivitis, angular cheilitis, geographic tongue, enamel hypoplasia, and dental caries is higher compared to healthy individuals (Yanushevich O.O. et al., 2014; Shcherbakova A.Yu. et al., 2014).

Studies (Khaykin M.B. et al., 2006; Moiseeva M.V., Belova E.V., 2011; Yanushevich O.O. et al., 2013; Kosoyuga S.Yu., Varvanina S.E., 2015; Nerobeev A.S. et al., 2018) have shown that peptic ulcer disease of the stomach and duodenum significantly alters the acid-base balance in the oral cavity, leading to the development of multiple caries, enamel erosion, inflammatory processes in periodontal tissues, and changes in the ratio of various organic acids in saliva. Based on the literature, we decided to identify the relationship between pathology of the mucosa and oral tissues in patients with gastrointestinal tract diseases.

The aim of the study was to investigate the nature of changes in certain biochemical blood parameters in the mixed saliva of patients suffering from gastrointestinal tract diseases.

Materials and Methods:

In the outpatient setting of the Tashkent State Dental Institute from 2020 to 2022, 140 patients with gastrointestinal tract pathology were examined, including 98 men (70%) and 42 women (30%), with an average age of 51.9 years. According to endoscopic studies, patients had lesions of various parts of the GIT (chronic gastritis; peptic ulcer disease of the stomach and duodenum). The control group consisted of 25 practically healthy individuals.

Diagnosis of lesions in various parts of the GIT was based on classical criteria [Vasilenko V.Kh. et al., 1987; Ivashkin V.T. et al., 2001] and was carried out taking into account clinical-endoscopic, functional, and morphological data. Verification of chronic gastritis was carried out according to the classification criteria proposed by the International Association of Gastroenterologists (Sydney, 1990; Houston, 1996), taking into account the traditional views for Russia [Aruin L.I. et al., 1998], based on endoscopic and morphological criteria. Observation of patients and healthy individuals was carried out according to a unified program, which included general clinical examination, esophagogastroduodenoscopy (EGD). Biomaterial was collected in the morning, on an empty stomach, in graduated test tubes. In all patients, oral fluid samples were collected before the administration of any medication. Before the procedure, the patient rinsed their mouth with distilled water for 30 seconds, followed by 5 minutes of rest. Then the patient swallowed all the accumulated saliva, after which the actual collection of material began for 15 minutes. At the end, the test tube was tightly closed, placed in a container with ice, and delivered to the laboratory within an hour and a half. In the laboratory, the test tubes were centrifuged at 3000 rpm for 10 minutes at 4°C, after which the saliva sample was frozen and stored at -80°C until analysis. To determine biochemical markers in mixed saliva, "HUMAN" reagent kits were used for direct enzyme-linked immunosorbent assay according to the manufacturer's instructions. Statistical processing of the data was performed on a personal computer using the standard package of applied statistical analysis programs (Statistica for Windows v. 7.0). The critical reliability level of the null statistical hypothesis was taken as 0.05.

Results:

As is known, the spectrum of oral cavity lesions in various comorbidities is wide. At the same time, comorbidities contribute to the development of pathological conditions in the tissues of the oral cavity, and against their background, various drugs are used for their correction. It is also important to consider the gerontological population, which is the main consumer of medications.

When analyzing the nosologies of gastrointestinal tract diseases, atrophic and chronic gastritis prevailed. According to the data obtained, 63% of patients with GIT pathology reported the presence of bad breath (halitosis). Dryness of the oral cavity was reported by 28% of respondents. Changes in the color of the tongue and gums were noted by 52% of those surveyed. A burning sensation in the oral cavity was reported by 8% of respondents, and 12% of patients reported hypersalivation.

On external examination, no pathologies of the soft tissues or abnormalities in the facial bone structures were found. Regional lymph nodes were not enlarged and painless. The skin was clean without pathological elements. During the examination of the oral mucosa, attention was paid to the architecture, color, moisture, and the presence of pathological elements (ulcers, erosions, crusts, cracks). According to the data obtained, in 16% of cases, patients had a pale oral mucosa. Hyperemia of the oral mucosa was observed in 11% of cases, dryness in 53%, mucosal hyperplasia in 14%, and ulcers and erosions in 7% of cases. Special attention was paid to the condition of the tongue in patients with GIT pathology. Among GIT patients, hyperemia of the tongue (41%) and a white coating on the dorsal surface of the tongue (38%) prevailed, tongue fissures were noted in 21%, tongue enlargement in 18%, and a folded tongue in 16%. In the oral cavity, the presence of superficial deposits on teeth (54%) and dental crowding (17%) predominated. Signs of hyperemia (26%), bleeding (41%), gum swelling (26%), and gingival papilla hyperplasia (8%) indicated significant marginal periodontium involvement against the background of polymorbid conditions. The most frequent dental pathologies were caries (8.9%) and wedge-shaped defects (7.1%).

