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Saliva and thyroid disease; a review of controversies

Foad Akhoondinasab[a], Mehran Bahrami[b], Azra Mohiti[c*], Maryam Vahdat[d]

a Department of Prosthodontics, School of Dental, Tehran University of Medical Sciences, Tehran, Iran
b Department of Prosthodontics AND Dental Research Center, School of Dental, Tehran University of Medical Science, Tehran, Iran
c Department of Oral Disease, School of Dentistry, Shahid Sadoughi University of Medical Science, Yazd, Iran
d Student, School of Dentistry, Shahid Sadughi University of Medical Sciences, Yazd, iran

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**Corresponding author:*
Azra Mohiti
Department of Oral Disease, School of Dentistry, Shahid Sadoughi University of Medical Science, Yazd, Iran

Tel: +98-351-625881
Fax: +98-351-6250344
Email: amohiti63@gmail.com

ABSTRACT

Introduction: Saliva as a simple non-invasive method of gaining body fluids has been used to detect the thyroid hormones. A single method for determining these hormones has not been clearly stated in the literature. Furthermore, thyroid diseases would affect the salivary glands and may compromise salivary flow.

Materials and Methods: A comprehensive search was conducted using PubMed and Medline.

Conclusion: Saliva can successfully be used as a non-invasive method for determining thyroid hormones and for detecting and monitoring thyroid dysfunctions. Thyroid dysfunctions also have a great impact on salivary gland functions and saliva.

Keywords: Saliva, Salivary Glands, Thyroid Disease

Introduction

Tyroid hormones are critical for biological activities in the body including growth, metabolism, neurodevelopment, and the synthesis of proteins. To diagnosis the thyroid diseases, circulating thyroxine (T4) concentrations should be measured in the blood samples. Furthermore for monitoring treatment protocols, regular blood samples have to be drawn from patients. Serum free T4 is currently being used to diagnose thyroid disorders [1]. In many studies, a suitable replacement for serum in diagnosing and monitoring systemic diseases such as thyroid diseases has been proposed [1, 2].

Saliva is one of the most critical body fluids and plays an important role in preservation and maintenance of oral health. However, usually only changes in its quality and quantity would be noticed. In the recent years as the medical significance of saliva has been understood better. Many studies have focused on salivary gland dysfunction and if they are correlated to systemic diseases itself or as side-effects of medications used for treating these diseases [2-4]. Furthermore, it has been established that certain systemic diseases could directly or indirectly affect salivary glands resulting in changes of the quantity and quality of the secreted saliva, consequently [4]. All these changes in the saliva composition may compromise the oral health of the individual [5]. Hypothyroidism and hyperthyroidism are common thyroid dysfunctions that affect all the organs of the human body; however, their effects on salivary gland function are still inconclusive [6].

Saliva has also been used as a non-invasive systemic sampling method for medical diagnostic purposes and research. Many studies have shown a correlation between plasma free hormone levels and saliva concentrations, but a certain conclusion is not obtained [7]. The objective of this article is to review the use of saliva for diagnosing thyroid diseases and the mutual effects of these diseases on the salivary glands and saliva.

Why is saliva useful for diagnostic purposes?

1. First of all collecting saliva does not need a needle, and there is no need for skin perforation there for it has a major preference over drawing blood for those who are afraid of this procedure [8]

2. It has been established that free-hormone rather than the protein-bound-hormone is considered to be the active component in blood [9]. The steroid hormones in saliva are thought to reflect the free-hormone concentrations in blood. Therefore, saliva levels reflect more accurately active hormones in the body especially for steroid hormones which are strongly bound in blood by specific binding globulins [9, 10].

3. Because saliva is stable at the room temperature for a longer period of time compared to the blood saliva collection is a less technique-sensitive method [11]

4. The risk of blood-borne diseases due to cross-contamination among patients and health care providers is minimal for saliva collection. Also, because saliva has low concentrations of HIV and hepatitis antigens the risk of infection is very low [12, 13].

Why is collecting saliva not a good idea?

1. Since the act of "spitting which is impolite in many cultures, this could mean a major drawback for this procedure and a disadvantage which could not be over ruled" [12].

2. Patient suffering from xerostomia will have a really hard time collecting the amount of saliva needed for tests [12]

3. A standard routine has been established for saliva collection, but it is not used universally there for the results of tests might be compromised [13, 14].

Collecting saliva samples

The most common way to collect saliva is by direct spitting into a tube [14]. The collected saliva could be ultra filtrated using some commercial devices able but in most of the tests the whole saliva is used [15-17].

