

“Alterations in blood thyroid hormone levels on palpation of thyroid gland”.

Abstract

Introduction: Manipulation of the thyroid gland leads to alteration of thyroid hormones levels. As palpation is the commonest form of manipulation during clinical examination of thyroid gland, its effect has been studied here.

Objective: As various factors influence the serum thyroid hormone levels, our aim was to find out whether palpation of thyroid gland during clinical examination altered its levels or not.

Methods: The blood samples of 89 (85 females ;4 males) patients were collected twice after a gap of 120 minutes following palpation of the gland in the test group and without palpation in the comparison group by the same examiner and at fixed hours to estimate Free Thyroxine(FT4),Free Triiodothyronine(FT3) and Thyroid Stimulating Hormone(TSH) levels.

Results: Serum FT4 level decreased significantly ($p < 0.05$) 2 hours after palpation only in euthyroid patients but hypothyroid or hyperthyroid patients had no significant ($p > 0.05$) change in the serum thyroid hormone levels.

Conclusion:There is statistically significant fall in serum FT4 levels 2 hours after palpation of thyroid gland among euthyroid subjects which is very small to alter the clinical picture.

Key words:Thyroid Hormones, Palpation, Thyroid gland,Thyroxine

1.Introduction

Pathologies of the thyroid gland are responsible for a spectrum of diseases, from subclinical hormonal abnormalities to life-threatening conditions. A goitre is defined as a condition when “each of the lateral lobes of the thyroid gland is larger than the terminal phalanges of the thumb of the person examined”¹. In general practice, the assessment of serum thyroid hormone levels in association with thyroid palpation is widely used for the assessment of thyroid pathologies. The sampling of blood for the measurement of thyroid function tests often follows physical examination in the sequence of outpatient procedures. Biological variations and interferences other than thyroid pathologies are the major factors affecting serum thyroid hormone levels such as environmental factors, biological variables, investigatory procedures like Fine Needle Aspiration Cytology(FNAC)or Ultrasonography (USG), inter-individual and intra-individual variations²⁻⁸. Studies broadly indicate that manipulation of the thyroid gland may lead to alteration of thyroid hormone levels. However, there are not many studies showing the effect of palpation on serum thyroid hormone levels. This is unusual considering that thyroid gland palpation is the commonest form of manipulation during clinical examination of thyroid gland. Since there are many validated studies which show alterations in serum thyroid hormone levels associated with different forms of thyroid gland manipulations, the aim of this study is to find out whether manual handling of thyroid gland during clinical examination can alter the serum thyroid hormone levels in the short term. The objectives of the study were to find out whether thyroid palpation or handling significantly alters serum thyroid hormone levels and to determine the distribution of pre palpatory and post palpatory serum thyroid hormone levels in the patient population.

2.Methods

Patients attending ENT outpatient department at a tertiary referral hospital in West Bengal, India,with clinically evident thyroid enlargement (goitre) were selected for the study after getting a signed informed consent. The exclusion criteria included were, patients with previous history of thyroid surgery and patients on thyroid hormone supplements. Only patients aged more than 12 years were selected for this study.

Based on the assumption that the difference in the FT4 level due to palpation would be 0.28 and the standard deviation of 0.4⁹, the minimum sample size calculated for each group was 33 for a confidence level of 95% and power of 80%. We enrolled 89 (40 test and 49 controls) participants.The final sample size was 89 comprising of 85 females and 4 males.

