# Oral manifestation biochemical and IgA analysis of saliva in hyperthyroid (Grave's disease) patients (Comparative study)

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## ABSTRACT

Background: Hyperthyroidism occurs due to over production of thyroid hormones, one types of hyperthyroidism was Graves' disease. Hyperthyroidism is characterized by high level of serum thyroxin, triiodothyronine and low level of thyroid stimulated hormones.

Material and Methods: fifty two hyperthyroid patients, thirty patients under treatment with carbimazole and other twenty two patients under treatment with radioactive iodine, and sixty healthy control group. The average salivary flow rate was calculated as ml/5mint.The concentration of calcium, potassium, and total protein were determined in the salivary supernatant sample. This is done through different biochemical tests. Determination of salivary IgA is done by ELIZA.

Results: The most prevalence oral manifestation was dry mouth; there were highly significant differences in salivary flow rate between the two studied groups. There were differences in concentration of total salivary protein and salivary IgA between the two studied groups although statistically non-significance. However there a significant differences in calcium concentration between the two studied groups, also there was a sequential decrease in potassium concentration between the two studied groups and control group.

Conclusions: Those type of patients need dental evaluation especially those who are taking radioactive iodine.

Keywords: Hyperthyroidism, Graves' disease, radioactive iodine, Carbimazole. (J Bagh Coll Dentistry 2013; 25(1):82-86).

## INTRODUCTION

Hyperthyroidism is characterized by high level of serum thyroxin, triiodothyronine and low level of thyroid stimulated hormones. The main causes of hyperthyroidism are Graves's disease, toxic multinodular goiter and toxic adenoma. About 20 times more women than men have hyperthyroidism. (1)

The oral manifestation in patients with hyperthyroidism is due to the disease process, and those are associated with drug intake used to treat hyperthyroidism. Oral manifestation due to the disease process include: Accelerated dental eruption in children , maxillary or mandibular osteoporosis, enlargement of extra glandular tissue (mainly in lateral posterior tongue) increase susceptibility to caries , periodontal disease , burning mouth syndrome and development of connective tissue diseases like Sjogren's syndrome or systemic lupus erythematosus.(2,3)

On the other hand oral manifestation that were associated with drug intake used to treat hyperthyroidism include : Xerostmia , taste changes , infection , increase susceptibility to caries , facial nerve involvement , stomatitis , sialoadenitis ,candidiasis , neoplasia , salivary gland neoplasia.(4,5,6)

Also there were changes in the composition of whole stimulated saliva that the concentration of urate and potassium ions were increased, while concentration of total protein, calcium ions and lactate dehydrogenase activity significantly decreased. (7) Other researchers illustrated excess salivation and swollen of salivary glands. (5)

This study was designed to:

1 –Determine the prevalence of oral manifestation in hyperthyroid' patients treated with antithyroid drugs (carbimazole and radioactive iodine).

2 – Determine the level of total salivary protein, concentration of salivary calcium and potassium in hyperthyroid patients treated with antithyroid drugs (carbimazole and radioactive iodine) and to compare with clinically healthy individuals.

3 – Investigate the (IgA) changes in saliva of hyperthyroid patients receiving antithyroid drugs (carbimazole and radioactive iodine) and compare with clinically healthy individuals.

## MATERIALS AND METHODS

A comparative study was performed in Al-Yarmuk Teaching Hospital in Baghdad. The study Samples consist of fifty two hyperthyroid patients, Thirty patients under treatment with carbimazole (methimazole) and other twenty two patients under treatment with radioactive iodine, and sixty healthy control group with no sign and symptom of any systemic disease.

