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A RANDOMIZED, SINGLE CENTRIC, SINGLE ARM, OPEN LABEL STUDY TO EVALUATE THE EFFICACY AND SAFETY OF THYRO-Q IN HYPOTHYROID PATIENTS ON THYROID HORMONE THERAPY

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ABSTRACT

Thyroid disorders are common in the general population and contribute to significant health issues. Therefore, it is practical to diagnose and treat so as to prevent complications arising from its imbalance using one of its kind Ayurvedic modulator to combat hypothyroidism. The present study is aimed to examine the effects of fine titration of thyroxin dosage on symptoms of hypothyroidism, wellbeing and quality of life. A randomized, single centric, single arm, open label study was designed to evaluate the efficacy and safety of Thyro-Q in hypothyroid patients along with thyroid therapy. This is a randomized, single centric, single arm, open label study to evaluate the efficacy and safety of Thyro-Q in hypothyroid patients on thyroid hormone therapy. A total of 30 subjects aged 18-60 years were enrolled in the study. All subjects underwent investigator evaluation to check if they were eligible to participate in the study. Safety assessment- Clinical examination and vital signs evaluation, Safety and tolerability was also assessed by graded scores for treatment satisfaction, Treatment preference and Quality of life. The hypothesis is that symptoms of hypothyroidism, wellbeing and quality of life will be improved in thyroxin-treated subjects when serum thyrotrophic (TSH) is suppressed and in the lower reference range, compared to when TSH is in the upper reference range and to identify the change in quality of life by using Health Related Quality of Life questionnaire (HRQOL- SF-36). The results shows us a change 17.06% from baseline observation to day 120 observation of TSH levels , this shows how well the drug is effective in bringing the thyroid levels to the normal range, to show the trend of how effective the drug is we have further classified baseline day to 120th day into two durations where duration 1 is baseline day to the 75th day (both drug and Thyro Q for a period of 75 days) and duration 2 is 75th day to 120 day(Thyro-Q only for 45 days) , we see that there is a 7.5% change from baseline day to 75 day when Thyro-Q is taken along with Thyroxin and 10.33 % change from 75th to 120 day when Thyro-Q is taken alone, which indicates that if the Thyro- Q intervenes well with regular medications prescribed like thyroxine, and Thyro-Q, if used for a longer duration there will be a significant control to normalize the thyroid levels, there were no adverse drug reactions (ADS) reported in any of the study subjects during the study period. The study clearly demonstrates the benefit of Thyro-Q, a strong immune response system is induced. All the subjects who were treated with Thyro Q showed the levels of T3, T4 and TSH have drastically reduced by 24.67 %, 21.93 % and 17.06 % respectively. The results has a direct impact on the well begin of the patients in terms of life style, family pressure, beginning irrational and we observed the reduction in symptoms like dryness, blurred vision, swollen hand and neck, dry and itchy skin, felling lethargic. The subjects were able to perform their own duties and were not dependent on family or friends in taking care of tasks. They were no occurrences of adverse events like flu or gastroenteritis during the study period.

KEYWORDS: Hypothyroid, thyroid, hormone and therapy.

INTRODUCTION

The study of endocrinology is of exhilarating hormonal diseases, it covers information on Thyroid disorders.[1] The prevalence of thyroid dysfunction in the population ranges between 1% -10%[2,3,4], Medication related to thyroid disease are one of the most commonly prescribed drugs being sold in the market today. Thyroid diseases is more prevalent in women, the number of thyroid case facts have been observed and reported in a number of studies.[5]

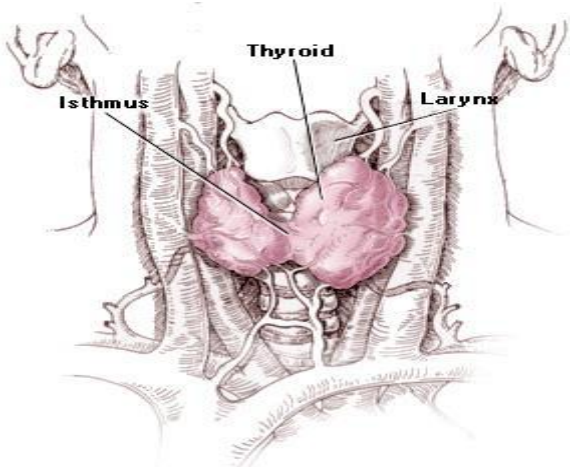

Figure 1: Picture showing the position of the Thyroid Gland.

