The use of parotid gland activity analysis in patients with gastro-esophageal reflux disease (GERD) and bulimia nervosa

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Abstract

Purpose: In patients with vomiting or reflux episodes, specific pathognomic signs may occur in the oral cavity. The significance of salivary gland activity in this type of disorder is a matter of dispute. The purpose of this study was to evaluate the parotid gland activity of patients with bulimic type eating disorder (group B) compared with patients affected by gastro-esophageal reflux (GERD) (group A) and healthy control subjects (group C).

Material and methods: Parotid saliva was collected during the clinical examination by means of a modified Lashley cap under unstimulated and stimulated conditions and the flow rate was determined. The concentrations of Na^+, K^+, Ca^+ (mmol/l) were determined by a colorimetric photometry method (Effox 5053, Eppendorf, Germany). Buffering capacity as a concentration of bicarbonates (mmol/l) and the pH, were measured by an automatic ion-selective electrode (ABL TM 520, Radiometer, Denmark). For the statistical analyses Kruskal Wallis one way ANOVA on Ranks with Dunn's method all pairwise multiple comparisons procedures were used with significance set at $p \leq 0.05$.

Results: The results showed that the flow rates in the subjects in group A and B were significantly lower than in the controls. There were also significant differences in the concentration of sodium, with the lowest level in group B, and calcium where the highest level occurred in group A.

Conclusions: Since patients may deny frequent vomiting (bulimia) or are unaware of the reflux (GERD) the changes in electrolyte levels revealed by this study appear to be of use in the diagnosis of these conditions.

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Introduction

In the mouth one of the intrinsic factors which leads to a reduction in salivary pH and tooth erosion is gastric acid which has a pH of 1-1.5 [1]. Gastric acid is one of the most important factors in the etiology of erosion in developed countries [2]. Gastro-esophegeal reflux disease (GERD) is the term used to describe a number of conditions where the gastric contents leak into the lower esophagus. Similar conditions apply in conditions such as psychosomatic conditions, eating disorders and alcoholism [3].

The American Psychiatric Association states that bulimic patients regularly binge and purge to keep control of their body weight, "the purging type of bulimia nervosa", or have periods of food restriction and strenuous physical exercise ("the non purging type of bulimia nervosa") [4]. Hoek and Hoeken [5] reported that the incidence of bulimia nervosa in woman is 29: 100000 and in men 1:100000 of those aged between 18 and 29. Epidemiological studies on the incidence of bulimia nervosa, conducted in the United States and Europe, show an increase over the last 40 years [6].

Gastro-esophageal reflux disease is common, and affects between 5-50% people in western countries [7]. Gastro-esophageal reflux is the movement of stomach juices upwards through the lower esophageal sphincter. In healthy individuals small amounts of gastric juice often reflux into the esophagus after eating and may be associated with belching. If the clearance mechanisms cannot return the reflux to the stomach the symptoms become chronic. The reason for this is failure of the lower esophageal sphincter [8, 9]. Two of the constituents of the gastric juice – hydrochloric acid and pepsin are implicated in the pathology of reflux because of their potential to damage the esophageal mucosa. Such a reflux also causes dental erosion and probably changes in saliva [10-12].

Figure 1. **Flow rates of parotid saliva (ml/min) in each group of subjects. 1 – unstimulated saliva, 2 – 3% citric acid saliva stimulated, 3 – stimulated by mastication saliva**