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All the patients examined by a single examiner, under standardized conditions; the oral cavity examined in an artificial light using mouth mirror according to WHO (1987). The oral manifestations were classified according to:

A-Dry mouth: was diagnosed according to the anamenesis below: Does your mouth feel dry? Do you experience any difficulties in chewing dry foods? Do you experience any difficulties in swallowing dry foods? Are you aware of any recent increase in the frequency of liquid intake? [8]

B-Burning mouth sensation: The diagnostic criteria for burning mouth syndrome in this study was :Pain in the mouth present daily and persisting for most of the day, Oral mucosa is of normal appearance, Local and systemic diseases have been exclude.[9]

C-Dysguesia (taste alteration): Taste alteration can be diagnosed in this study according to the criteria taken from the European Organization for Research and Treatment of Cancer (EORTC): Have you had problems with your sense of taste? and Did food and drink taste different from usual?[10]

Saliva collection was done according to the Wu-Wang procedure[11], to avoid circadian variation the sample was collected between 9 a.m and 1.00 p.m. All samples were centrifuged for 10 min. at 3000 RPM .then supernatants stored at -70 C freezers until analysed. [12]

Then biochemical analysis was performed on salivary supernatants, so the concentrations of salivary calcium, potassium, and total salivary protein were determined. This is done through biochemical tests:

A-Determination of salivary minerals {Calcium , and Potassium. }:

This was done by atomic absorption Spectrophotometer (AAS) using standardized (Stock Standard for $K^{+1}$ 1mg/L,and -Stock Standard for $Ca^{+2}$ 1mg/L) by air acetylene.

B-Determination of total salivary protein.

- Using Total protein kit (SPINREACT) by spectrophotometer at 598nm.

After that the average salivary flow rate was obtained from the total volume collected in the study time, [13] and salivary flow rate calculated as ml/5mint.

Finally the determination of salivary IgA is done by Enzyme Link Immunosorbent Assay, using Demeditec Secretory IgA ELISA (DEXK276) kit.

**Statistical analysis**

Levene test for testing the homogeneity of variances for equality of variances, one-way ANOVA for equality of means with (LSD) Least significant difference, Fisher's Exact Test, Contingency Coefficients test, and Odds Ratio coefficient.

# RESULTS

Table (1) shows the distribution of oral manifestation according to the type of treatment, with all types of manifestation studied ,the difference was non-significance. Whereas Odds Ratio criteria illustrated extremely difference between oral manifestation in those of treatment N (Carbimazole) compared with those of treatment R (Radioactive iodine) with proportion of 10:43, N:R, in dry mouth,10:13 in dysguesia, and 10:42 in burning mouth respectively.

In table (2) another statistical methodology was used but in this instances all type of treatment were compared against the control groups, with the mean, standard deviation, standard errors, (95%) Confidence interval for population Mean of Score values, minimum and maximum values**.**

Table (3) showed the results of multiple comparisons by LSD method which represented statistically differences at $P<0.01$ between Study - Neomercazole and Study - Radioactive Iodine at the parameter Salivary flow rate and at $P<0.05$ between the preceding of the study groups at the parameter Calcium as well as at $P<0.01$ between the two study groups and control group and with a non significant at $P>0.05$ were recorded with the leftover.

# DISCUSSION

**Oral Manifestations**

Dry mouth considered the most prevalence oral manifestation seen in this study, female is more prevalence among hyperthyroid patients and so dry mouth seen more in female. This explained by the fact that hormonal changes in female lead to several oral alterations including xerostomia and burning mouth syndrome.[14] Also, dry mouth seen more in hyperthyroid patients treated with radioactive iodine than those treated with carbimazole. On the same line Khonle,[15] stated that one of the possible complications of RAI therapy was dry mouth. While Ford[7] suggested that after RAI therapy there was an increase in salivary flow rate.

Dysguesia was the second oral manifestation in this study, again dysguesia was seen more in female than male due to the fact that female is more prevalence among hyperthyroid patients than male **,** dysguesia seen among hyperthyroid patients treated with carbimazole rather than those

treated with radioactive iodine. This could be explained by the fact that the anti-thyroid agent (carbimazole) had adverse effect either by interfering with chemical composition or flow of saliva or by affecting taste receptor function or signal transduction that cause taste alteration. [16]

Burning mouth was least oral manifestation that seen in this study, it seen more in female than male owing to the fact that the female is more prevalence among hyperthyroid patient than male. [17]

**Salivary flow rate**

This study concluded that hyperthyroid patients treated with radioactive iodine showed decrease in salivary flow rate in compared with control, this in line with Wolfram,[18] While Ford[7] suggested that after RAI therapy there will be an increase in salivary flow rate.