Transfer of hormones to saliva keeping the upper digestive tract mucosa moist and helping to swallow is one of the roles that saliva plays in maintaining the oral health. Saliva takes part in digestion and immune response by amylase enzyme and secretory immunoglobulin A respectfully [12]. Additionally, saliva is a carrier fluid for signal molecules, which could be produced by the gland themselves or transported from blood into the glands [18]. The lipophilic layers of the capillaries and glandular epithelial cells controls the speed of hormone transferred from blood into saliva. In result, the transfer rate of lipophilic molecules, such as steroids is more rapidly than hydrophilic molecules, such as peptides [19].

In contrary to insulin which is transported into saliva from its tissue of origin other proteins such as cytokine are produced by the salivary glands themselves [20].

Peptides which are oriented from salivary glands are secreted into the acinar lumen by exocytose there for concentrations of peptide hormones in saliva does not always correlate as well as steroid hormones which are transported passively though to the acinar lumen from blood vessels, there for many studies have been conducted to come up with better methods for measuring peptide hormones in the saliva including T4 hormone [9-11].

Techniques for the collection of saliva

Whole saliva is the best method for collecting saliva and is used as a routine method in many studies [16].

This routine includes the participants spitting or drooling directly into the collection tube. In this method, unstimulated saliva is collected. The patient is asked to sit upright in a chair and spit in the tube every minute until the required volume is collected. Furthermore, the patient is forbidden to eat, drink or smoke at least 90 minutes before collection time. Because the collection procedure should not affect salivary concentrations, any absorption devices should be avoided [16-18].

Analytical methods for the measurement of hormones in salivary

Because peptides are more likely than steroids to be attached to the surface of collection tubes, and this may result in the loss of significant amount of the peptide in the sample handling saliva samples for measuring peptic hormones is more critical and needs greater attention. Moreover, the proteolytic content in saliva that rapidly degrades peptide hormones is yet another difficulty in peptide hormone analysis using saliva. These problems could be overcome by using appropriate collection devices, low-protein-binding cryotubes for storage, and adding ethylenediaminetetraacetic acid which is preservative [21-24].

Immunological methods

Immunoassays have been widely used for analyzing salivary hormones because:

1. This method is simple and requires minimal expertise
2. The volume required for this method is smaller than other methods [25].

Chromatographic methods

Modern liquid chromatography coupled with mass spectrometric detection, have provided vast improvements in analytical specificity and sensitivity. Their usage for detecting protein-hormones has been studied, and some promising results have been achieved [26, 27].

Another aspect of this topic is the effect of thyroid disease and its treatment on the salivary glands and saliva. Animal experiments have shown the effect of thyroid dysfunction on salivary glands [28-30].

A study which investigated the effect of hypothyroidism on salivary glands in humans used salivary scintigraphy which does not fully reflect the function of salivary glands [31]. Salivary flow rate and individual gland sialometry are the best methods for assessing salivary gland function. Clearance of microorganisms and dietary components from the oral cavity is a critical role of saliva which is measured by the salivary flow rate [1, 32]. Unfortunately, the only study assessed the salivary flow rate in hypothyroid subjects and its

treatment, has only used the parotid salivary flow rate without considering secretions from the other salivary glands [33]. As it was stated previously salivary flow rate is an important measurement for the assessment of salivary gland function; taken in consideration that whole saliva which includes secretions from all the salivary glands is shown to be functionally more relevant for evaluation of systemic disorders compared to the assessment of secretions of only one individual gland. An alteration in the pH of the saliva is resulted from hormonal and metabolic changes, as well as compromised general health [34]. Some studies demonstrated that the prevalence of hypo-salivation in patients with thyroid dysfunction was lower than other common endocrine disorders, i.e., diabetes [3]. Greater body mass among males and a smaller gland size among females results in higher salivary flow rates in males compared to female individuals [34, 35]. The pH of saliva among the patients with thyroid dysfunction was compatible to the healthy control subjects, but the buffering capacity at baseline among thyroid subjects was lower than that reported among the healthy subjects [28, 36]. Muralidharan et al. [1] demonstrated that hypothyroid subjects showed improvement of salivary flow rate after treatment in both male and female subjects.

These findings suggest that correction of the thyroid status improves the salivary parameters particularly among hypothyroid subjects [1, 3].

Dixit et al. in their study [35] showed that hypothyroidism and its treatment did not cause a significant decrease in stimulated parotid flow rates using both cross-sectional and longitudinal data. Some studies have shown that chronic-hypo-salivation results in various oral complications including atypical dental caries, oral mucositis, difficulty in eating, and halitosis. All of these complications would cause a lower quality of life among patients who suffer from chronic diseases such as thyroid dysfunction [37].