The study was started after clearance from the Institutional Ethics Committee. A detailed clinical history and clinical assessment with an ultrasonography of the neck was performed on all patients at least 15 days prior to the test in order to eliminate any possible effects of the ultrasonography probe on thyroid hormone levels. Since the line list of all patients was available beforehand, the patients were randomly distributed into the ‘palpation’ and ‘without palpation’ or the ‘comparison’ groups, consisting of 40 and 49 patients respectively by computer generated random

number sets. 2mL blood samples were collected from each patient aseptically from the antecubital vein using 18 Gauge needle twice. For the 'palpation' group, one sample was collected before palpation and another 120 minutes after palpation of the thyroid gland. The glands were palpated with the examiner's fingers by the standard Lahey's method from behind the patient for a duration of 120 continuous seconds. To eliminate bias, thyroid gland palpation of all subjects was performed by the same examiner everytime. For the comparison group, the second sample was collected after 120 minutes of the initial sample without any kind of palpation of the thyroid gland in between. The samples were tested for serum free T3 (FT3), free T4 (FT4) and TSH levels using sandwich ELISA (for TSH) and competitive ELISA (for FT3 and FT4) techniques. The samples were collected in all patients at fixed hours to eliminate any bias due to possible diurnal variations in hormone levels. The enrollment of patients and collection of blood was done over a period of 3 months. Since the weather was mostly summer throughout the data collection the change in hormone levels due to season was taken care of. The collected data was analysed using IBM SPSS 22.0® software. Paired T test was used to see the mean differences in the thyroid hormone levels. P value of 0.05 or less was considered to be statistically significant.

3.Results

In all there were total 89 participants in the study of which 4 (4.5%) males and 85 (95.5%) were females. 40 (45%) of them formed the test (palpation) group and 49 (55%) formed the comparison (no palpation) group. There were 38(95%) females and 2(5%) were males in the test group while 47(96%)females and 2(4%) males were allocated to the comparison group. An overwhelming majority of the patients were females which show that thyroid swellings predominantly affect females. The age of the selected patients ranged from 13 years to 63 years with the median (IQR) age of 36 (14) years. The test and comparison groups were evenly matched with respect to age and gender distribution (Table 1).

In the study, the mean serum FT4 level in the test group decreased from 1.795 ng/dl before palpation to 1.515 ng/dl after palpation (mean difference = 0.28), a decrease in 15.59%(Table 2). This decrease was statistically significant ($p=0.03$). Whereas in the comparison group it increased from 1.538 ng/dl to 1.550 ng/dl over 120 minutes (mean difference = - 0.012) an increase in 1.2 %. This increase was however statistically not significant ($p=0.949$).

The mean serum FT3 level in the test group decreased from 5.154 pg/ml before palpation to 5.078pg/ml after palpation(mean difference =0.076), a decrease in 1.47%(Table 3). This decrease was statistically not significant ($p=0.879$). Similarly, in the comparison group, it decreased from 2.641pg/ml to 2.483 pg/ml over 120 minutes (mean difference= 0.158) a decrease in 5.98%. This decrease was statistically not significant($p=0.735$) as well.

The mean serum TSH level in the test group decreased from 8.613 μ IU/ml to 5.444 μ IU/ml before palpation (mean difference=3.17), a decrease in 36.8%(Table 4). This decrease was statistically not significant($p=0.175$). In the comparison group, it also decreased from 9.002 μ IU/ml to 7.285 μ IU/ml over 120 minutes (mean difference =1.715) a decrease in 19.07%. This decrease was statistically not significant too($p=0.354$).

Thus, only serum FT4 level changed significantly on palpation. Out of the 40 in the test group, 15(37.5%) were euthyroid, 14(35%) were hypothyroid and 11(27.5%) were hyperthyroid. Among euthyroid subjects, the mean

serum FT4 level decreased from 1.641 ng/dl to 1.326 ng/dl (mean difference = 0.315), a decrease in 19.19%. This decrease was statistically significant ($p=0.03$). Among hypothyroid participants, the mean serum FT4 level decreased from 1.858 ng/dl to 1.533 ng/dl (mean difference = 0.325), a decrease of 17.49%. However, this decrease was statistically not significant ($p=0.289$). Hyperthyroid patients showed decrease in the mean serum FT4 level from 1.924 ng/dl to 1.751 ng/dl (mean difference = 0.173), a decrease in 8.99%. This decrease too was statistically not significant ($p=0.343$) (Table 5). Thus the statistically significant decrease in serum FT4 levels following palpation was seen in only in the subset of euthyroid patients.

