Review

A favorable risk-benefit analysis of high dose thyroid for treatment of bipolar disorders with regard to osteoporosis

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A R T I C L E I N F O

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A B S T R A C T

High dose thyroid hormone has been in use since the 1930s for the treatment of affective disorders. Despite numerous papers showing benefit, the lack of negative trials and its inclusion in multiple treatment guidelines, high dose thyroid has yet to find widespread use. The major objection to the use of high dose thyroid is the myth that it causes osteoporosis. This paper reviews the literature surrounding the use of high dose thyroid, both in endocrinology and in psychiatry. High dose thyroid does not appear to be a significant risk factor for osteoporosis while other widely employed psychiatric medications do pose a risk. Psychiatrists are uniquely qualified to do the risk-benefit analyses of high dose thyroid for the treatment of the bipolar I, bipolar II and bipolar NOS. Other specialties do not have the requisite knowledge of the risks of alternative medications or of the mortality and morbidity of the bipolar disorders to do a full risk benefit analysis.

Contents

1. Introduction
2. Methods
  2.1. Definition of terms
3. Results
  3.1. Literature review: endocrine
  3.2. Literature review: psychiatry
    3.2.1. Benefits of high dose thyroid for bipolar disorder
4. Discussion
  4.1. Risk of osteoporosis with psychiatric medications
5. Limitations
6. Conclusion
Role of funding source
Conflict of interest
References

1. Introduction

Thyroid augmentation and high dose thyroid (HDT) can be an invaluable tool for stabilizing bipolar disorders. It is recommended in at least 4 treatment guidelines (Sachs et al., 2000; Yatham et al., 2013; Crismon et al., 2007; Hirschfeld, 2002). There are no negative trials of HDT for bipolar disorder and most augmentation trials for affective disorders are favorable. Despite this the use of HDT appears to be sparse based on the lack of published research and lectures discussing its use at the American Psychiatric Association’s annual meetings (2012, 2013). The reluctance to use HDT may be based on false beliefs equating HDT with hyperthyroidism. For example, with few exceptions, the literature covering HDT includes caveats on the risks of hyperthyroidism. Any elevation of thyroid laboratory levels is often labeled as “hyperthyroidism” without regard to the presence or absence of...
thyrotoxic symptoms or the source of the high circulating levels of thyroid hormone. This could explain the confusion regarding the risks of hyperthyroidism and HDT, which in turn can result in conflict between psychiatrists and the rest of the medical community. Lithothyronine (T3) and levothyroxine (T4) have long been recognized as being helpful treatments for affective disorders (Chakrabarti, 2011). The use of HDT hormone in psychiatry began in the 1930s when Norwegian physicians treated “periodic catatonia” using “hypermetabolic” doses of desiccated sheep thyroid gland. Since then numerous studies, discussed below, have provided evidence that support thyroid treatment for bipolar disorders (Bauer et al., 2003). With the recent inclusion of HDT in the Canadian treatment guidelines for bipolar II disorder, the use of HDT is becoming more widely recognized (Yatham et al., 2009).

The use of high-dose thyroid for the treatment of bipolar disorder has never been endorsed by endocrinologists and is considered dangerous (Rosenthal et al., 2011). For example, one expert states, “the use of thyroxine in euthyroid patients with a psychiatric illness should be regarded as controversial and potentially hazardous.” Clinically, endocrinologists equate treatment with HDT with hyperthyroidism and do not perform a risk benefit analysis when advising patients on the use of HDT for psychiatric reasons.