In the other hand, this study revealed that hyperthyroid patients treated with carbimazole shows increase in salivary flow rate in compared with control, this is not in line with a study done by Scully and Sebastian,[17] they stated that antithyroid drug (carbimazole) may cause salivary gland swelling as a side effect of prolong used.

**Salivary IgA**

Hyperthyroid patients treated with radioactive iodine showed increase in the concentration of salivary IgA than those treated with carbimazole, that's to say there is improvement in salivary IgA concentration after treatment with RAI, this result is in line with study done by Ford done on hyperthyroid patients after administration of RAI.[7]

**Total salivary protein**

This study showed low salivary total protein among hyperthyroid patients treated with radioactive iodine, than hyperthyroid patients treated with carbimazole. This not in line with Ford[7] whom suggested that after RAI therapy there is improvement in the concentration of total salivary protein.[7] This could be explained by the fact that total salivary protein decrease among hyperthyroid patients before treatment.[7] Recently Al-Rubbaey[18] stated that total salivary protein increase among hyperthyroid patients, in this study carbimazole treated patients shows increase in total salivary protein than radioactive iodine treated patients this may explained by the fact that due to improvement in their toxic state.

**Salivary calcium**

The present study showed slight higher concentration of salivary calcium in hyperthyroid patients receiving carbimazole than those receiving RAI.This in line with Fisher[19] who's declared that hyperthyroidism consider as a cause of hypocalcaemia. In the other hand Ford[7] found a decrease in salivary calcium among hyperthyroid patients.

**Salivary potassium**

There was increase in salivary potassium concentration in the two studied groups in compared with control. The same as with that seen by Ford [7] among group of hyperthyroid patients.[7]However, benign thyroid disease such as hyperthyroidism can influence the composition and flow of saliva, although the exact mechanism is unknown [7, 20].

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**Table 1: Distribution of the Oral manifestations at the two different of the studied treatments groups with comparison's significant**

| Oral manifestation | Treatment | Freq. & Percent | Absent | Present | Total | C.S. (*) P-value |
|---|---|---|---|---|---|---|
| (Dry mouth) | Neomercazole | Freq. | 13 | 17 | 30 | FEPT P=0.0.052 NS |
| | | % within Groups | 43.3% | 56.7% | 100% | |
| | Radioactive Iodine | Freq. | 4 | 18 | 22 | CC=0.450 P=0.056 NS |
| | | % within Groups | 18.2% | 81.8% | 100% | |
| | Total | Freq. | 17 | 35 | 52 | |
| | | % within Groups | 32.7% | 67.3% | 100% | Odds Ratio (1 : 3.441) (N : R) |
| (Dysguesia) | Neomercazole | Freq. | 21 | 9 | 30 | FEPT P=0.0.425 NS |
| | | % within Groups | 70% | 30% | 100% | |
| | Radioactive Iodine | Freq. | 14 | 8 | 22 | CC=0.067 P=0.629 NS |
| | | % within Groups | 63.6% | 36.4% | 100% | |
| | Total | Freq. | 35 | 17 | 52 | |
| | | % within Groups | 67.3% | 32.7% | 100% | Odds Ratio (1 : 1.333) (N : R) |
| (Burning mouth) | Neomercazole | Freq. | 25 | 5 | 30 | FEPT P=0.0.183 NS |
| | | % within Groups | 83.3% | 16.7% | 100% | |
| | Radioactive Iodine | Freq. | 21 | 1 | 22 | CC=0.184 P=0.176 NS |
| | | % within Groups | 95.5% | 4.5% | 100% | |
| | Total | Freq. | 46 | 6 | 52 | |
| | | % within Groups | 88.5% | 11.5% | 100% | Odds Ratio (1 : 4.202) (R : N) |

