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Review article

Human saliva as a diagnostic material

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ABSTRACT

Today blood biochemical laboratory tests are essential elements to the diagnosis and monitoring of the treatment of diseases. However, many researchers have suggested saliva as an preferable diagnostic material. The collection of saliva is simple, painless, cheap and safe, both for patients and medical staff. An additional advantage of saliva is the fact that it may be retrieved several times a day, which makes repeat analysis much easier. Furthermore, saliva has very high durability. Although 94–99% of salivary content is water, saliva also contains numerous cellular elements and many organic and inorganic substances, including most biological markers present in the blood and urine that may be used in the early detection and monitoring of many dental and general diseases.

Contents

1. Introduction

Biochemical laboratory tests are an essential part of human disease diagnosis and monitoring. For biochemical analysis various biological fluids or tissues are collected, however, blood is still the most commonly used diagnostic material. Unfortunately, blood collection is an invasive procedure that may involve some risk to the health of medical staff and patients (e.g. HIV, HBV) as well as a very large discomfort for many groups of patients. Therefore, many researchers have recommended saliva as the ideal non-invasive diagnostic material. Human saliva may be used in the early diagnosis and monitoring of many systemic diseases (e.g. cancer, infectious or cardiovascular disorders) [1], in the pharmacokinetic studies, in therapeutic drug monitoring [2,3]. Using saliva as a diagnostic material is possible, because a number of major inorganic and organic substances (e.g. proteins, carbohydrates and lipids) as well as drugs and their metabolites are secreted into saliva. In addition, salivary collection is painless, easy, inexpensive, and completely safe for patients and health professionals [4–7]. Therefore, the analysis of the concentrations of various salivary

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components is becoming increasingly important in the laboratory medicine for diagnosis and monitoring of many oral [2,5] and systemic disorders [8–11].

2. Saliva

Saliva – a fluid excreted by the large and small salivary glands, is one of the most important factors affecting the homeostasis of the oral cavity. Salivary composition and secretion depends on the gland from which saliva is secreted, as well as a patient's age, gender and type of stimulating factor [11–13]. Human saliva is composed mainly of water (94–99%), however an important fraction of saliva is made up of proteins (especially glycoproteins) and lipids. Saliva is also rich in carbohydrates, salts and contains non-protein nitrogen (urea, uric acid, amino acids and creatinine) [14]. Besides the excretions of salivary glands, saliva includes gingival fluid, serum components, bacteria and bacterial metabolites, exfoliated epithelial cells and leukocytes. Adults secrete about 0.5–1 liters of saliva daily of which 80% is due to food intake. The secretion of saliva is controlled by the autonomic nervous system (Fig. 1). Quantitative and qualitative changes of saliva are also caused by a variety of oral and systemic diseases, for example: Alzheimer's disease [15], diabetes [13], cystic fibrosis [16,17] and oncological diseases (especially head and neck tumors) [6,8].

A major role of saliva is to create a protective environment for teeth and oral mucosa against a variety of harmful mechanical, biological and chemical stimuli. In addition, saliva takes part in the initial phase of food digestion and participates in the perception of taste. Saliva exhibits antibacterial, antifungal and antiviral properties that are conditioned by the presence of salivary immunoglobulins as well as innate immunity proteins, such as lactoferrin [18] and lysozyme [19]. Waszkiewicz et al. [18,19] reported a decrease in salivary lactoferrin [18] and lysozyme [19] output in chronically intoxicated alcohol-dependent patients, in comparison to social drinkers. Decrease in salivary lactoferrin and lysozyme output in chronically intoxicated alcohol-dependent persons, reflects the inhibition of synthesis and an increase in lactoferrin and lysozyme catabolism, caused by harmful action of ethyl alcohol and its toxic metabolites e.g. acetic aldehyde. Decrease in output of salivary immunoproteins induces deterioration of the paradontium of chronically intoxicated alcohol-dependent persons, in comparison to social drinkers [18,19]. Protection of the paradontium from harmful agents, next to immunoglobulins include enzymatic (e.g. peroxidase, catalase) and non-enzymatic antioxidant activity created by e.g. uric acid, polyphenols, ascorbic acid, reduced glutathione or albumin, protecting oral cavity against free radicals and other environmentally derived oxidative stress-induced agents [20]. Reduction of antioxidant activity can lead to the onset of inflammation in the oral cavity [21–25].