To determine the intensity of the carious process in patients with GIT pathology, the DMF index was used. The DMF index in patients was 8.48±0.91, which corresponds to a moderate level of caries intensity. The number of filled teeth ranged from 1 to 6. The number of extracted teeth was slightly lower than the number of filled teeth, ranging from 1 to 24 teeth. The DMF index values were reliably positively dependent on the diagnosis of GIT nosology. The lowest DMF index values were found in patients with chronic gastritis, and the highest in patients with peptic ulcer disease of the stomach and duodenum.

In addition to clinical examination of the oral tissues, patients with GIT pathology underwent a study of mixed saliva, which reflects changes occurring in the oral cavity.

As can be seen from the presented research results, patients with GIT pathology showed an increase in all studied parameters in mixed saliva. Against the background of an increase in total protein content in mixed saliva in patients with GIT pathology, there was an increase in the activity of enzymes, especially mitochondrial enzymes compared to plasma enzymes. Thus, in patients with GIT pathology, there was a significant increase in AST activity in saliva, as well as a pronounced tendency to increased ALP and ALT activity, which reflects periodontal status disturbances. LDH activity was also higher compared to the control group. These data indicate pronounced inflammation of the oral tissues, associated both with the growth of pathogenic microflora and with impaired blood supply and weakened defense systems of the oral mucosa.

One of the main indicators of mucosal immunity is the content of secretory immunoglobulins. It should be noted that the ratio of immunoglobulins in the oral cavity differs from that in blood serum. Secretory antibodies in oral fluid are immunoglobulins of classes IgA and IgM and have a local origin. They are produced by plasma cells located under the basement membrane in the connective tissue layer of the mucosa (M.J. Taba, J. Kinney et al., 2005; Polushina L.G., 2019). The main role of sIgA antibodies is to prevent the attachment of bacteria and microbial toxins to the epithelium and absorb harmful xenobiotics. Saliva contains much more sIgA than other immunoglobulins: for example, in saliva secreted by the parotid glands, the IgA/IgG ratio is 400 times higher than that in blood serum (C.A. Janeway, P. Travers, 1996). The study of the level of secretory immunoglobulin A in mixed saliva in patients with GIT diseases averaged 167.24±10.09 mg/L, whereas this indicator in the group of healthy individuals was 86.23±7.24 mg/L.

As is known, the sIgA level reflects the status of local immunity aimed at forming defense mechanisms in the oral cavity. An increase in sIgA level leads to a shift from effective cellular

immunity to impaired humoral (Th1/Th2) immunity as GIT disease progresses. A similar trend was observed regarding lactoferrin levels in the mixed saliva of patients with GIT diseases. Thus, if the lactoferrin concentration in oral fluid in healthy individuals was 7127.13±82.78 ng/mL, in the group of patients with GIT diseases it was 61456.28±71.15 ng/mL, indicating an inflammatory process in the oral cavity. It should be noted that the increase in LF level in GIT diseases is due not only to an increase in the number of neutrophils but also to their intensive degranulation caused by hyperactivation of cells by bacterial substances, complement components and their fragments, and pro-inflammatory cytokines. It is also important to note that objective indicators of the condition of the oral cavity are dental indices—DMF, OHS-S, PMA, PI—determined during the examination by a dentist. All of them were significantly increased in patients with GIT diseases and correlated with the severity of the pathological process. The most pronounced changes were observed in PMA and PI, which is logical and consistent with dental concepts. PMA quantitatively reflects the intensity and prevalence of the inflammatory reaction of soft tissues, while PI indicates the severity of the disease, reflecting not only gingival inflammation but also pocket formation and alveolar bone resorption. This was also confirmed by the results of the physicochemical analysis of mixed saliva in patients with GIT diseases, in particular by the levels of secretory immunoglobulin A and lactoferrin.

Conclusions: In patients with GIT diseases, along with stimulation of mucosal immunity, an increase in the concentration of lactoferrin and secretory immunoglobulin A in mixed saliva was also detected, as well as an increase in enzymes in mixed saliva, which indicates Th-2 dependent activation of cellular immunity.

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