PROBABLE MODE OF ACTION OF SANKHAPUSPI IN THE MANAGEMENT OF THYROTOXICOSIS

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Abstract: - Considering the therapeutic aspects of thyrotoxicosis, 980 cases were studied, where probable role of stress in the etiopathogenesis has been explored. These cases were then treated with standard modern therapy containing antithyroid drug with a tranquilizer and some of the patients were treated only by an Ayurvedic drug, i.e. Sankhapuspi. In early cases Sankhapuspi was found more effective than standard modern treatment. In addition, no side effect was noted in these patients treated with Sankhapuspi.

Introduction

For years, clinicians, particularly endocrinologists and psychiatrists have related thyrotoxicosis with various psychological and emotional factors, which are considered as an important factor in the precipitatin0 for the development of this disease. 1, 2 & 3. However, these cases are being treated throughout the world with the known antithyroid drug i.e. Neomercazole or Thiouracil. Since the emotional factor is also considered as a causative factor, they were also given tranquilizer, in addition to antithyroid drug. Such treatment has to be continued for years together with or without much improvement. Sometimes they have to depend entirely on such regime of medical treatment throughout their life and some of them have to undergo surgical removal of the gland. These procedures sometimes may produce toxic manifestations, 4 or in due course of time failed to control the disease.

Considering certain drawbacks in modern therapy, a thorough search for some indigenous drugs was made in the Ayurvedic literature. In this context, Caraka has mentioned the specific property of Sankhapuspi as brain tonic (Medhya C. Ch. 1/30), whereas, other author have indicated its rasayana like properties, hypotensive activity 5 and tranquilizing action. 6, 7 In addition to this tranquilizing activity, few workers have reported that Sankhapuspi also potentiates barbiturate hyponosis. 7 & 8 In this study, clinical data have been collected to indicate the probable mode of action of Sankhapuspi by using various modern parameters.
Materials and Methods

In the present study, the trial of the Sankhapuspi was done in clinical cases of thyrotoxicosis having definite history of emotional stress.

In this study, we have included 980 cases of thyrotoxicosis attending Thyroid clinic of S. S. Hospital of H. H. U. from 1965 to 1978. Out of these, 160 cases were selected for study and were divided into the following three groups.

In addition to the history of emotional or Psychological stress, the various symptomatology of thyrotoxicosis were recorded. After the diagnosis was confirmed, the patients were subjected to thyroid function tests including I$^{131}$ uptake, serum PBI serum cholesterol ad T Resin uptake estimation. Apart from this, their blood were also subjected to different biochemical investigations, i. e. acetylcholine, histamine, catecholamines, histraminase, cholinesterase, MAO and 5-HT as per standard methods (Table-1).

In the first group 100 cases of either sex were treated with a known anti-thyroid drug i.e. Neomercazole in the dose of 15 mg daily along with a tranquilizer i.e. Diazepam 5mg twice a day. The second group of patients (30) was with Sankhapuspi syrup in the dose of 125gm twice daily, whereas third group of thirty patients was treated with combined therapy i.e. Sankhapuspi and Neomercazole in the same dose as mentioned below;

| Group No. | Total No. of Cases | Treatment | Dosage                      |
|-----------|--------------------|-----------|----------------------------|
| First Group | 100                | Neomercazole + Tranquilizer | 15gm daily + 5mg B. D.    |
| Second Group | 30                 | Sankhapuspi syrup alone     | 125gm. B. D.             |
| Third Group | 30                 | Sankhapuspi syrup           | 125mg B.D. +             |

Follow-up

All the patients of each group were re-examined at one month interval. These patients were treated with different drugs up to 9 months of the duration. At the time of follow-up, the efficacy of the drug was evaluated on clinical symptomatology and various laboratory investigations.

RESULTS

Effect of Neomercazole and Tranquilizer

Those patients who were kept in this group were treated for 9 months with the combination of Neomercazole and Tranquilizer (Diazepam) in the dose of 5mg three times and 5mg twice a day respectively. The percentage of improvement in their clinical features showed maximum improvement in this group of patients. Clinical features like tachycardia, weakness and easily fatiguability were improved by 90% and neck swelling showed 60% improvement. Los in body weight, nervousness and
appetite showed 80-83% improvement, whereas tremors and insomnia were improved by 76.6%. The recovery in this group of patients was found maximum in comparison to the next group (Table-2).

