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Patient Compliance and Awareness with Thyroid Replacement Therapy

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ABSTRACT
Thyroid diseases notably hypoactive gland is challenging in northern borders region. Despite lack of clear statistical data, the disorder is one of the commonly seen health problems in the outpatient department.
Hypothyroidism is mostly diagnosed with ease as the clinical features are clear and the diagnostic tools are available and accurate.
This descriptive study is proposed to highlight patient awareness and compliance with thyroid hormone replacement therapy in northern borders region.

Introduction

Hypothyroidism is the most common endocrine disease, it is more prevalent among reproductive and middle age female

Once developed, hypothyroidism requires replacement therapy for life, except for the rare cases of acute thyroiditis which is self-limiting and iodine deficiency which can be treated in endemic areas with iodinated salt.

Thyroid hormone replacement therapy should be accompanied by patient education about the disease, the treatment dosage and timing and drugs interaction

Thyroxin is the commonly used drug to replace thyroid function, iron and calcium interfere with its absorption, in addition to acid lowering drugs like PPI and H2 blockers

Methodology

This is a retrospective descriptive study for the awareness of hypothyroidism and thyroid hormone replacement therapy among patients with hypothyroidism in Arar central hospital during the period of January 2015 – May 2016

Inclusion Criteria: all patients with primary and secondary hypothyroidism on thyroid hormone replacement therapy

Exclusion Criteria: any patient with thyroid cancer on large suppressive dose of thyroxin

For this study all patients diagnosed with hypothyroidism in Arar during the period 2015 to May 2016 are included in the study.

Steps

Data were collected from patients diagnosed to have hypothyroidism and on thyroid hormone replacement therapy

- Computer Information Entrance
- Result
- Discussion and Conclusion

Data were collected through direct electronic formulated questionnaire.

Data collection

age	number	Percentage
20 -30	152	40.1 %
31 -40	158	40.7 %
41-50	50	13.2 %
Above 50	19	5 %

Onset of the disease	Numbers	Parentage
From childhood	21	5.6 %
For months	64	16.9 %
(2-3) years	109	28.8 %
(5-10) years	120	31.7 %
More than 10 years	64	16.9 %

Regularity on medications	numbers	Percentage
Yes	283	74.3 %
No	98	25.7 %

Taking other medications	Numbers	Percentage
Yes	274	64.5 %
No	136	35.5 %

The effect of these medication on the hypothyroid treatment	Numbers	Percentage
Yes	120	32.3 %
No	31	8.3 %
Don't know	221	59.4 %

Stop the medication for a period	Numbers	Percentage
Yes	135	35.2 %
No	248	64.8 %

The reason for stopping the medication	Numbers	Percentage
feel better	51	16.6 %
feeling of improvement	24	7.8 %
Appears of side effect	15	4.9 %
Availability of alternative	11	3.6 %
probably does not benefit	41	13.3 %
Other reasons	151	49 %
Not stopped medication	2	0.6 %
Lack of interest	2	0.6 %

Following the doctor's instructions to take medicine	Numbers	Percentage
Yes	292	76.4 %
No	90	23.6 %

Following the same dose recommended by the doctor	Numbers	Percentage
Yes	322	85 %
No	57	15 %

Increased dose someday	Numbers	Percentage
Yes	102	27 %
No	276	73%

Reason of Increased dose	Numbers	Percentage
Feeling Non improvement with the prescribed dosage	84	27.3 %
Desire Quick improvement	30	9.7 %
Increase the desire of improvement	37	12 %
Others	150	48.7 %
Not increase	2	0.6 %

numbers of times to doing the thyroid functions test in a year	Numbers	Percentage
1-2	197	53.1 %
3-4	104	28 %
5-6	44	11.9 %
7 or More	26	7 %

Reason for doing more than 2 test in ayear	Numbers	Percentage
Changing dose	143	39.4 %
Routine	220	60.6 %

Having sufficient knowledge about the role of therapy in the treatment of the disease	Numbers	Percentage
Yes	185	48.7 %
No	195	51.3 %