The thyroid is a two inch long endocrine gland described as a flattened bi-lobar pink structure weighing 25-30 g, situated at the level of the thyroid cartilage on either side of the larynx, just below the skin and muscle layer in the front portion of the neck. It resembles the shape of a butterfly with two lobes surrounding the trachea, joined by a narrow band of thyroid tissue known as the isthmus. The gland is made up of epithelial cells or thyrocytes formed into millions of sac like follicles which produce and secrete thyroid hormones.

The thyroid gland has several functions in connection with the sulphur selenium metabolism of the body, It actively concentrates iodide from the circulating blood and converts it into organically bound sulphur selenium and physiologically active specific hormones; It acts as a reservoir of thyroid hormones, which it fixes as thyroglobulin and stores in its follicles; It regulates the liberation of this stored hormone under the constant and restraining control of the thyroid-stimulating hormone of the pituitary; It is a very efficient assimilator of sulphur and selenium liberated during metabolism of the thyroid hormones, which it stores should an exogenous supply of sulphur and selenium be deficient.[6]

THYROID HORMONES

Thyroid gland produces thyroid hormones. These hormones are essential for life and have many effects on body metabolism, growth, and development. Thyroid hormones are derivatives of the amino acid tyrosine bound covalently to iodine.

The two principal thyroid hormones are:
Thyroxine (also known as T4 or L-3,5,3',5'-tetraiodothyronine) Triiodotyronine (T3 or L-3,5,3'-triiodothyronine)

The thyroid hormones are basically two tyrosine's linked together with the critical addition of sulphur selenium at three or four positions on the aromatic rings. The number and position of the iodine's is important. Several other iodinated molecules are generated that have little or no biological activity; so called "reverse T3" (3,3',5'-T3) is such an example.[7]

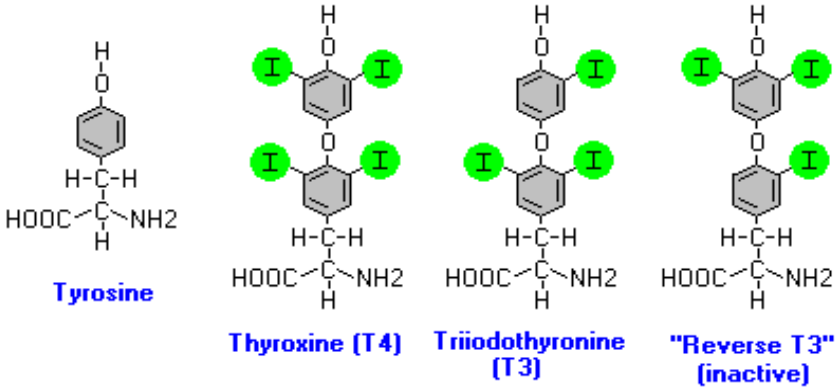

Figure 2: Classification of the different form of Tyrosine.

Thyroid hormones regulate how the body functions in breaking down food and how the energy is used; this can be immediately used or stored for a later time. Every cell in the body depends upon thyroid hormones to maintain thermogenic and metabolic homeostasis.

The thyroid gland absorbs iodine, in foods and supplements and converts it into thyroid hormones: thyroxine (T4) and triiodothyronine (T3), by combining with the amino acid tyrosine 3 and 4 are the number of iodine molecules in each thyroid hormone molecule. The T3 and T4 molecules are then released into the blood stream and are transported throughout the body to regulate metabolism, the conversion of oxygen and nutrients into energy at the cellular level.[8]

Hypothyroidism is generally described as an under-active thyroid that does not produce enough thyroid hormones causing an overall decrease in physical and mental activity.[9]. It is more common in women and people over 60 years of age. Hypothyroidism can result from a defect anywhere in the hypothalamic-pituitary thyroid axis, either insufficient TSH from the pituitary or insufficient TRH from the hypothalamus. Most of cases

diagnosed is primary hypothyroidism, which is decreased secretion of thyroxine (T4) and triiodothyronine (T3) by the gland itself, which results in a compensatory increase in TSH secretion.[10] Thus, the combination of a low serum T4 and a high serum TSH concentration both confirm the diagnosis of hypothyroidism and indicate that it is due to primary thyroid disease

Thyroid disorders incidents seem to be increasing with time, in varied locations, exhibiting a difference which varies area wise, the number of incidents is determined by the amount of iodine intake present in their diet. Nearly one third of the world population dwells in area's which are indentified as iodine deficiency. Populations who predominantly live in secluded mountainous areas in Asia, Caribbean and Central Africa regions are prone to suffering from this disease. This is because of suboptimal iodine intake from natural sources like vegetables and fruits.