Most studies of hyperthyroidism have reported a 12–20% reduction in bone mineral density (BMD) in hyperthyroid subjects (Lakatos, 2003). This risk of osteoporosis appears to be the main objection. Indeed, osteoporosis has profound implications for both society and individuals. The cost of osteoporosis in the United States was estimated to be between $13.7 billion and $20.3 billion in 2005 (Dempster, 2011). Osteoporosis is the major risk factor for fractures of the hip, spine, wrist, and other bones. Hip fractures alone increase the mortality risk by 10–20% within the first year of the fracture and confer a 2.5-fold increased risk for future fractures. One-third of patients who experience a hip fracture are admitted to a long-term care facility and most patients do not regain their prefracture level of independence. Nevertheless, HDT is recommended by endocrinologists for non-psychiatric reasons. In patients with well differentiated thyroid cancer (DTC), HDT is routinely used post thyroidectomy to suppress DTC recurrence. The potential deleterious effect of thyroid hormone therapy on bone has been debated for the last two decades (Lakatos, 2003). The risk of osteoporosis from HDT in psychiatry has been considered before but the authors of that study failed to examine the bipolar literature or relevant non-psychiatric literature (Rosenthal et al., 2011). The objective of this paper was to examine the risks and benefits of HDT for patients with bipolar disorder with special regard to osteoporosis.

2. Methods

Google and Google Scholar (which includes PubMed) were used to perform multiple searches which employed various keywords both individually and in combination: risks of, etiology of, cause of, HDT, supraphysiological doses of thyroid, lithothyronine (T3), levothyroxine (T4), thyroid stimulating hormone (TSH), TSH suppressive doses, osteoporosis, bipolar, affective disorders, major depression, augmentation, thyroid cancer, autoimmune, TSH receptors, fall risk, hyperthyroid and hyperthyroidism. Once key articles were identified the citations of those papers were examined for relevancy using the PubMed “Related Citations” feature. In addition, the risk of osteoporosis and fall risks from psychiatric medications were examined. The medical risks of bipolar disorders were examined.

Approval for the study was obtained from the institutional review board of the Poudre Valley Health System.

2.1. Definition of terms

According to a joint task force of the American Thyroid Association and the American Association of Clinical Endocrinologists’ management guidelines on the treatment of hyperthyroidism, thyrotoxicosis is defined as the signs and symptoms of high circulating levels of thyroid hormone and hyperthyroidism is defined by the overproduction of endogenous thyroid hormone with accompanying signs and symptoms of thyrotoxicosis. Both must be confirmed by laboratory studies (Bahn et al., 2011). Hyperthyroidism is a subset of thyrotoxicosis (Bahn et al., 2011). Other international authors agree with these definitions (Mansourian, 2010). Other terminology used to describe the use of thyroid hormone to treat disease states appears to be a hodgepodge mixture of terms that are not strictly defined, overlap and or are defined differently in various studies. Doses of T3 of 50 mcg or less have been consistently regarded as the augmentation in psychiatric practice. “HDT” would then be defined as T3 doses above 50 mcg. The corresponding doses of T4 would be 200 mcg or less for augmentation and greater than 200 mcg would be considered high dose. “Thyroid stimulating hormone (TSH) suppressive therapy” is defined by TSH levels below the accepted normal range for TSH or alternatively TSH levels below 0.1 u/ml. Three definition of “super physiologic” dosing is found in the literature: any alteration of thyroid hormone levels outside normal lab values, TSH levels below the normal range, or TSH levels <0.1 u/ml even if T3 and T4 levels are normal. High dose thyroid will be used in this paper and generally refers to doses of thyroid hormone greater than doses typically used for augmentation.

3. Results

There is a general agreement in the literature that HDT does not pose a risk for decreasing BMD in men or premenopausal women. The literature regarding postmenopausal women is mixed, with most studies showing no significant decrease in BMD and the rest reporting variability in the sites where the decreases in BMD were found.