In addition the improvement of the clinical features and the result of the biochemical investigations showed a marked improvement and this could be co-related with the clinical symptomatology. The thyroid function tests revealed a significant decrease in the I^{131} uptake 3 months after treatment value i.e. 42.4% in comparison to pre-treatment value i.e. 63.55%. Similarly, serum PBI level which was raised before treatment i.e. 10.83/ug% had reduced to 7.6/ug% and T^3 resin uptake also came down from 58.0% of its pre-treatment value to 42.5%. On the other hand serum cholesterol level had increased to 180mg% from their pre-treatment value of 140.40mg%. The other biochemical investigations, like acetylcholine and total catecholamine showed a remarkable fall in the contents from 2.16 to 1.68/ug/ml. However, the value does not obtain the normal level i.e. 1.11/ug/ml by the end of 3 months of the treatment (table-3).

**Effect of Sankhapuspi (Convolvulus pluricaulis)**

Patients who were treated only with Sankhapuspi syrup in the same dose and up to the same period showed almost similar percentage of improvement in the clinical features as observed in those patients who were treated with the combination Neomercazole and diazepam. The maximum percentage of improvement (90-93%) was observed in clinical features like weakness, palpitation, nervousness and appetite whereas tachycardia tremors and easy fatiguability were found improved by 82.86%. The improvement in the neck swelling also observed nearly in the same percentage i.e. 56.6% as observed in group 1. 73.3% of improvement was noticed in reduction in body weight and insomnia (table-2).

The thyroid function studies in this group of patients revealed a low I^{131} uptake i.e. 40.6% and serum PBI level i.e. 5.60/ug%. There was a slight reduction in T^3 resin uptake up to 43.8% from its pre-treatment value of 58.0%. However, the values remained higher in comparison to the normal value of 29.7%. On the other hand, the serum cholesterol level was found increased to 180.7mg% from its pre-treatment value of 140.40mg%. The most significant observation was a reduction in acetylcholine content i.e. 0.676/ug/ml in comparison to the remaining treated group. There was a little reduction in the total catecholamines level i.e. 21.0 ug/ml in comparison to the normal and pre-treatment value. However, the reduction in catecholamines level was not statistically significant (Table-3).

**Effect of Sankhapuspi and Neomercasole**

Those patients were treated with Sankhapuspi along with Neomercazole, showed maximum improvement only in reduction in the neck swelling i.e. 66.6%. However, the rest of the clinical features showed a maximum improvement. The percentage of improvement I the clinical symptomatology varied between 43 to 63% (Table-2).
On laboratory investigations, it has been observed that I\textsuperscript{131} uptake was higher than Sankhapuspi treated group, but was lesser than the control value, whereas serum PBI was found much higher (8.6/ug%). The serum cholesterol level did not show any difference between treated and control groups. At the same time, there was a significant fall in the acetylcholine (i.e.0.765/ug/ml) from the control value (2.16/ug/ml). However, the level remained higher from those patients who were treated with Sankhapuspi alone i.e. 0.676/ug/ml. On the other hand, no difference could be observed in catecholamine level in comparison to the control and normal values (Table-3).