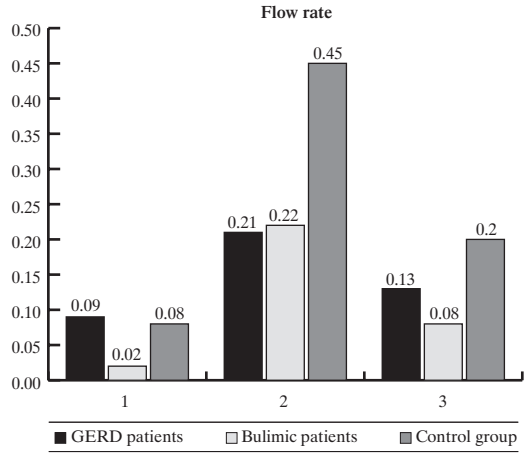
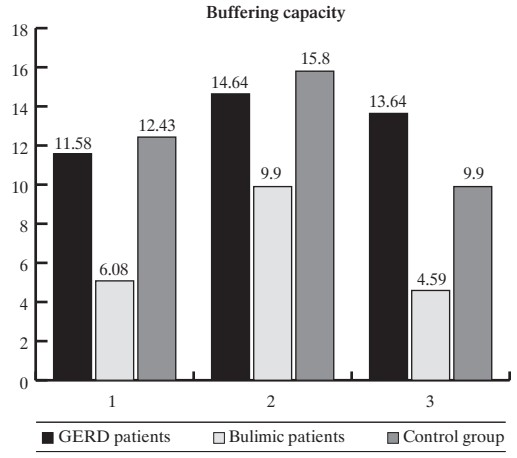


Figure 2. **Mean concentration of bicarbonates (mmol/l) in parotid saliva. 1 – unstimulated saliva, 2 – 3% citric acid saliva stimulated, 3 – stimulated by mastication saliva**



The role of saliva as a neutralizing factor has been reported in a previous research [11]. On the tooth surface, both the formation of the pellicle and a phosphate and calcium saturated condition may protect the teeth from acid. Bicarbonate ions are responsible for the buffering capacity of saliva due to their ability to rise with an increasing flow rate. An explanation for the reduction in both pH and flow rate requires parotid gland activity studies. Because of the changes in oral health which occur in patients with GERD and eating disorders there is a significant need to determine parotid gland efficiency and the nature of changes in the saliva of patients with these conditions.

Material and methods

The purpose of this study was to compare the flow rates and inorganic content of the parotid saliva of 3 different groups, namely 18 gastro-esophageal disease patients (group A), 33 bulimics (group B), and 51 healthy controls (group C). The ethical committee of Poznan University of Medical Sciences granted its approval for this study. The nature of the investigation was explained to the 102 participants, all of whom signed a consent form. The patients in group A, with a confirmed diagnosis of GERD, were referred to the University's Clinical Surgery Department. The mean age of this group was 35±3.2 years, with a mean onset of gastric reflux having occurred 4±2.1 years previously.

The patients in group B, with a confirmed diagnosis of bulimia nervosa of the purging type according to DSM IV (American Psychiatric Association 1994) criteria, were referred to the University's Clinical Psychiatric Department. The mean age of this group was 21.2±3.2 years, with a mean onset of eating disorder having occurred 3.5±2.4 years previously. The mean frequency of binge-purging was 2.0/day. The fifty-one female, age-matched control subjects from group C all denied any history of an eating disorder or gastro-esophageal reflux. Other control selection criteria included: good health, not pregnant, no medication being taken (birth control agents excluded) and no tobacco use. These controls had a mean age of 25.5±4.6 years.

Parotid saliva was collected under both unstimulated and stimulated conditions. All individuals were instructed to refrain from eating or drinking for 1 hour prior to saliva testing. All the saliva collections were performed between 9.00 a.m. and noon and collected by the same examiner. Parotid saliva was collected by a modified Lashley cap placed over Stensen's duct under three different salivary flow conditions: after 15 min rest, physiologically stimulated using 3% citric acid applied to the tongue at 30 s interval and finally when stimulated by the mastication of wax tablets for 5 min. The secretion rate was calculated and recorded in ml/minute. The concentration of the various inorganic components, such as sodium, potassium and calcium (mmol/l) was determined by a colorimetric photometry method (Effox 5053, Eppendorf, Germany). An automatic ion-selective electrode was used for pH determination and bicarbonate concentration (mmol/l) (ABL TM 520, Radiometer, Denmark). Flow rate estimation and electrolyte analysis were performed within 2 hours of saliva collection.