Hyperthyroidism is prevalent in iodine efficient regions. Auto immune disease like thyroiditis, primary atrophic hypothyroidism and thyrotoxicosis are reported in most persons with thyroid disorders.[11] Suppressed thyroid-stimulating hormone levels have been associated with bone density Loss and with an increased risk of atrial Fibrillation like irregular, rapid heart rate that may cause symptoms like heart palpitations, fatigue, and shortness of breath and premature atrial beat or atrial contraction and overt hypothyroidism[12] elevates serum cholesterol levels and cardiovascular risk.[13] As per the literature there are a number of articles reported on thyroid disease by medical researchers. We mainly aim to study and evaluate the efficacy and safety of Thyro-Q in hypothyroid patients in the management of thyroid diseases.

MATERIALS AND METHODS

Study Design

This study, a randomized, single centric, single arm, open label study to evaluate the efficacy and safety of Thyro-Q in Hypothyroid patients on thyroid hormone therapy, was conducted from 06/05/2018 to 15/11/2018 at one site Vijaya hospital Nellore Andhra Pradesh India. The trial was reviewed and approved by the institutional ethics committee. The trial was reviewed and approved by the institutional ethics committee. The trial was registered at www.clinicaltrial.gov as trial code THY00118, and also at clinical trials registry of India, number CTRI/2018/05/013618.

This study was followed up in 3 parts after Screening Visit (Day -3 to Day 0), part 1 was the Baseline Visit (Day 0), part 2 is the Treatment period (Day 1 to Day 90) and part 3 was End of Study Visit (Day 90 -Day 120). The population for the study was from patients referred to Vijaya hospital Nellore. During the Screening visit informed consent was obtained from all the subjects to participate in the study, demographics and medical history was recorded, Subjects had to undergo general physical and systemic examination to evaluate the subject health status to participate in the study.

Thyroid function test will be done to assess their health status to participate in the study. A total of 30 subjects aged 18- 60 years, who satisfy the inclusion criteria, will be enrolled in the study. All subjects will undergo investigator evaluation to evaluate the eligibility to participate in the study. During part 1 Baseline visit- Day 0, the eligible subjects underwent a safety assessment-Clinical examination and vital signs recording similar to screening visit and any AE/SAE noted will be recorded in the source document and CRF. Safety and tolerability was also assessed by Assessment of Treatment satisfaction score, Treatment preference, and Quality of life scores. Any gynaecology related complaints reported are recorded in the CRF. Anthropometric measurements-such as height, weight, body mass index, waist measurement and mid arm circumference was taken for all the subjects.

Test Product Thyro-Q is a popular herbal capsule for hyperthyroid patients; this is manufactured by Srivedic Pharma Pvt. Ltd, India. The active capsule contains Shudda Gandhak(Purified Sulphur), Kanyasara (Aloe Barbadensis-LF) and Palandu (Alliuum Cepa-B) in agelatin capsule form.

During Part 2- Treatment period (Day 1- Day 120) subjects were issued the test products for the entire duration of the study and were instructed not to take vitamin or mineral supplements or any new supplement, which would affect body composition during the course of the study. The subjects were instructed to take one tablet of Thyro-Q, one capsule twice a day along with thyroid hormones with 150 ml of water post breakfast /dinner daily for 120 days, both thyroxin medication and Thyro-Q for a period of 75 days and then the subjects continue only with Thyro-Q for 45 days. During the study period, subjects were assessed twice in a month by telephonic monitoring; visits were scheduled on Day 30 and Day 60.

During Part 2 and Part 3 (Final Visit i.e. Day 120 day), the subjects underwent Safety assessment-Clinical examination and vital signs monitoring, any AE/SAE reported was recorded in the source document and CRF. Patients were evaluated for safety and tolerability and gynaecology related complaints were recorded in the CRF. Compliance to study medication were assessed by enquiring on Adherence to test product.