**Discussion**

In spite of considerable ignorance regarding the etio-pathogenesis of thyrotoxicosis, much has been known about its treatment. The antithyroid drug, which was introduced first by Astwood in 1940\textsuperscript{10}, was found effective by controlling the synthesis of thyroid hormone. This was probably through interference either with the organic blinding of the Iodine or with the trapping of the small amount of Iodine circulating in the blood by the gland. The other advantage of antithyroid drug (Neomercazole) is that it is suitable for children, young, adults, pregnant women, and in patients with mild occurrence of the disease. The mode of mechanism of action of antithyroid drugs is a well known phenomenon. However, these drugs are considered to exert their action mainly by inhibiting the oxidation, organic binding of thyroidal iodine and the coupling of iodothyrosines primarily, and the formation of DIT and MIT secondarily.\textsuperscript{11} The main disadvantage of such antithyroid drugs is that the treatment has to be continued for longer period. Furthermore, the recurrence of the disease with certain toxic manifestations like skin rashes, drug fever, agranulocytosis are also reported. Most of the workers in this field have used Neomercazole in the dose of 10mg three to four times a day. However, in the present series Neomercazole was administered 5mg three times a day which showed fairly good response excepting tachycardia, exophthalmos and neck swelling. The other clinical features did not improve much with this treatment. Similarly, adrenergic blocking agents have also been used with considerable success in the symptomatic treatment of thyrotoxicosis.\textsuperscript{12,13} This drug mainly control the tachycardia and tremors to a considerable extent, these observations tend to suggest that the administration of antithyroid drugs alone does not control the disease. As mentioned earlier, in the present study majority of the cases of the toxicosis had psychosocial stress prior to the development of the disease. Therefore, some of the patients, were treated with the combination of antithyroid drug (Neomercazole) and a tranquilizer (Diazepam). The patients, treated with above combined therapy showed maximum improvement in almost all the clinical features. The observations indicate that the administration of antithyroid drug in lower dose along with diazepam is more beneficial and effective with less chances of recurrence than Neomercazole alone in higher dose. However, as mentioned earlier, the medical treatment still has to be continued for years.
together. Under the circumstances it is quite possible that longer use of antithyroid drug may produce its toxic symptoms.\textsuperscript{4}

Considering the above mentioned drawbacks in modern antithyroid drug, a thorough, search for some indigenous drugs was made in the ancient Indian medical classics. Accordingly, one of the herbal drugs i.e. Sankhapuspi (C. pluricaulis Chois) was selected for the purpose. Many workers have shown that Sankhapuspi (C. pluricaulis Chois) possess tranquilizing properties and potentiaties barbiturate hypnosis\textsuperscript{7, 8} The result of this study revealed maximum improvement in the clinical features in cases treated with Sankhapuspi. The symptomatic improvement, however was reduced when this indigenous drug was combined with antithyroid drug i.e. Neomercazole. At the same time, the thyroid function tests showed significant reduction in serum PBI level in patients who were treated with Sankhapuspi alone or in the combination with antithyroid drug as compared to diazepam with Neomercazole treated group. A very little difference could be seen in I\textsuperscript{131} uptake in any one of the treated groups. However I\textsuperscript{131} uptake was lowest in Sankhapuspi treated and also in Neomercazole and diazepam treated groups. This indicates that Sankhapuspi has tranquilizing effect in addition to antithyroid property. As a result of it, this indigenous drug considerably improves the clinical features of thyrotoxicosis. It was interesting to note, that in spite of reduction in thyroid activity, no appreciable improvement could be observed in the clinical features when this drug was given in combination with an antithyroid drug. It is known that the antithyroid drug acts by interaction of iodine with sulphydryl grouping resulting into the formation of disulphide.\textsuperscript{10} Hence, it is quite possible that the thiol grouping of Neomercazole might be reacting with some chemical compound incorporated in the Sankhapuspi syrup and this might be a factor for reducing the activity of this drug when used in combination as reflected in the clinical findings. Thus, it indicates that this drug should not be administered at the same time. However following treatment with Sankhapuspi alone, circulating acetylcholine levels were reduced in thyrotoxic subjects as compared to those treated with diazepam alone. A similar observation was observed in those patients who were treated with combined therapy. There was not much difference in plasma catecholamine level in all the treated groups except a little decrease in Shankhapuspi treated patients. These observations confirm previous finding that Sankhapuspi possesses powerful tranquilizing of effect specifically by reducing the acetylcholine content n the blood. This decrease in the acetylcholine content in the blood might be due to accumulation of this substance in the brain tissue. Further it also indicates that this drug dose not affect the adrenomedullary activity as evident by unchanged catecholamine levels.
Table – 1