During the clinical examination a level of toothwear was measured using a Smith and Knight Tooth Wear Index [3].

For the statistical analyses Kruskal Wallis one way Anova on Ranks with Dunn's method all pairwise multiple comparison procedures were used. The significance level was set at $p \leq 0.05$.

Results

The results of parotid saliva analyses of the subjects are presented in *Fig. 1* to *7* and *Tab. 1* and *2a*, *b*. Evaluation of parotid secretion showed that in group B the flow rates were significantly lower than in the group A and control group C subjects at rest and under stimulation (*Fig. 1*), 40% of the subjects in group B had unstimulated salivary flow rates <0.01 ml/min. The results present statistically significant differences for pH in the unstimulated saliva between the bulimic group B and control group C

Figure 3. **Mean pH of parotid saliva for all groups. 1 – unstimulated saliva, 2 – 3% citric acid saliva stimulated, 3 – saliva stimulated by mastication**

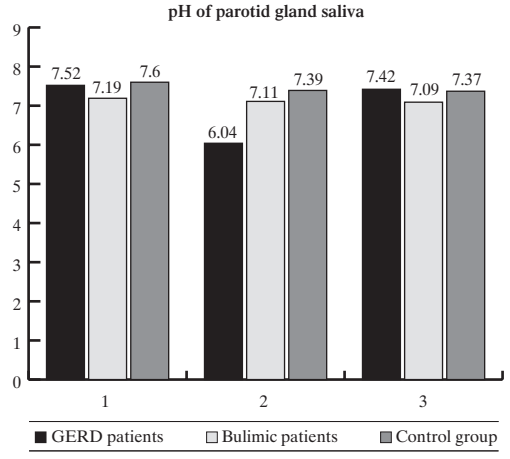


Figure 4. **Mean sodium concentration in parotid saliva (mmol/l). 1 – unstimulated saliva, 2 – 3% citric acid saliva stimulated, 3 – saliva stimulated by mastication**

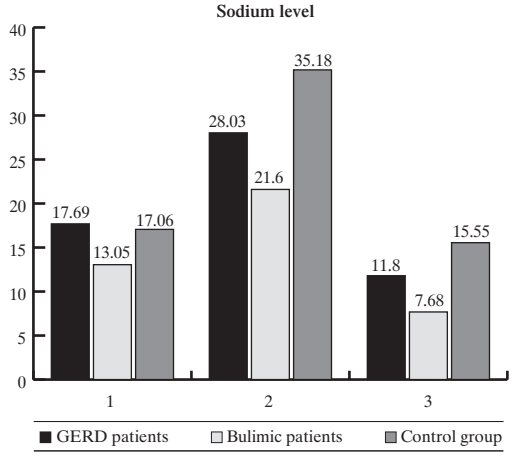


Figure 5. **Mean potassium concentration in parotid saliva (mmol/l). 1 – unstimulated saliva, 2 – 3% citric acid saliva stimulated, 3 – saliva stimulated by mastication**

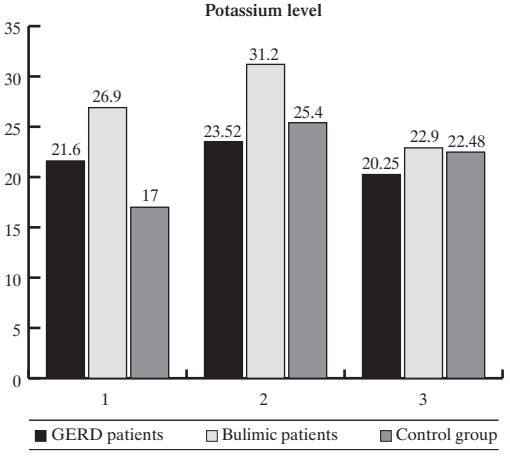


Figure 6. **Mean calcium concentration in parotid saliva (mmol/l). 1 – unstimulated saliva, 2 – 3% citric acid saliva stimulated, 3 – saliva stimulated by mastication**