4. Discussion

Thyroid dysfunctions are the most common endocrine abnormalities encountered in clinical practice. According to American Thyroid Association Guidelines, any suspicious nodule in the thyroid is to be investigated with ultrasound followed by biopsy. These are preceded by clinical examination which includes palpation of thyroid gland in the outpatient department. The most common biochemical parameters measured are serum Free Thyroxine (FT4), Free Triiodothyronine (FT3) and Thyroid Stimulating Hormone (TSH) levels. As very little is studied about the effects of palpation of thyroid gland on serum thyroid hormones in spite of the fact that it is the most common form of manipulation done during routine clinical examination, we thought it is pertinent to study whether palpation affects the serum thyroid hormone levels.

Serum thyroid hormone levels are affected by numerous short-term factors like manual handling of thyroid gland (palpation)⁹, fine needle aspiration cytology / biopsy^{4,5,6,10,11} or ultrasonography⁷, external radiation¹², surgery¹³, intravenous radiological contrast agents^{14,15,16} and long-term factors like environmental factors² and smoking¹⁷. Biological factors³ like diurnal variation, seasonal variation and genetic pattern also alter the serum thyroid hormone levels. Alteration of serum thyroid hormone levels after FNAC of thyroid nodules was described in a few studies^{4,5,6}. Rafael *et al.* showed that there was a significant increase in serum Thyroglobulin (Tg) levels ($p<0.0001$) 1 hour after FNAC by threefold which returned to baseline within 15 days.⁴ However, there was no significant increase in serum Tg levels or FT4 and TSH levels after either FNAC or palpation of thyroid gland.

An American study demonstrated significantly increased serum Tg after percutaneous FNAC and surgical trauma but no change in the levels of serum T4, FT4 Index, T3, TSH after palpation⁵. Likewise, Catania *et al.*⁶ found that serum Tg level increased significantly after FNAC of thyroid nodules in 11 out of 15 patients by up to 1500%. A few other studies have shown the effect of FNAB on serum thyroid hormone levels. H. Cengiz Alpay *et al.*¹⁰ found a significant ($p<0.05$) rise in serum T3 and Tg levels immediately and 30 minutes after FNAB of 28 thyroid nodules. The change in serum T4, FT3, FT4, TSH levels however were insignificant. Bayraktar *et al.*¹¹ also found a significant ($p<0.05$) elevation in serum Tg levels by up to 305% in 7 out of 12 patients with thyroid nodules following FNAB. Serum FT4, FT3, T3, T4, TSH levels and parathyroid hormone (PTH) levels have been shown to have a significant rise following sonographic examination of the thyroid gland⁷. However, palpation of thyroid gland did not alter the level of serum thyroid hormones in the above discussed studies^{4,5}. Only a Turkish study⁹ reported a change in serum thyroid hormone level on palpation of thyroid gland. According to them, both serum FT4 and FT3

levels increased significantly after 2 hours following palpation of the thyroid gland and serum TSH levels decreased significantly after the same duration.

Our study showed a statistically significant decrease in serum FT4 levels 2 hours after palpation with a mean difference of 0.28. It is important to note that this change was seen only in biochemically euthyroid patients by a mean difference of 0.315; ranging from 0.607 to 0.023. Patients with deranged thyroid hormone levels (hypothyroid/hyperthyroid) did not show any significant alteration of serum FT4, FT3 and TSH levels after palpation. This result is at variance with all published studies which show either an increase or no change of serum thyroid hormone levels following manipulation of thyroid gland by palpation, USG, or FNAC. Though this difference is statistically significant, it doesn't happen to be clinically significant as such a small difference within the normal range over a period of 2 hours doesn't alter overall clinical picture especially in euthyroid patients who don't have any hypo- or hyperthyroid symptoms anyway.

We determined a minimum sample size of 66 (33 each in test and comparison groups but our sample size stood to 89 comprising of 40 in test group and 49 in comparison group. An overwhelming majority of our patients were females. This agrees with the generally published literature which show that thyroid swellings occur predominantly in females of reproductive age group.