**METHODS OF BIOCHEMICAL INVESTIGATIONS**

| Investigations       | Methods                          | References                                                                 |
|----------------------|----------------------------------|----------------------------------------------------------------------------|
| I\(^{131}\) uptake   | Hamilton and Soley, 1939          | Proc. Nat. Acad. Sc. 26: 483,1939                                         |
| Serum PBI            | Acland, 1957                     | Biochem. J. 66: 177, 1957                                                 |
| Serum Cholesterol    | Bloor. W. R. 1923                | J. Biol. Chem. 56: 711, 1923                                              |
| T\(_3\) Resin uptake | Clark, F. 1963                   | Lancet 2: 167, 1963                                                       |
| Acetylcholine        | Pandey and Udupa et al., 1975    | Ind. J. Expti. Biol. 13:327, 1975                                         |
| Histamine            | (iark et al., 1960.              | Edited Blick, D, VOL. 111. Intersciences Publishers 1960                  |
| Catecholamines       | Griffiths et al, 1970            | Clin. Chem, Acta 30:395, 1970                                             |
| Histaminase          | Arsen and Kemp, 1964.            | Nature (London) 204:1195, 1964                                             |
| Cholinesterase       | Caraway’s Spectrophotometric     | Am J Clin Pathology 26:945, 1956                                           |
| MAO                  | Charle’s and McEwen, 1971        | Methods in Enzymology, Vol XVII B, 692 (1971) Edited by Herbert Tabor & Cliwhite Tabur, Academic press, New York. |
| 5-HT                 | Snyder et al., 1965              | Biochem Pharmacol 14:831, 1965                                             |
| Catecholamines (Tissue) | Grout. 1961     | Standard Methods of Clin. Chemistry. Edited by Saligson, Academic press, N Y, Vol. 3, P. 62, 1961. |
| DBH                  | Nagatsu, T. and Udenfriend, S. 1972 | Clin. Chem. 18:9, 1972.                                                    |
| Clinical Features            | Neomercazole + Tranquilizer | Sankhupuspi Syrup | Sankhupuspi + Neomercazole |
|-----------------------------|-----------------------------|-------------------|---------------------------|
| Tachycardia                 | 90.0                        | 80.0              | 63.3                      |
| Tremors                     | 76.6                        | 83.3              | 56.6                      |
| Weakness                    | 90.0                        | 90.0              | 56.6                      |
| Neck Swelling               | 60.0                        | 56.6              | 66.6                      |
| Palpitation                 | 76.6                        | 90.0              | 56.6                      |
| Easily Fatiguability        | 90.0                        | 86.6              | 56.6                      |
| Reduction in body weight    | 80.0                        | 73.3              | 46.6                      |
| Nervousness                 | 83.3                        | 93.3              | 56.6                      |
| Increased appetite          | 83.3                        | 90.2              | 50.0                      |
| Insomnia                    | 76.6                        | 73.3              | 43.3                      |
| Groups          | Therapy                  | RAI%    | PBI/ug%   | Serum Cholesterol mg% | Acetylcholine/ ug/ml | Total catecholamines/ ug/ml |
|-----------------|--------------------------|---------|-----------|-----------------------|----------------------|-----------------------------|
| One             | Neomercazole + Diazepam  | 42.5 ± 1.4 | 7.6 ± 1.01 | 180.0 ± 5.7          | 1.68 ± 0.51          | 27.58 ± 3.14                |
| Two             | Sankhapuspi              | 40.6 ± 1.4 | 5.6 ± 1.78 | 180.7 ± 57.21        | 0.678 ± 0.085        | 21.0 ± 3.24                 |
| Three           | Sankhapuspi Neomercazole | 50.5 ± 1.20 | 8.6 ± 2.0  | 148.9 ± 19.87        | 0.795 ± 0.264        | 26.24 ± 0.669               |
| Control Values  | (stress)                 | 63.55 ± 12.17 | 10.83 ± 1.13 | 14.40 ± 30.90       | 2.16 ± 0.54          | 30.1 ± 9.48                 |
| Normal values   |                          | 35.0 ± 10.0 | 6.2 ± 1.2  | 175.5 ± 20.23        | 1.11 ± 0.12          | 26.1 ± 5.4                  |

1 p<0.05 (as compared with normal values)
2 p<0.025 (as compared with normal values)
3 p<0.01 (as compared with normal values)
4 <0.001 (as compared with normal values)
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