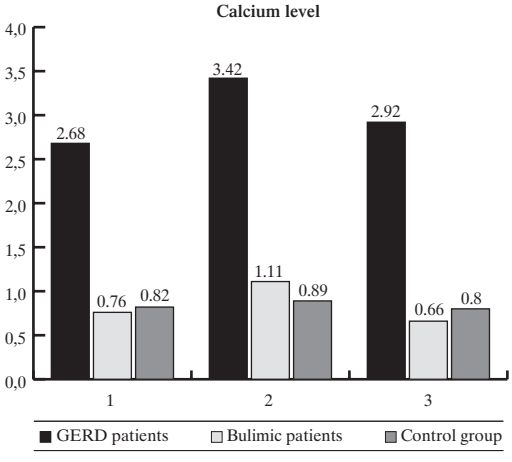
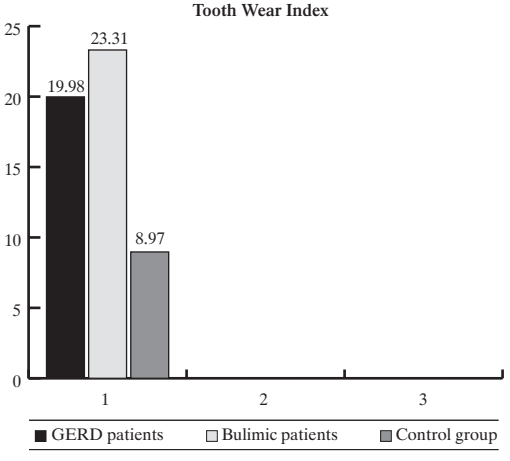


Figure 7. **Mean level of tooth wear in each group measured by the Smith and Knight Tooth Wear Index (%)**



and the bicarbonate level indicating differences between both groups (*Fig. 2*, *3*). Parotid sodium levels increased after stimulation in all three groups but the increase was lowest in the bulimics. A significant difference in sodium levels occurred between groups B and C after chemical stimulation with 3% citric acid (*Fig. 4*). The concentrations of potassium and calcium increased with parotid gland stimulation (*Fig. 5*, *6*). There were significant differences between all groups, especially in the calcium level in groups A and C after chemical stimulation, with the highest concentration in the GERD group A. All the experimental groups (A and B) had significantly more abnormal toothwear than the controls, with the differences being most marked in the bulimic group (*Fig. 7*).

Discussion

The quantity of parotid saliva in bulimics was reduced under both unstimulated and stimulated conditions. Most stud-

Table 1. **Unstimulated flow rate (ml/min), pH, bicarbonates ions and sodium, potassium, calcium concentrations of parotid saliva (mmol/L). Results are expressed as the mean, S.D. and P value (ns – not significant)**

Saliva data	Group A	Group B	Group C	Comparison	Dunn's multiple comparisons test mean rank difference	P value
salivary flow (ml/min)	0.09±0.06	0.02±0.01	0.08±0.05	A vs B	41.71	***P<0.001
				A vs C	3.21	ns P>0.05
				B vs C	-38.49	***P<0.001
pH	7.5±0.3	7.2±0.7	7.6±0.5	A vs B	10.87	ns P>0.05
				A vs C	-6.54	ns P>0.05
				B vs C	17.42	* P<0.05
bicarbonates ions (mmol/L)	11.58±6.9	6.08±6.1	12.4±11.2	A vs B	60.57	ns P>0.05
				A vs C	8.5	ns P>0.05
				B vs C	52.07	ns P>0.05
sodium concentration (mmol/L)	17.7±12.3	13.05±8.7	17.06±13.7	A vs B	20.67	ns P>0.05
				A vs C	6.08	ns P>0.05
				B vs C	14.59	ns P>0.05
potassium concentration (mmol/L)	21.6±6.4	26.9±8.3	25±5.6	A vs B	-67.6	ns P>0.05
				A vs C	-35.53	ns P>0.05
				B vs C	-25.14	ns P>0.05
calcium concentration (mmol/L)	2.7±1.3	0.8±0.2	0.8±0.3	A vs B	85.64	* P<0.05
				A vs C	86.31	** P<0.01
				B vs C	-0.67	ns P>0.05