Material and Methods

This article reviewed the biomedical literature on thyroid diseases and normal salivary composition, flow, and function. Literature review was conducted by using the Medline and PubMed search engines (from 1970 to 2014).

Conclusion

A clear, relatively acidic muco-serous secretion of the exocrine glands is called saliva. The whole saliva is a complex mixed secretion from major and minor salivary glands, also consisting of gingival cervicular fluid, which contains oral bacteria and food debris. Saliva is contains various electrolytes which magnesium, potassium, sodium, calcium, bicarbonate, and phosphates can be mentioned [3]. Proteins, enzymes, immune globulins, mucins, urea, and ammonia are also present in saliva. On the contrary of what is believed saliva is not an ultra filtrate of plasma, but it is considered a good equivalent [1, 3]. A few studies have under taken the relevancy of hormones circulating in the plasma and saliva and concluded that there is an absolute relevancy between these two bodily fluids. Many years ago the correlation between saliva and lipid-hormones has been marked and proven; but this correlation for protein-hormones, such as thyroid hormones is yet to be defined entirely [8]. In many studies, the use of saliva instead of blood samples for diagnostic use has been suggested [5, 8, 9].

Saliva as a non-invasive method for the assessment of diseases has proven its worthy cause and many studies have been conducted to prove this matter. Furthermore, subjects with chronic-hypo-salivation should have a thyroid function assessment especially if no other known cause of hypo-salivation has been proven. Furthermore, patients with uncontrolled hypothyroidism should be evaluated for signs of hypo-salivation and its complications to implement necessary preventive regimens.

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References

[1] Muralidharan D, Fareed N, Pradeep PV, Margabandhu S, Ramalingam K, Ajith Kumar BV. Qualitative and quantitative changes in saliva among patients with thyroid dysfunction prior to and following the treatment of the dysfunction. Oral Surg Oral Med Oral Pathol Oral Radiol. 2013; 115(5): 617-23.

[2] Hofman LF. Human saliva as a diagnostic specimen. J Nutr. 2001; 131(5): 1621S-5S.

[3] Humphrey SP, Williamson RT. A review of saliva: normal composition, flow, and function. J Prosthet Dent. 2001; 85(2): 162-9.

[4] Roth G, Calmes R. Salivary glands and saliva. St Louis: Mosby, 1981. pp. 196-236.

[5] Mohiti- Ardekani A, Hasan Karbassi M, Mohiti-Ardekani J, Akhondinasab F, Haji Mirza Mohammad M. Evaluation of salivary IgA in diabetic and non-diabetic patients: a case-control study. Iran J diabetes Obes. 2012; 4(4): 167-71.

[6] Putz Z, Vanuga A, Veleminsky J. Radioimmunoassay of thyroxine in saliva. Exp Clin Endocrinol. 1985; 85(2): 199-203.

[7] Kaufman E, Lamster IB. The diagnostic applications of saliva--a review. Crit Rev Oral Biol Med. 2002; 13(2): 197-212.

[8] Groschl M. Current status of salivary hormone analysis. Clin Chem. 2008; 54(11): 1759-69.

[9] Simionescu L, Aman E, Museteanu P, Dinulescu E, Giurcaneanu M. Peptide hormones in saliva. I. Insulin in saliva during the oral glucose tolerance test in female

