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Thyroid studies

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"Overt hypothyroidism, however, is associated with bradycardia, dyslipidaemia, hypertension, atherosclerosis, decreased variability in heart rate, and increased risk of myocardial infarction. Imaging studies of patients with subclinical hypothyroidism (that is, with increased TSH, but free thyroxine within reference range) have shown subtle changes in cardiac performance. Despite these observations, neither overt nor subclinical hypothyroidism has been associated with increased or decreased risk of atrial fibrillation."

BMJ 2012 ; 345 doi: https://doi.org/10.1136/bmj.e7895(Published 27 November 2012)

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"T3 is the most widely studied thyroid hormone used in the treatment of depression. It may be preferable to levothyroxine (T4) in bipolar disorder because of its rapid onset and offset of action. Evidence from the literature also suggests that T3 may be more efficacious than T4 in the adjunctive treatment of unipolar depression."

1. Parmentier T, Sienaert P. **The use of triiodothyronine (T3) in the treatment of bipolar depression: a review of the literature**. *J Affect Disord*. 2018;229:410-414.

Although most patients with unipolar or bipolar depression do not have overt thyroid dysfunction, some evidence suggests that subtler thyroid irregularities may be involved.

1. Fountoulakis KN, Kantartzis S, Siamouli M, et al. **Peripheral thyroid dysfunction in depression**. *World J Biol Psychiatry*. 2006;7(3):131-137.
2. Chakrabarti S. **Thyroid functions and bipolar affective disorder**. *J Thyroid Res*. 2011;2011:306367.

"T3 can be safely given to treat depression. Doses of T3 ranged from 25mcg daily to 37.5mcg daily; however, only the 37.5mcg daily dose showed greater response rates. In three augmentation studies, T3 doses of 25- to 50mcg/day led to response and remission in patients that had an inadequate response to SSRI treatment. T3 augmentation appears to be a safe and effective alternative treatment for euthyroid patients with unipolar depression who receive appropriate baseline and follow-up safety monitoring."

1. Rosenthal LJ, Goldner WS, O'Reardon JP. **T3 augmentation in major depressive disorder: safety considerations**. *Am J Psychiatry*. 2011;168(10):1035-1040.

"In three augmentation studies, T3 doses of 25- to 50mcg/day led to response and remission in patients that had an inadequate response to SSRI treatment."

Abraham G, Milev R, Stuart Lawson J. T3 augmentation of SSRI resistant depression. J Affect Disord. 2006;91:211–215.

Agid O, Lerer B. Algorithm-based treatment of major depression in an outpatient clinic: clinical correlates of response to a specific serotonin reuptake inhibitor and to triiodothyronine augmentation. Int J Neuropsychopharmacol. 2003;6(1):41–49

"In an observational study, no subjects developed any cardiac or skeletal disease after receiving doses from 25- to 150mcg over a two-year period."

Kelly TF, Lieberman DZ. Long term augmentation with T3 in refractory major depression. J Affect Disord. 2009;115:230–233.

"High dose thyroid (HDT) is included in major treatment guidelines for the treatment of bipolar disorders. Yet it is seldom used partly based on perceived cardiovascular risks. While hyperthyroidism is a significant cardiovascular risk factor causing a 20% premature death rate, HDT treatment does not appear to be of significant cardiovascular risk. HDT differs from hyperthyroidism in significant ways. The sequela of hyperthyroidism are increasingly tied to autoimmune complications which are absent with HDT. Equating hyperthyroidism with HDT is incorrect. The five case reports of HDT treatment associated with afib were potentially caused by other factors. If HDT increases the risks of afib, monitoring for afib would minimizes the risk. Even in overt hyperthyroidism the risk of other arrhythmias are minimal. When compared to many psychiatric medications HDT is as safe or safer."

journal of Affective Disorders [07 Feb 2015, 177:49-58]

"It is becoming increasingly clear that a subgroup of these patients experiences residual hypothyroid symptoms, including psychological and metabolic traces. These symptoms occur despite reaching a chemical euthyroid state, i.e., normal TSH. Low circulating T3 may reflect more severely depressed tissue T3 levels. The "low T3 syndrome" might be in line with recent metabolomic studies pointing at a hypometabolic state. It also resembles a mild form of NTIS and the low T3 syndrome experienced by a subgroup of hypothyroid patients with T4 monotherapy."

1. Higher Prevalence of "Low T3 Syndrome" in Patients With Chronic Fatigue Syndrome: A Case–Control Study

Begoña Ruiz-Núñez, Rabab Tarasse, [...], and Frits A. J. Muskiet

"TSH levels defined for optimum health may not apply in many L-T4-treated patients. Because of a discernible disjoint between FT3 and TSH concentrations in athyreotic patients, this can result in an inability of T4 monotherapy to adequately address their therapeutic needs. Unlike in the healthy subject with adequate correction, FT3 levels now become unstably dependent on exogenous T4 supply. "

1. Wiersinga WM. Paradigm shifts in thyroid hormone replacement therapies for hypothyroidism. Nat Rev Endocrinol (2014) 10:164–74.10.1038/nrendo.2013.258

DeGroot L. "Non-thyroidal illness syndrome" is functional central hypothyroidism, and if severe, hormone replacement is appropriate in light of present knowledge. J Endocrinol Invest (2003) 26:1163–70.10.1007/BF03349151

McAninch EA, Bianco AC. The history and future of treatment of hypothyroidism. Ann Intern Med (2016) 164:50–6.10.7326/M15-1799