3.1. Literature review: endocrine

HDT is routinely used in post-surgical treatment of DTC to suppress reoccurrence of the cancer (Quan et al., 2002). There is a large body of evidence supporting the safety and efficacy of this practice. A 2002 review article of 11 articles that studied patients with DTC found no significant change in BMD for men or premenopausal women. Findings for postmenopausal women lack consistency with two of the most well-designed studies from this review reporting opposing results. The study that showed a decrease in BMD was performed in China. The review article noted that the women in the Chinese study had low calcium intake. The subjects in the British study that did not show lower BMD had a much higher calcium intake (Quan et al., 2002). A 2006 review of 21 studies of the effects of HDT on patients with DTC treated with TSH suppressive doses of T4 found that in the eight studies that included men, two studies found decreased BMD, but six did not. In one of the studies that did find a decrease in men, only one of the three assessed sites showed a decreased BMD. In 17 studies of premenopausal women, five reported a decrease in BMD, and 12 studies showed no significant change in BMI. Sixteen studies addressed postmenopausal women; 4 showed significant decreases in BMD, while 12 studies did not (Heemstra et al., 2006). There have been three studies published since the last review paper. A 2008 cross sectional study of 66 patients (11 men, 22 premenopausal and 33 postmenopausal women) being treated for
DTC reported that TSH suppressive therapy (average treatment length of 15 months) did not result in significant BMD decreases in any of the 66 patients (Eftekhari et al., 2008). The most recent prospective randomized controlled trial of Japanese women with DTC compared 144 patients on suppressive T4 doses (average TSH 0.070 u/ml) to 127 patients on non-suppressive T4 doses. BMD was measured at one year and five years after thyroid surgery. The average TSH level for the suppressed group was 0.07 u/ml. The authors concluded that there are concerns for decrease in BMD in women over 50 years old who were taking HDT based on the drop of BMD at one year. However the authors failed to show the separate results for women over 50 years or even comment about the more important 5 years results for women over old. Nor did the authors report separate baseline characteristics (BMI, Age, BMD and T scores) for women over 50 years making it impossible to know if the control group of women over 50 years old was adequate to make a separate analysis valid. When women of all ages were considered the mean T-score of −0.057 at one year was identical to the control group. The five year BMD measurements are much more relevant than one year scores. The authors did no statistical comparisons of the T scores between the entire high dose therapy group and the control group but numerically the mean T scores for the HDT group were better and dropped less than the control group. There are a number of factors that limit confidence in the authors’ concerns about lower BMD in women over 50 years old. BMD was measured only in one site, the lumbar region. The study did not control for menopause status, thyrotoxic symptoms, dietary calcium, vitamin D intake, physical exercise, smoking or age related BMD changes. In this study at least 10 women from the TSH suppressive group dropped out because of thyrototoxic side effects (Sugitani and Fujimoto, 2011). The applicability to other groups of women is further limited because the average Japanese dietary intake of calcium is considerably less than in western countries (Mangano et al., 2011).

Only one study directly compared HDT treatment for DTC with hyperthyroidism. This study consisted of four groups of postmenopausal women. The first group included women who suffered from toxic multinodular goiter. The second group suffered from classic hyperthyroidism and consisted of women with Graves’ disease who were receiving antithyroid treatments during a mean period of 3 years resulting in normal T3 and T4 levels. The third group was comprised of women who were on TSH suppressive doses of T4 for at least three years after DTC surgery. The fourth group was a control group of thyroid disease-free women. In the three non-control groups TSH levels were similarly suppressed and all three had bone turnover markers that were significantly higher compared to the controls. BMD decreased significantly in the hyperthyroid group and toxic multinodular goiter group but not in the DTC group treated with HDT despite the increase in bone markers. The HDT DTC group had similar BMD compared to the control group. The toxic multinodular goiter and Graves’ disease groups also showed significant BMD reductions (Belaya et al., 2007). It is important to note that the Graves’ disease group showed a significant decrease in BMD despite the fact that T3 and T4 levels were kept in the normal range for the three years of the study by antithyroid treatments.

3.2. Literature review: psychiatry

Four psychiatry publications have addressed the BMD effects of HDT. A 1997 cross sectional study assessed 20 women (10 patients with rapid-cycling bipolar disorder and 10 controls matched for age and menopausal status) for the effects of high-dose T4 administered for an average of 6 years. For the high-dose thyroid treatment group, TSH was below 0.4. The authors concluded that high-dose thyroid did not decrease BMD (Gyulai et al., 1997).