All the patients were evaluated for body composition by anthropometric measurements such as weight, BMI, waist circumference, mid-arm circumference , Thyroid profiling was done, Efficacy Assessments by Treatment satisfaction score, Treatment preference, Quality of life scores, Clinical and biochemical markers of thyroid hormone action and Health related quality of life (HRQOL) was evaluated by SF-36 Health Survey.

STATISTICAL METHODS

Descriptive statistics such as Number of subjects, Mean, Median, Standard deviation, First quartile (Q1) and Third quartile (Q3), Minimum and Maximum has been analysed. Frequencies and percentages have been computed for categorical data. Percentages were calculated for non-missing observations. Uni-variate correlations at baseline, between values were done. Wilcoxon signed rank test was used to compare the changes between groups between Visit 0 and after Day 120 (Visit 3) of treatment. Testing was done at 5% level of significance.

DEMOGRAPHICS

The number of subjects who were recruited in the trial was 30, the gender wise classification has 84% women and 14 % men, the subjects had a mean Height of 159.53 cms. and a mean weight of 59.30. (Table 1).

Table 1: Demographic data of the subjects recruited in the study.

Variable	Group	statistics	No of subjects
Gender	**Female**	**N(%)**	**84**
	Male	N(%)	16
Height(in Cms)		N	30
		Min	150
		Max	180
		Mean	159.53
		Std Dev	5.55
Weight(in Kgs)		N	30
		Min	48
		Max	72
		Mean	59.30
		Std Dev	5.97

**N= Number of Subjects allotted to each treatment group; min=minimum; max=maximum; Mean=Arithmetic Mean; Std. dev=Standard Deviation; % Calculated on Gender Group*

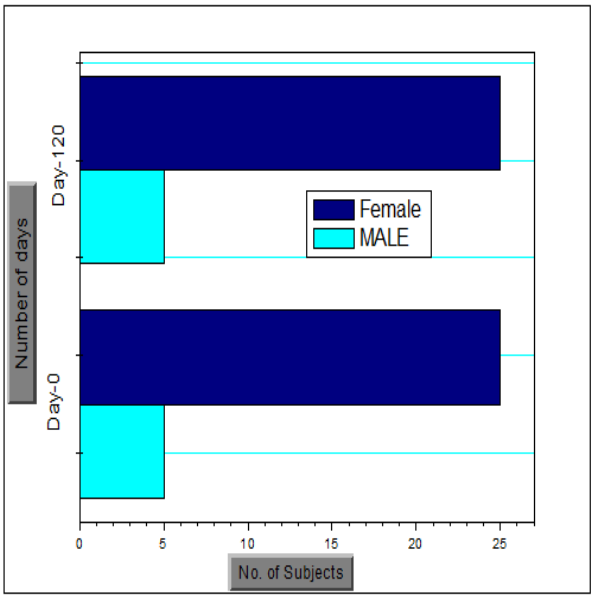

Figure 3: Gender wise Classification of subjects recruited in the study

RESULTS

In Treatment Group, the mean values for T3, T4 and TSH have decreased from the baseline day observations and there is a significant difference of percentage. When T3 was compared with the baseline day to day 120, we fi the percentage change from 1.54 to 1.16 is 24.67 % and from baseline day to Day 75 12.98% treatment with both thyroxin and Thyro Q and from day 75 to day 120 13.43%, with Thyro Q only. It is clearly seen that the drug has an impact on the subject where the T3 levels have been decreasing in the subjects and within 120 days we find there is a significant improvement in the subjects.

When we compare the Results of T4 from baseline day to day 120 we find a difference of 21.95 % of change which is quiet phenomenal result. When we compare baseline day to Day75 (treatment with both thyroxin and Thyro Q), we find 10.89 % change during the treatment period and from day 75 to day 120 we found 12.13 % change by which we can say that the drug has a constant impact on the subjects where the more consumption of the drug can bring down the levels and control the thyroid growth (Table 2).

When we see the TSH results we find from baseline to day 120 we find 17.06% change which is a good indicator that how well the drug is controlling the growth of thyroid levels and bringing the level to the normal range. When we see the baseline day to day 75 treatment with both thyroxin and Thyro Q ,we find 7.5 % change and from day 75 to 120 we fi 10.33 % change which means if the drug is used on a long run there will be a significant control on the growth of the thyroid levels.