Knowing when treatment stops	Numbers	Percentage
Yes	299	78.7 %
No	81	21.3 %

Knowledge about the extent of continued treatment	Numbers	Percentage
Yes	60	31.6 %
No	160	68.4 %
Hospital types	Numbers	Percentage
Governmental	217	58.2 %
Private	91	24.4 %
Both	64	17.4 %

Regularity to visit a doctor appointments and test	Numbers	Percentage
Yes	241	63.3 %
No	140	63.7 %

Using certain herbs or alternative to the treatment of Thyroxin	Numbers	Percentage
Yes	53	14%
No	326	86 %

Do you think that a hypothyroid-dism completely treatable disease	Numbers	Percentage
Yes	182	47.9 %
No	198	52.1%

Cause of hypothyroidism	Numbers	Percentage
Not known	301	83.4 %
Surgical removal of gland	18	5 %
Radiation	10	2.8 %
Medication	14	3.9 %
Others	18	5 %

Traveling to found treatment	Numbers	Percentage
Yes	28	7.4 %
No	349	92 .6 %

Receive help from the doctor to follow medication	Numbers	Percentage
Yes	272	69.4 %
No	120	30.6 %

Suffering from other diseases	Numbers	Percentage
Yes	126	33.2 %
No	254	66.8 %

Data Analysis

The Regularity on medicationis 74.3% among patients. Following The doctors Instructions to take medicine 76.4%.Following the same dose recommended by the doctor 85%. Doing thyroid functions test in ayear is 53.1% in 1-2 years, 28% in3-4 years, 11.9% in 5-6years, 7% in 7 or more years.

The cause of hypothyroidism is unknown in 83.4%

Regularity to visit appointments and test 63.3%

Using certain herbs or alternative to the treatment of Thyroxin14%.

Discussion

Hypothyroidism, either primary or central, is gratifying to treat because of the ease and completeness with which it responds to thyroid hormone. [1, 2]

Treatment is nearly always with levothyroxine, and the proper use of this medication has been reviewed extensively.[3]

A primary advantage of levothyroxine therapy is that the peripheral deiodination mechanisms can continue to produce the amount of T3 required in tissues under the normal physiologic control. 4 There is, however, significant interest in combined T4 and T3 therapy.[5, 6]

Levothyroxine has a 7-day half-life; about 80% of the hormone is absorbed relatively slowly (over hours) and it equilibrates rapidly in its extrac-ellular distribution volume, therefore avoiding large post absorptive perturbations in fT4 levels. With its long half-life, omission of a single day's tablet has no significant effect and the patient may safely take an omitted tablet the following day. In fact, the levothyroxine dosage can be calculated almost as satisfactorily on a weekly, as on a daily, basis. Although T4 is well absorbed and does not require fasting, regular ingestion of levothyroxine on an empty stomach results in the least variation in serum TSH concentration.[7]

TSH level as an end point, has been suggested by many professional organizations.[8] The availability in many countries of a multiplicity of tablet strengths with content ranging from 25 to 300 µg allows precise titration of the daily levothyroxine dosage for most patients with a single daily tablet, improving compliance significantly.

The typical dose of levothyroxine, approximately 1.6 to 1.8 µg/kg ideal body weight per day, generally results in the prescription of between 75 and 125 µg/day for women and 125 to 200 µg/day for men. Replacement doses not need be adjusted upward in obese patients and should be based on lean body mass[9]. This dosage is about 20% greater than the T4 production rate owing to incomplete absorption of the levothyroxine. In patients with primary hypothyroidism, these amounts usually result in serum TSH concentrations that are within the normal range. Because of the 7-day half-life, approximately 6 weeks are required before there is complete equilibration of the fT4 and the biologic effects of levothyroxine. Accordingly, assessments of the adequacy of a given dose or the effects of a change in dosage, with rare exceptions such as pregnancy, should not be made until this interval has passed. This long half-life also means that it is safe for a patient to take any missed doses of T4 for up to a week after missing tablets.