patients. Endocrinologie. 1985; 23(3): 179-87.
[10] Riad-Fahmy D, Read GF, Walker RF, Griffiths K. Steroids in saliva for assessing endocrine function. Endocr Rev. 1982; 3(4): 367-95.
[11] Lewis JG. Steroid analysis in saliva: an overview. Clin Biochem Rev. 2006; 27(3): 139-46.
[12] Nguyen S, Wong DT. Cultural, behavioral, social, and psychological perceptions of saliva: relevance to clinical diagnostics. J Calif Dent Assoc. 2006; 34(4): 317-22.
[13] Mandel ID. Salivary diagnosis: promises, promises. Ann N Y Acad Sci. 1993; 694: 1-10.
[14] Tenovuo J. Antimicrobial function of human saliva--how important is it for oral health? Acta Odontol Scand. 1998; 56(5): 250-6.
[15] Chang K, Chiou WL. Interactions between drugs and saliva-stimulating parafilm and their implications in measurements of saliva drug levels. Res Commun Chem Pathol Pharmacol. 1976; 13(2): 357-60.
[16] Hold KM, de Boer D, Zuidema J, Maes RA. Evaluation of the Salivette as sampling device for monitoring beta-adrenoceptor blocking drugs in saliva. J Chromatogr B Biomed Appl. 1995; 663(1): 103-10.
[17] Groschl M, Kohler H, Topf HG, Rupprecht T, Rauh M. Evaluation of saliva collection devices for the analysis of steroids, peptides and therapeutic drugs. J Pharm Biomed Anal. 2008; 47(3): 478-86.
[18] Vining RF, McGinley RA, Symons RG. Hormones in saliva: mode of entry and consequent implications for clinical interpretation. Clin Chem. 1983; 29(10): 1752-6.
[19] Popa M, Simionescu L, Dumitriu E, Dimitriu V, Giurcaneanu M, Bartoc R, et al. Serum-to-saliva transfer of the immunoreactive insulin (IRI) in children with obesity associated with insulin-resistance. Endocrinologie. 1987; 25(3): 149-55.
[20] Cui CY, Lu WL, Xiao L, Zhang SQ, Huang YB, Li SL, et al. Sublingual delivery of insulin: effects of enhancers on the mucosal lipid fluidity and protein conformation, transport, and in vivo hypoglycemic activity. Biol Pharm Bull. 2005; 28(12): 2279-88.
[21] Chen YM, Cintron NM, Whitson PA. Long-term storage of salivary cortisol samples at room temperature. Clin Chem. 1992; 38(2): 304.
[22] Groschl M, Wagner R, Rauh M, Dorr HG. Stability of salivary steroids: the influences of storage, food and dental care. Steroids. 2001; 66(10): 737-41.
[23] Nimmagudda RR, Ramanathan R, Putcha L. A method for preserving saliva samples at ambient temperatures. Biochem Arch. 1997; 13(3): 171-8.
[24] Bourque J, Sulon J, Demey-Ponsart E, Sodoyez JC, Gaspard U. A simple, direct radioimmunoassay for salivary progesterone determination during the menstrual cycle. Clin Chem. 1986; 32(6): 948-51.
[25] Vitorino R, Lobo MJ, Ferrer-Correira AJ, Dubin JR, Tomer KB, Domingues PM, et al. Identification of human whole saliva protein components using proteomics. Proteomics. 2004; 4(4): 1109-15.
[26] Jonsson BA, Malmberg B, Amilon A, Helene GA, Orbaek P. Determination of cortisol in human saliva using liquid chromatography-electrospray tandem mass spectrometry. J Chromatogr B Analyt Technol Biomed Life Sci. 2003; 784(1): 63-8.
[27] Higashi T, Ichikawa T, Shimizu C, Nagai S, Inagaki S, Min JZ, et al. Stable isotope-dilution liquid chromatography/tandem mass spectrometry method for determination of thyroxine in saliva. J Chromatogr B Analyt Technol Biomed Life Sci. 2011; 879(13-14): 1013-7.
[28] Lenander-Lumikari M, Loimaranta V. Saliva and dental caries. Adv Dent Res. 2000; 14: 40-7.
[29] Axelsson P. Diagnosis and risk prediction of dental caries. New York, NY: Quintessence Publishing Company, 2000. p. 91-148.
[30] Clark PG, Muhler JC, Shafer WG. The inhibition of hypophysectomy-induced changes in the rat submaxillary glands. Endocrinology. 1956; 59(5): 516-21.
[31] Henrikson TD, Armbrust LJ, Hoskinson JJ, Milliken GA, Wedekind KJ, Kirk CA, et al. Thyroid to salivary ratios determined by technetium-99m pertechnetate imaging in thirty-two euthyroid cats. Vet Radiol Ultrasound. 2005; 46(6): 521-3.
[32] RYAN E, KIRKWOOD S. Explanation of the effect of feeding desiccated thyroid on the incidence of dental caries in the rat. Science. 1955; 121(3136): 175-6.
[33] Navazesh M, Christensen C, Brightman V. Clinical criteria for the diagnosis of salivary gland hypofunction. J Dent Res. 1992; 71(7): 1363-9.
[34] Navazesh M, Kumar SK. Measuring salivary flow: challenges and opportunities. J Am Dent Assoc. 2008; 139(Suppl): 35S-40S.
[35] Dixit PS, Ghezzi EM, Wagner-Lange LA, Ship JA. The influence of hypothyroidism and thyroid replacement therapy on stimulated parotid flow rates. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1999; 87(1): 55-60.
[36] Fenoll-Palomares C, Munoz Montagud JV, Sanchiz V, Herreros B, Hernandez V, Minguez M, et al. Unstimulated salivary flow rate, pH and buffer capacity of saliva in healthy volunteers. Rev Esp Enferm Dig. 2004; 96(11): 773-83.
[37] Wikner S, Soder PO. Factors associated with salivary buffering capacity in young adults in Stockholm, Sweden. Scand J Dent Res. 1994; 102(1): 50-3.

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