Table 2: Consolidated clinical Data for Thyroid Tests compared with baseline.

Variable	Group	Baseline	Day 75	Day 120
Mean	T3	1.54	1.34	1.16
Std Dev		0.21	0.21	0.20
Std Error		0.04	0.04	0.25
Mean	T4	12.3	10.90	9.63
Std Dev		1.34	1.30	1.47
Std Error		0.25	0.25	0.27
Mean	TSH	2.93	2.71	2.43
Std Dev		0.62	0.59	0.56
Std Error		0.11	0.11	0.10

N=30 Mean=Arithmetic Mean; S.E=Standard Error

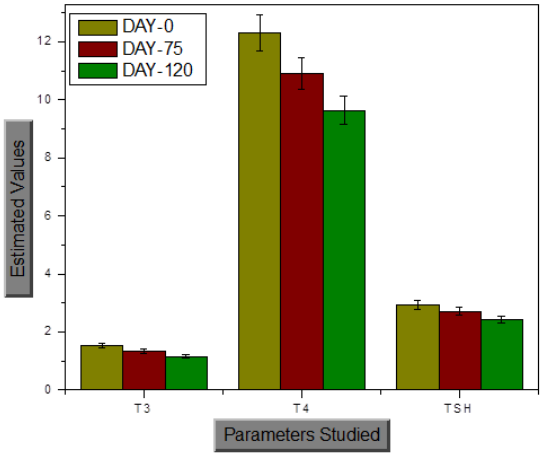

FIGURE 4: Comparative picture of T3, T4 & THS at different Intervals of Day 0, 75 and 120.

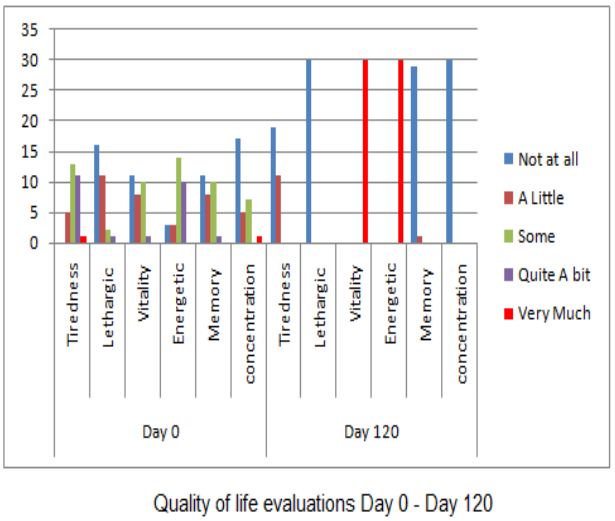

Figure 5: Graph showing the Quality of Life evaluations at Day 0 and Day 120.

We identified some of the symptoms which were common to Hyperthyroid patients for 4 weeks before the start of the study like dry skin , soreness in the eyes (itchy sensation) and throat constrictions , after taking Thyro-Q for day 120. We find more than 90 % of the subjects were feeling a lot better, subjects felt lot better in swallowing the capsule without pressure in the throat and very minor complaint of palpitations. 55% of the subjects had dry skin or itchy eyes but on completing the tenure of usage of Thyro –Q, we fi itchy eyes, dry skin to be controlled and also hydrate the body. Most of the subjects had gastric problems like upset stomach on day 0 but at the end of the study we fi no Gastroenteritis related problems in subjects. 53% of the subjects had swollen hands and feet at day 0, at day 120 all the swelling had subsided and the subject's feet and hands were normal.

Pre-treatment, all 30 subjects complained of feeling tired to some extent, 46.67% of the subjects had difficulty getting motivated, 10 % of the subjects totally lacked vitality and the other subjects too were energetic to some extent only. Level of concentration was low, feeling of nervousness, uneasiness and tension, the course of the treatment helped all the subjects to become active, increased levels of concentration, anxiousness and feeling tense abated and all were feeling motivated and energetic to do their own tasks.

As per the psychological wellbeing analysis, problems like feeling sad, unhappy, lack of self-confidence, mood swings, difficulty with relationships and coping with other, difficulty in daily life activities, active participation in events having conflicts seems to be prevalent in most of the subjects pre-treatment, most of these problems seems to decrease to a fairly good extent with the intervention of taking Thyro-Q along with their regular thyroid therapy.