Table 2a. **Stimulated by 3% citric acid flow rate (ml/min), pH, bicarbonates ions and sodium, potassium, calcium concentrations of parotid saliva (mmol/L). Results are expressed as the mean, S.D. and P value (ns – not significant)**

Saliva data	Group A	Group B	Group C	Comparison	Dunn's multiple comparisons test mean rank difference	P value
salivary flow (ml/min)	0.2±0.1	0.2±0.1	0.4±0.2	A vs B	-31.8	*** P<0.001
				A vs C	-4.7	ns P>0.05
				B vs C	-27.05	*** P<0.001
pH	6.04±2.8	7.1±0.7	7.4±0.3	A vs B	-1.4	ns P>0.05
				A vs C	-14.4	ns P>0.05
				B vs C	13.0	ns P>0.05
bicarbonates ions (mmol/L)	14.6±17.5	9.9±9.9	15.8±8.8	A vs B	10.4	ns P>0.05
				A vs C	-40.03	ns P>0.05
				B vs C	50.5	ns P>0.05
sodium concentration (mmol/L)	28.03±9.3	21.6±6.4	35.2±2.4	A vs B	21.1	ns P>0.05
				A vs C	-22.4	ns P>0.05
				B vs C	43.5	* P<0.05
potassium concentration (mmol/L)	23.5±7.7	31.2±8.3	25.4±6.5	A vs B	-68.2	ns P>0.05
				A vs C	-14.9	ns P>0.05
				B vs C	-53.2	ns P>0.05
calcium concentration (mmol/L)	3.4±1.4	1.1±1.8	0.9±0.3	A vs B	94.52	** P<0.01
				A vs C	101.5	*** P<0.001
				B vs C	-6.97	ns P>0.05

ies concerning salivary gland activity in bulimics have reported hyposalivation of different degrees [13-15], except for that reported by Howat et al. [16]. Unfortunately, these authors only examined 11 patients with bulimia and measured the pH, without measuring unstimulated salivary flow.

One possible explanation for the hyposalivation and glandular swelling, which can accompany bulimia could be morphological gland changes caused by inflammation. However, histological investigations have revealed only fatty infiltration and fibrosis, without inflammatory changes [17]. Another explanation for hyposalivation relates to the frequent vomiting or gastric reflux in bulimics which can cause reduced salivary gland output. Other studies have found that the composition of saliva may be changed in bulimic subjects because of dehydration. To support this hypothesis Ship and Fisher [18] conducted an investigation in healthy adults abstaining from eating and

Table 2b. **Stimulated by mastication flow rate (ml/min), pH, bicarbonates ions and sodium, potassium, calcium concentrations of parotid saliva (mmol/L). Results are expressed as the mean, S.D. and P value (ns – not significant)**