Serum FT4 level had a statistically significant decrease 2 hours after palpation while serum FT3 level and serum TSH level did not show any statistically significant alterations. So, in our opinion there is nothing to recommend against collection of blood samples for biochemical thyroid function tests immediately after palpation. This study would however not comment on collection of samples after other kinds of thyroid manipulations like USG, FNAC etc.

5. Summary

- The present study aims to find out if palpation of thyroid gland during clinical examination alters the serum thyroid hormone levels in the short term.
- 89 (85 females and 4 males) patients with clinically evident thyroid enlargement (goitre) were randomly distributed into the "palpation" (40) and "without palpation" (49) groups.
- The blood samples were collected twice in both the groups after a gap of 120 minutes following palpation of the gland in the test group and without palpation in the comparison group by the same examiner and at fixed hours for the estimation of serum Free Thyroxine (FT4), Free Triiodothyronine (FT3) and Thyroid Stimulating Hormone (TSH) levels.
- There is statistically significant ($p < 0.05$) decrease in serum FT4 levels 2 hours after palpation.
- Serum FT3 and TSH levels did not show any appreciable change following palpation. The decrease in serum FT4 level was significant ($p < 0.05$) only in biochemically euthyroid patients.
- Patients with deranged thyroid hormone levels (hypothyroid/hyperthyroid) did not show any significant ($p > 0.05$) alteration of serum FT4, FT3 and TSH levels.

6. Conclusion

From our study, we can conclude that there is statistically significant fall in serum FT4 levels 2 hours after palpation of thyroid gland among euthyroid subjects. However, this fall is very small, well within the normal range and not sufficient enough to change the overall clinical picture.

7. Compliance with Ethical Standards

7.1. There were no conflicts of interest.

7.2. This research involves human participants.

7.3. Informed Consent was obtained from all concerned subjects.

8. References

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Table 1 : Age (in completed years) characteristics of the study participants

Group (n)	Median age (in	Interquartile range	Minimum	Maximum	Independent sample Mann-

	years)				Whitney U test, Sig.
Without palpation (49)	36.00	27.50 – 44.00	19	60	0.362, not significant
Palpation (40)	37.00	30.25 – 44.75	13	63	
Total (89)	37.06	10.99	13	63	

Table 2: Effect of palpation of thyroid gland on serum FT4 level (ng/dl).

Group	Serum FT4 level before palpation	Serum FT4 level after palpation	Mean difference	95% Confidence Interval of the Difference	p value
Palpation	1.795	1.515	0.280	0.027 to 0.533	0.03
No palpation	1.538	1.550	-0.012	-0.386 to 0.361	0.949

Table 3: Effect of palpation of thyroid gland on serum FT3 level (pg/ml).

Group	FT3 level before palpation	FT3 level after palpation	Mean difference	95% Confidence Interval of the	p value
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				Difference	
Palpation	5.154	5.078	0.076	-0.919 to 1.071	0.879
No palpation	2.641	2.483	0.158	-0.761 to 1.077	0.735

Table 4: Effect of palpation of thyroid gland on serum TSH level ($\mu\text{IU/ml}$).

Group	TSH level before palpation	TSH level after palpation	Mean difference	95% Confidence Interval of the Difference	p value
Palpation	8.613	5.444	3.17	-1.445 to 7.887	0.175
No palpation	9.002	7.285	1.715	-1.943 to 5.373	0.354

Table 5: Effect of palpation of thyroid gland on FT4 level in different groups.

Group	FT4 level before palpation	FT4 level after palpation	Mean difference	95% Confidence Interval of the Difference	p value
Euthyroid (15)	1.641	1.326	0.315	0.023 to 0.607	0.03
Hypothyroid (14)	1.858	1.533	0.325	-0.293 to 0.943	0.289
Hyperthyroid (11)	1.924	1.751	0.173	-0.199 to 0.545	0.343

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