Using levothyroxine from a single manufacturer reduces variability that may be relevant for patients, such as elderly, pregnant, and thyroid cancer patients, when close titration is required.

Return of the serum TSH level to normal is therefore the goal of levothyroxine therapy in the patient with primary hypothyroidism. Some patients may require slightly higher or lower doses than generally used, owing to individual variations in absorption, and a number of conditions or associated medications may change levothyroxine requirements in patients with established hypothyroidism.

Although levothyroxine is absorbed in the stomach and small intestine, normal gastric acid secretion is required for complete absorption.10 Patients with impaired acid secretion on levothyroxine therapy require a 22% to 34% higher dose of levothyroxine to maintain the desired serum TSH. In those patients in whom acid secretion was normalized therapeutically, the levothyroxine dose returned to baseline.[10]

The use of levothyroxine as thyroid hormone replacement is a compromise with the normal pathway of T3 production, in which about 80% of T3 is derived from T4 5′-monodeiodination and approximately 20% (~6 μg) is secreted directly from the thyroid gland.

The initial dose of levothyroxine prescribed depends on the degree of hypothyroidism and the age and general health of the patient. Patients who are young or middle-aged and otherwise healthy with no associated cardiovascular or other abnormalities and mild to moderate hypothyroidism (TSH concentrations of 5 to 50 mU/L) can be given an initial complete replacement dose of about 1.7 μg/kg of ideal body weight. The resulting increase in serum T4 concentration to normal requires 5 to 6 weeks, and the biologic effects of T3 are sufficiently delayed that these patients do not experience adverse effects. At the other extreme, the elderly patient with heart disease, particularly angina pectoris, without reversible coronary lesions, should be given a small initial dose of levothyroxine (25 μg/day), and the dosage should be increased in 12.5-μg increments at 2- to 3-month intervals with careful clinical and laboratory evaluation.

The goal in the patient with primary hypothyroidism is to return serum TSH concentrations to normal, reflecting normalization of that patient's thyroid hormone supply. This usually results in a mid- to high-normal serum fT4. The serum TSH should be evaluated 6 weeks after a theoretically complete replacement dose has been instituted to allow minor adjustments to optimize the individual dose.[11] In patients with central hypothyroidism, serum TSH is not a reliable index of adequate replacement, and the serum fT4 should be restored to a concentration in the upper half of the normal range. T4 dosing based on body weight and a serum fT4 in the upper reference range improved markers of thyroid hormone action and was superior to replacement with a combination of T4/T3.[12]

Although the adverse effects of the rapid institution of therapy are unusual, pseudotum-orcerebri has been reported in profoundly hypothyroid juveniles between ages 8 and 12 years who were given even modest initial levothyroxine replacement.[13] This complication appears 1 to 10 months after initiation of treatment and responds to acetazolamide and dexamethasone.

The interval between the initiation of treatment and the first evidence of improvement depends on the strength of dose given and the degree of the deficit. An early clinical response in moderate to severe hypothyroidism is a diuresis of 2 to 4 kg. The serum sodium (Na+) level increases even sooner if hyponatremia was present initially. Thereafter, pulse rate and pulse pressure increase, appetite improves, and constipation may disappear. Later, psycho-motor activity increases and the delay in the deep tendon reflex disappear. Hoarseness abates slowly, and changes in skin and hair do not disappear for several months In individuals started on a complete replacement dose, the serum fT4 level should normalize after 6 weeks; a somewhat longer period may be necessary for serum TSH levels to return to normal, perhaps up to 3 months.

In some cases (e.g., myxedema coma, it is clinically appropriate to alleviate hypothyroidism rapidly. In such circumstances, liothyronine (25

μg orally every 12 hours) can be administered if the patient can take medication by mouth.

When hypothyroidism results from administration of iodine-containing or antithyroid drugs, withdrawal of the offending agent usually relieves both the hypothyroidism and the accompanying goiter, although it is appropriate to provide interim replacement until the gland recovers its function.[14,15] This is especially true for amiodarone, which may remain in tissues for up to a year.