3. Salivary glands

Saliva is produced and secreted by the large salivary (parotid, submandibular and sublingual) as well as 800–1000 minor salivary glands located throughout the oral mucosa (Fig. 1) [4,26]. Cells of the salivary glands produce mucinous or serous human saliva. We may distinguish purely serous salivary glands (e.g. parotid or von Ebner's glands), purely mucous salivary glands (i.e. the glands located on the palate and base of tongue) and mixed (tubulo-alveolar) salivary glands. The mixed salivary glands include: the submandibular, sublingual, labial, buccal and molar salivary glands [27,28].

Large and medium size salivary glands have a lobular structure. The majority of human salivary glands are constructed with segments generating secretion (one layer of cuboid secreting cells wrapped with dense net of blood vessels) and tubes secreting saliva into the oral cavity. Individual salivary glands differ mainly in the structure of secretory segments and the type of produced saliva. Small salivary glands may be histologically distinguished from large and medium size salivary glands, as they are devoid of lobular structure and connective tissue capsule [27–30].

3.1. The parotid gland

The parotid gland is the largest (15–30 g), usually single (occasionally, there is an additional parotid gland) salivary alveolar gland, with a typical serous nature, located on the lateral side of the oral cavity [29] (Fig. 1). The parotid gland is found located in the vicinity of the submandibular salivary gland, separated by the bands of connective tissue. The parotid gland is surrounded by a capsule of connective tissue, divided by numerous septa connected with capsule and variable amounts of fat tissue. The salivary duct located at the frontal edge of the parotid gland perforates buccal muscle and leads to the vestibule of the oral cavity at the region of the second cheek tooth. The parotid gland is parasympathetically innervated by the glossopharyngeal and sympathetically by spinal nerve (Fig. 1) [21,29].

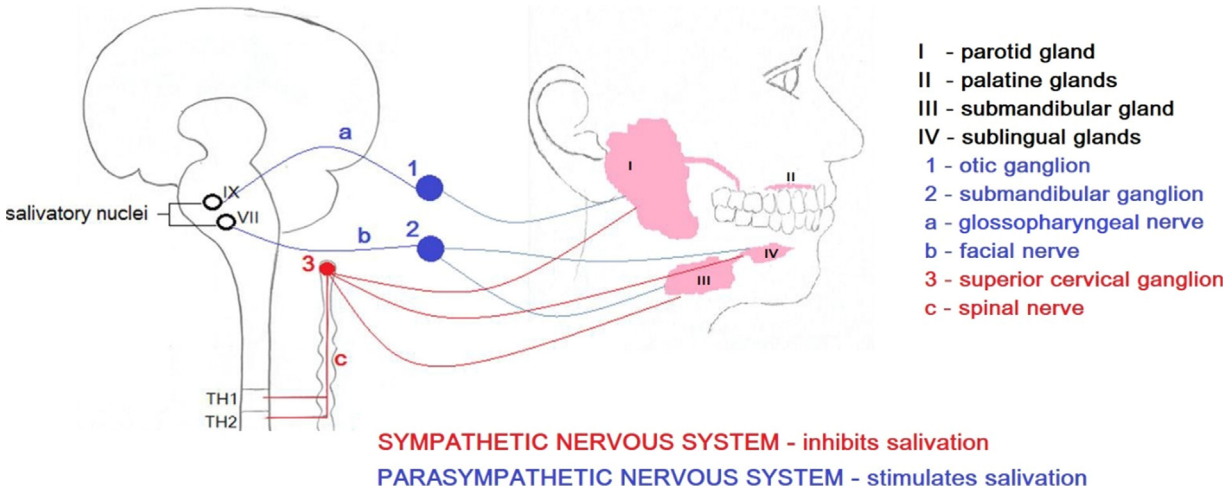

Fig. 1. Salivary glands and their vegetative innervation.