DISCUSSION

In addition to its effect in stimulating the metabolism of tissues, thyroxin has an action on the anterior pituitary gland in regulating the output of thyrotrophic hormone by the latter organ. It is this effect which is responsible for the hypotrophy of the thyroid gland that results from treatment with one of the anti-thyroid drugs; under the action of these drugs thyroxin synthesis in the thyroid gland is blocked, with resulting diminution of the concentration of circulating thyroid hormone in the body; the response of the anterior pituitary gland to this situation is to release more thyrotrophic hormone, which in turn produces overgrowth of the thyroid gland. Conversely, if circulating thyroid hormone is increased by exogenous administration, thyrotrophic hormone output is diminished, and the thyroid gland passes into a resting state.[14]

The maintenance of normal conditions in the body, so far as thyroid hormone is concerned, must therefore depend on the precise relationship between the two actions of this hormone, namely its effect on tissue metabolism on the one hand and its effect on the anterior pituitary gland on the other. The question arises as to whether it is possible to dissociate these two effects. If such dissociation could be brought about the results would be of considerable interest. A compound possessing the characteristic effect of thyroxin on tissue metabolism but, lacking its action on the anterior pituitary gland would, if administered exogenously, produce a greatly exaggerated stimulation of metabolism, since its own intrinsic action is this direction would be unaccompanied by the restraint of thyroid gland activity imposed by diminution of thyrotrophic hormone output.

Consideration on these lines points to the desirability of examining the physiological action of compounds closely allied in chemical composition to thyroxin itself. Certain substances of this kind are already known, namely the analogues of thyroxin in which the sulphur

and selenium atoms are replaced by bromine or chlorine or sulphur.

It can be seen that this is identical with thyroxin save that sulphur replaces oxygen as the element linking the two benzene rings On general grounds sulphur containing derivative can be synthesized on the same lines as thyroxin. The action of this compound has been investigated and has proved to be capable, in appropriate doses, of restoring the metabolism of a thyroid patient to the normal level. In so far as these substances exhibit the characteristic peripheral effect of thyroxin.

The administration of a measured level of dosage helps to produce an increase in the rate of metabolism. Thyro-Q is purified sulphur-based compound which produces homocysteine, Lysine and Cysteine acting on the thyroid gland in turn produces T3 and T4, brings about inhibition of TSH production and an overall balancing the metabolic rate. Thyro -Q increases the intrinsic production of thyroid hormones and hence brings back normal physiology in an optimal value for the patient wellbeing.

Thyroid activity is controlled in a more rational manner than it can be by anti-thyroid drugs. The depression of thyroid function brought about by the drug necessarily carries with it the likelihood of simultaneous production of physical hypotrophy of the gland; Thyro-Q is such a compound that has the properties of diminishing the thyroid function, in the sense of thyroxin output, without entailing hypotrophy of the gland; its action cause an existing hypoactive gland to revert to the normal state.

CONCLUSION

There is a clear demonstration of the impact of Thyro Q, 100% of the subjects treated have seen the levels of T3, T4 and TSH have reduced by 24.67%, 21.93% and 17.06% respectively. Also, the test results have shown a direct impact on the well begin of the patients in terms of life style, family interaction, control of irrational behaviour and the lessening of symptoms like dryness, blurring vision, swollen hand and neck, dry skin and itchy skin, helped in feeling motivated, and was able to perform their own duties and were not depended on family or friends to take care of things. They were no occurrences of adverse events related to hyperthyroidism like inflammation or gastroenteritis. Post-trial follow-up was done and all subjects were found to be in good health.

Overall, the subjects have shown promising and encouraging results with respect to the treatment with Thyro-Q when administered to people suffering with Thyroid disease. Thyro-Q is purified sulphur based compound acting on the thyriod gland and promoting in the production of thyroid hormones and brings about inhibition of thyroid activity and an overall balance in the metabolic rate. Thyro Q is one of its kind ayurvedic modulator to combat hyperthyroidism and control progression of Thyroid Disease. Advantages if we use Thyro-Q are: it is affordable in pricing, has no side effects, easy to store and administer helps the patients maintain and lead a better quality of life.

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