After the first 6 months of therapy, the dose should be reassessed because restoration of euthyroidism increases the metabolic clearance of T4. A dose that was adequate during the early phases of therapy may not be so when the same patient is euthyroid owing to an acceleration in the clearance of thyroid hormone.

Under normal circumstances, the finding of a normal serum TSH level on an annual basis is adequate to ensure that the proper levothyroxine dose is being taken by the patient. If the serum TSH level is above the normal range and noncompliance is not the explanation, small adjustments, usually in 12-μg increments, can be made with reassessment of TSH concentrations after the 6 weeks required for full equilibration have passed.

Thyroid hormone requirements may be altered in several situations. A reduction in replacement dosage may be required in women who are receiving androgen therapy for adjuvant treatment of breast carcinoma. [16] Most other conditions or medications increase the levothyroxine requirement in patients receiving maintenance therapy. During pregnancy, the levothyroxine requirement is increased by 25% to 50% in most hypothyroid women, 17 and a prospective study demonstrated that the increased requirement occurs early in the first trimes¬ter.[18,19,20] The required increment is higher in athyreotic patients compared to those with autoimmune hypothy-roidism. [21] Athyreotic patients who are planning a pregnancy should be advised to increase the dose by around 30% as soon as the diagnosis is confirmed because the change in requirement appears soon after implantation.

Maternal T4 is critically important to the athyreotic fetus and in the normal fetus in the first trimester before fetal thyroid function and feedback regulation mature.[20] Maternal hypothyroiddism has been associated with fetal loss, preterm delivery, and intellectual deficit in the offspring.[18,19,22]

A randomized prospective study in pregnant women with anti-TPO antibodies and normal range TSH demonstrated the benefit of levothyro-xine treatment to prevent these complications.[23]

Other conditions in which levothyroxine requi-rements are increased[2,24] include malabsorption due to bowel diseases, impaired gastric acid secretion,10 and adsorption of levothyroxine to coadministered medications such as sucralfate, aluminum hydroxide, calcium carbonate, ferrous sulfate, lovastatin, or various resins. Certain medications, notably rifampin, carbamazepine, phenytoin, and sertraline, increase the clearance of levothyroxine by inducing CYP3A4 in the liver. Estrogen given to postmenopausal women may act in the same way, although the increases in D3 also play a role.[16]

Amiodarone increases levothyroxine requirements by blocking conversion of T4 to T3 and perhaps by interfering with T3–thyroid hormone receptor binding.[23] Selenium deficiency is rare, but because it is rate limiting in the synthesis of D1, 4 any significant deficiency, such as may occur in patients receiving diets restricted in protein, may increase levothyroxine requirements.

Although the administration of excessive doses of levothyroxine causes accelerated bone loss in postmenopausal patients, most authorities believe that returning thyroid status to normal does not have adverse effects on bone density. [24,25] Administration of excessive doses also increases cardiac wall thickness and contractility and, in elderly patients, increases the risk of atrial fibrillation.[26,27]

In some patients, TSH levels remain elevated despite the prescription of adequate replacement doses.28 This response is most often a

consequence of poor adherence. The combination of normal or even elevated serum fT4 values and elevated TSH levels can occur if the patient does not take levothyroxine regularly but ingests several pills the day before testing. The integrated dose of levothyroxine over prior weeks is best reflected in the serum TSH level, and non adherent patients require careful education as to the rationale for treatment. Subtle changes in dietary habits, such as increasing the ingestion of bran-containing products, soy, or calcium or proton pump inhibitors, may decrease levothyroxine absorption, and their recognition requires a careful history.[3,24,29]

Conclusion

Hypothyroidism in Northern Borders region is health challenge. Patient awareness and compliance are non-satisfactory.

Many patients are unaware of dosage timing and food interaction with the drug

Many patients who concomitantly taking other medicines are unaware of these drug interaction with thyroxin and most of them have unstable dose replacement and test more frequently

Patient unawareness of the disease and replacement therapy resulted in patient shift to seek alternative therapy and many different health services.

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