Saliva data	Group A	Group B	Group C	Comparison	Dunn's multiple comparisons test mean rank difference	P value
salivary flow (ml/min)	0.1±0.07	0.08±0.02	0.2±0.1	A vs B	20.2	* P<0.05
				A vs C	-15.6	ns P>0.05
				B vs C	35.8	*** P<0.001
pH	7.4±0.4	7.1±0.4	7.4±0.4	A vs B	16.7	ns P>0.05
				A vs C	2.7	ns P>0.05
				B vs C	14.0	ns P>0.05
bicarbonates ions (mmol/L)	13.3±14.7	4.6±3.8	9.9±8.3	A vs B	63.5	ns P>0.05
				A vs C	11.3	ns P>0.05
				B vs C	52.1	ns P>0.05
sodium concentration (mmol/L)	11.8±9.4	7.7±5.1	15.5±11.1	A vs B	23.8	ns P>0.05
				A vs C	-6.0	ns P>0.05
				B vs C	29.8	ns P>0.05
potassium concentration (mmol/L)	20.2±7.3	22.9±9.7	22.5±6.3	A vs B	-32.7	ns P>0.05
				A vs C	-16.9	ns P>0.05
				B vs C	-15.8	ns P>0.05
calcium concentration (mmol/L)	2.9±1.6	0.6±0.3	0.8±0.3	A vs B	115.6	*** P<0.001
				A vs C	104.2	*** P<0.001
				B vs C	11.4	ns P>0.05

drinking for 24 hours and stated that reduced levels of hydration may cause diminished salivary output.

Another possible explanation lies in an electrolyte imbalance resulting from the changes mainly observed in the sodium and calcium levels. Out of all the inorganic components investigated in this study, the most significant statistical differences were found in the sodium levels. Normally, the sodium level increases with the salivary flow rate [19], so the lack of such an increase in the level of this element in bulimic subjects can be additional confirmation of reduced secretion or hyposalivation. Potassium is more independent of the flow rate and is more sensitive to the inflammatory process, due to a breakdown of salivary-blood barriers. The absence of a significant change in the potassium concentration agrees with previous histological studies confirming a non-inflammatory process in vomiting-associated glands [20-22]. A decrease in both these components in the group B, lower salivary flow rate and sodium concentration, suggest that the function of the parotid glands is more affected than that of the other salivary glands. This assumption supports previous studies concerning patients with primary Sjogren's syndrome, after head and neck radiotherapy or neuroleptic treatment. All these hyposalivation groups tended to have an imbalance in salivary sodium concentration [23,24].

The association between vomiting and erosive toothwear was not linearly proven. Reviews in the dental literature showed an increase of erosion with the increase of the frequency of vomiting and gastric reflux. There are also studies that reported no difference in the level of erosion between those who vomited more or less frequently [25,26]. The higher prevalence of erosive toothwear in bulimic patients than in GERD patients may be explained by the fact that the gastric content is not always aspirated to the oral cavity. The regurgitation in GERD patients occurs many times during day but the amount of acidic content is lower comparing with bulimic patients. It is also relevant that among GERD patients the regurgitation may be limited only to esophagus and respiratory system. However, the changes in salivary secretion, electrolyte imbalance and low bicarbonate level may act as a co-factor in erosion.

Conclusions

1. Hyposalivation and lower sodium and calcium levels were found in both Group A (GERD) and Group B (bulimic) subjects which support previous findings of hyposalivation and electrolyte imbalance in such patients.

According to our data bulimic patients have reduced a lover salivary flow from the parotid glands both at rest and under stimulation. It is assumed that this electrolyte imbalance and hyposalivation in group B could account for the greater tooth wear index in this type of patient.

2. According to the results of salivary flow rate is an unreliable indicator of bulimia nervosa and reflux disease. The change of electrolyte level in stimulated saliva could be a more reliable confirmation of symptoms in eating disorder and GERD.

References

1. Azzopardi A, Bartlett DW, Watson TF, Smith BGN. The measurement and prevention of erosion and abrasion. J Dent 2001; 29: 305-12.

2. Eisenburger M, Addy M. Evaluation of pH and erosion time on demineralization. Clin Oral Invest, 2001; 5: 108-11.

3. Bartlett DW, Blunt I, Smith BGN. Measurements of tooth wear in patients with palatal erosion. Br Dent J, 1997; 182: 179-84.