(*) NS : Non Significant at P> 0.05

**Table 2: Descriptive statistics for the studied parameters at the two different of the studied treatments groups**

| Parameters | Treatment | No. | Mean | Std. D. | Std. Error | 95% C. I. for Mean | | Min. | Max. |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | L.B. | U.B. | | |
| Sal. flow rate ml / 5 min. | Neomercazole | 30 | 1.25 | 0.63 | 0.11 | 1.02 | 1.48 | 0.25 | 2.5 |
| | Radioactive Iodine | 22 | 0.78 | 0.31 | 0.07 | 0.65 | 0.92 | 0.25 | 1.5 |
| | Control | 16 | 1.00 | 0.66 | 0.17 | 0.65 | 1.35 | 0.25 | 2.5 |
| IgA mg/ml | Neomercazole | 30 | 159.25 | 49.97 | 9.12 | 140.59 | 177.90 | 48.0 | 265.5 |
| | Radioactive Iodine | 22 | 167.90 | 49.81 | 10.62 | 145.82 | 189.99 | 47.1 | 242.3 |
| | Control | 16 | 166.56 | 44.52 | 11.13 | 142.84 | 190.28 | 47.8 | 229.1 |
| Calcium mg / ml | Neomercazole | 30 | 5.55 | 0.82 | 0.15 | 5.25 | 5.86 | 4.2 | 7.2 |
| | Radioactive Iodine | 22 | 4.99 | 0.84 | 0.18 | 4.62 | 5.36 | 3.9 | 6.4 |
| | Control | 16 | 3.93 | 0.52 | 0.13 | 3.66 | 4.21 | 3.1 | 4.6 |
| Potassium µmol / L | Neomercazole | 30 | 9.92 | 2.78 | 0.51 | 8.88 | 10.95 | 6.2 | 16 |
| | Radioactive Iodine | 22 | 9.66 | 3.40 | 0.72 | 8.15 | 11.17 | 4.6 | 17.6 |
| | Control | 16 | 8.45 | 2.47 | 0.62 | 7.14 | 9.76 | 5.6 | 12.6 |
| Total Protein gm / L | Neomercazole | 30 | 0.72 | 0.16 | 0.03 | 0.65 | 0.78 | 0.36 | 0.9 |
| | Radioactive Iodine | 22 | 0.70 | 0.16 | 0.03 | 0.63 | 0.77 | 0.47 | 0.95 |
| | Control | 16 | 0.74 | 0.16 | 0.04 | 0.65 | 0.83 | 0.41 | 0.95 |

**Table 3: Multiple Comparison (LSD) among all pairs of different responding of the studied parameters in the studied groups**

| Dependent Variable | (I) Groups | (J) Groups | Sig. | C.S. |
|---|---|---|---|---|
| Sal. flow rate ml / 5 min. | Study - Neomercazole | Study - Radioactive Iodine | 0.004 | HS |
| | | Control | 0.151 | NS |
| | Study - Radioactive Iodine | Control | 0.241 | NS |
| IgA mg/ml | Study - Neomercazole | Study - Radioactive Iodine | 0.529 | NS |
| | | Control | 0.629 | NS |
| | Study - Radioactive Iodine | Control | 0.933 | NS |
| Calcium mg / ml | Study - Neomercazole | Study - Radioactive Iodine | 0.011 | S |
| | | Control | 0.000 | HS |
| | Study - Radioactive Iodine | Control | 0.000 | HS |
| Potassium µmol / L | Study - Neomercazole | Study - Radioactive Iodine | 0.755 | NS |
| | | Control | 0.111 | NS |
| | Study - Radioactive Iodine | Control | 0.213 | NS |
| Total Protein gm / L | Study - Neomercazole | Study - Radioactive Iodine | 0.707 | NS |
| | | Control | 0.609 | NS |
| | Study - Radioactive Iodine | Control | 0.423 | NS |