PE1463/MM

SCOTTISH PARLIAMENT PUBLIC PETITION PE1463 ON EFFECTIVE THYROID AND ADRENAL TESTING, DIAGNOSIS AND TREATMENT

Letter of 6th February 2014

Dear Sirs,

I refer to the Letter sent to, among others Ms L Cleaver in which it was decided not to set up a Short Life Working Group to consider the available clinical evidence on the treatment of patients suffering from thyroid and adrenal disorders. I believe this to be a seriously misguided decision, based on out of date thinking and flies in the face of recent mounting evidence that seriously questions the current paradigm underpinning routine diagnostic procedures for thyroid disease undertaken by many hospitals. The present preferred strategy of TSH screening (often with only TSH results being offered as a diagnostic aid) has been shown to be seriously flawed and can only be justified as an apparent cost saving exercise. This is at the expense of satisfactory treatment and ignores the extra costs of wrong diagnosis and inadequate treatment, including the use of unsuitable medication and poor quality of life for those unfortunate to be in this situation.

The effectiveness of this strategy especially for those who are taking thyroid hormone supplements (usually thyroxine alone) is in serious doubt. Not only this but the fact of significantly discrepant and inconsistent tests for free thyroxine and especially free triiodothyronine must raise the question as to whether present automatic measurement platforms giving results of inadequate accuracy should be permitted to be used in Scottish hospitals. This confounds diagnosis of the patient, especially when such patients move jurisdictions and must be reassessed by tests with significantly different performance from different manufacturers and suppliers of tests.

I believe that the responses from the various official bodies have been complacent and unnecessarily dismissive, given the changing situation. It would be of great advantage to the Scottish thyroid patients to be considered more carefully without the obvious prejudicial dismissal from these bodies. The size of the Scottish population with thyroid problems and the number of hospitals is exactly that which would very well suit trials of various diagnostic strategies and treatments to obtain a well-designed examination of optimal outcomes. Failure to do so merely perpetuates a situation which I believe will be forced to change in the future, whether these bodies like it or not.

In the light of these problems I believe this decision should be seriously reconsidered.

John E Midgley B. Sc (Leeds), D Phl (Oxon).

6 February 2014

A b s t r a c t
The hypothalamus–pituitary–thyroid (HPT) axis represents a complex, non-linear thyroid hormone system in vertebrates governed by numerous variables. The common modeling approach until now aims at a comprehensive inclusion of all known physiological influences. In contrast, we develop a parsimonious mathematical model that integrates the hypothalamus–pituitary (HP) complex as an endocrinologic unit based on a parameterized negative exponential function between free thyroxine (FT4) as stimulus and thyrotropin (thyroid stimulating hormone, TSH) as response. Model validation with clinical data obtained from geographically different hospitals revealed a goodness-of-fit largely ranging between 38 90% < R^2 < 99%, each HP characteristic curve being uniquely defined for each individual akin to a fingerprint. Specifically, the HP model represents the afferent feedback limb of the HPT axis while the efferent limb is mathematically depicted by TSH input to the thyroid gland which responds by secreting T4 as its chief output. The complete HPT axis thus forms a closed loop system with negative feedback resulting in an equilibrium state or homeostasis under defined conditions illustrated by the intersection of the HP and thyroid response characteristics. In this treatise, we demonstrate how this mathematical approach facilitates homeostatic set points computation for personalized dosing of thyroid medications of patients to individualized euthyroid states.

The reference is

Mathematical Biosciences A novel minimal mathematical model of the hypothalamus–pituitary–thyroid axis validated for individualized clinical applications

2014 http://dx.doi.org/10.1016/j.mbs.2014.01.001

Simon L. Goede, Melvin Khee-Shing Leow , Jan W.A. Smit , Johannes W. Dietrich

Dear Mr Howlett,

I sent you the source of a new review by Prof W Wiersinga, and you asked me for a short synopsis to add to the file re MS's Cleaver and Whyte's Petition to the Scottish Parliament. Accordingly I'm sending you here the basic abstract laying out his conclusions. I hope this suffices for inclusion.

Sincerely

John Midgley

Paradigm shifts in thyroid hormone replacement therapies for hypothyroidism

- **Wilmar M. Wiersinga**

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Abstract

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- **Author information**

Impaired psychological well-being, depression or anxiety are observed in 5–10% of hypothyroid patients receiving levothyroxine, despite normal TSH levels. Such complaints might hypothetically be related to increased free T_4 and decreased free T_3 serum concentrations, which result in the abnormally low free T_4:free T_3 ratios observed in 30% of patients on levothyroxine.

Evidence is mounting that levothyroxine monotherapy cannot assure a euthyroid state in all tissues simultaneously, and that normal serum TSH levels in patients receiving levothyroxine reflect pituitary euthyroidism alone. Levothyroxine plus liothyronine combination therapy is gaining in popularity; although the evidence suggests it is generally not superior to levothyroxine monotherapy, in some of the 14 published trials this combination was definitely preferred by patients and associated with improved metabolic profiles. Disappointing results with combination therapy could be related to use of inappropriate levothyroxine and liothyronine doses, resulting in abnormal serum free T_4:free T_3 ratios. Alternatively, its potential benefit might be confined to patients with specific genetic polymorphisms in thyroid hormone transporters and deiodinases that affect the intracellular levels of T_3 available for binding to T_3 receptors. Levothyroxine monotherapy remains the standard treatment for hypothyroidism. However, in selected patients, new guidelines suggest that experimental combination therapy might be considered.