4. Diagnostic and statistical manual of Mental Disorders (DSM-III--R), 4th edition, revised. Washington, DC: American Psychiatric Association; 1994

5. Hoek HW, Hoeken D. Review of the prevalence and incidence of eating disorders. Int J Eat Disord, 2003; 34: 383-96.

6. Fainburn ChG, Beglin SJ. Studies of the epidemiology of bulimia nervosa. Am J Psychiatry, 1990; 147: 401-7.

7. Małecka-Panas E. Nietypowe objawy choroby refluksowej – rozpoznanie i leczenie. Medical Advisor, 2002; 4: 1-6.

8. Barron RP, Carmicheal RP, Marcon MA, Sandor GKB. Dental erosion in gastro-esophageal reflux disease. J Can Dent Assoc, 2003; 69: 84-9.

9. Bartlett DW, Smith B. Clinical Investigation of Gastro-oesohageal Reflux: Part 1, Dental Update, 1996: 205-10.

10. Bartlett DW, Anggianash A, Smith BGN, Kidd EAM. The role of regurgitation and other symptoms of reflux disease in palatal dental erosion; an audit project. Ann R Coll Sug Engl, 2001; 83: 226-8.

11. Fisher S. Motor Disorders of the Gastrointestinal tract. New York: What's new & What's to do; 1993.

12. Kaczmarek U, Waśko-Czopik D, Kowalczyk-Zając M, Sommer-Szelepin E, Paradowski L. Dental erosion, selected salivary components and gastroesophageal reflux. Czas Stom, 2003; LVII; 5: 295-302.

13. Abrams RA, Ruff JC. Oral signs and symptoms in the diagnosis of bulimia. J Am Dent Assoc, 1986; 113: 761-4.

14. Altshuler BD, Dechow PC, Waller DA, Hardy BW. An investigation of the oral pathologies occurring in bulimia nervosa. Int J Eat Disord, 1990; 9: 191-9.

15. Little J. Eating disorders: dental implications. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 2002; 93: 138-43.

16. Howat PM, Varner LM, Wampold RL. The effectiveness of a dental/dietitian team in the assessment of bulimic dental health. J Am Diet Assoc, 1990; 90: 1099-102.

17. Burke RC. Bulimia and parotid enlargement – case report and treatment. J Otolaryng, 1986; 15: 49-51.

18. Ship JA, Fisher DJ. Metabolic indicators of hydration status in the prediction of parotid salivary-gland function. Arch Oral Biol, 1999; 44: 343-50.

19. Edgar M, Daves C, O'Mullane D. Saliva and oral health. London: British Dental Association; 2004, 32-50.

20. Tylenda CA, Roberts MW, Elin RJ, Li S-H, Altemus M. Bulimia nervosa its effect on salivary chemistry. JADA 1991; 122: 37-41.

21. Milosevic A, Dawson LJ. Salivary differences and erosion in vomiting bulimics. Caries Res, 1996; 30: 361-6.

22. Hunter KD, Wilson WS. The effects of antidepressant drugs on salivary flow and content of sodium and potassium ions in human parotid saliva. Arch Oral Biol, 1995; 40: 983-9.

23. Almstahl A, Wikstrom M. Electrolytes in stimulated whole saliva in individuals with hyposalivation of different origins. Arch Oral Biol, 2003; 48: 337-44.

24. Cowman RA, Baron SS, Daly TE, Drane JB, Davis ME, Strosberg AM. Changes in protein composition of saliva from radiation-induced xerostomia patients and its effect on growth of oral streptococci. J Dent Res, 1983; 62: 336-40.

25. Robb ND, Smith BGN, Geidrys-Leeper E. The distribution of erosion in the dentitions of patients with eating disorders. Br Dent J, 1995; 178: 171-5.

26. Roberts MW, Li SH. Oral findings in anorexia nervosa and bulimia nervosa: a study of 47 cases. JADA 1987; 115: 407-10.