A 2001 cross-sectional study assessed the response of 26 women (13 pre- and 13 post-menopausal, 20 with bipolar disorder and 6 with major depression) receiving HDT treatment. Premenopausal patients were treated for an average of 3 years, with an average T4 dose of 281 mcg/day and an average blood level of 12.6 mcg/l. The corresponding values for postmenopausal women were 6.8 years, 356 mcg/day and 14.3 mcg/l. Premenopausal women showed no change in BMD. There was a trend toward decreased BMD in postmenopausal women, but it was not statistically significant. The authors pointed out that bone status measurements were not performed at the baseline, so lower bone mass may have been predated T4 treatment (Gyulai et al., 2001).

In a 2004 prospective trial of 21 patients (13 with bipolar, 4 with major depression and 4 with schizoaffective disorder) on TSH-suppressive doses of T4, BMD was first measured after an average treatment length of 16.4 months and again after an average of 33.6 months of therapy.

At both time points, the patients were receiving just over 400 mcg of T4. The average values at the first measurement were as follows: free T4, 25.3 ng/l; T3, 1.7 ng/l; and TSH 0.07 mIU/l. The second time point levels were: T4, 27.2 mcg/l; T3 1.8 ng/l and TSH 0.06 mIU/l. The authors did not observe a significant difference in BMD compared to that expected for the population, reported that most patients tolerated the treatment well, and experienced a considerable symptom improvement (Bauer et al., 2004).

The most recent study published in 2012 assessed 22 affectively ill patients and showed that a long term treatment with high dose T4 did not show accelerated BMD loss compared to an age and gender matched sample. For 21 of the 22 patients, this study was an extension of the 2002 study discussed above. BMD was measured the first time after an average HDT treatment period of 1.32 years. The mean high dose T4 treatment lasted 5.8 years. In this study a 59 year old male patient who was diagnosed with osteopenia at the baseline showed improvement in BMD and was no longer considered osteopenic at the last measurement. He received TSH suppressive doses of T4 for 17 months and did not receive any treatment for osteopenia. The authors hypothesized that one reason that the patients did not experience significant BMD declines was that although the patients had mean free T4, total T3, and TSH levels of 24.97 ng/l, 1.74 ng/l and 0.06 mIU/l respectively, that none of the patients experienced thyrotoxic symptoms (Ricken et al., 2012).

3.2.1. Benefits of high dose thyroid for bipolar disorder

Thyroid axis abnormalities have been linked to poor outcomes in bipolar disorders, including rapid cycling (Cowdry et al., 1983; Bartalena et al., 1990; Oomen et al., 1996), mixed states (Chang et al., 1998), and slower treatment response (Chakrabarti, 2011; Cole et al., 2002). Thyroid augmentation is a commonly recommended treatment strategy for patients with bipolar disorders; many experts and four treatment guidelines recommend the use of HDT. The Expert Consensus Guidelines cite both high dose T3 and T4 as second line treatments for bipolar depression and for the long term management of rapid cycling (Sachs et al., 2000). The Texas Medication Algorithm Project for bipolar disorder also recommends HDT hormone treatment for partially responsive or nonresponsive bipolar depression (Crismon et al., 2007).

In a 2001 review article, Bauer, and Whybrow reviewed seven double blind placebo controlled studies of T3 augmentation of patients with unipolar or bipolar depression, dose range 20–67.5 mcg. T3 accelerated onset of improvement in five of the seven studies (Bauer and Whybrow, 2001). Four maintenance trials of T4 augmentation showed that > 50% of bipolar and unipolar patients were well maintained on T4 doses ranging from 50–60 mcg (Bauer and Whybrow, 2001). In an open-label HDT trial, 10 of 11 rapid
cycling bipolar patients with depression at the baseline and five of seven patients with mania at the baseline responded to high dose T4 that was added to their mood-stabilizing treatment regimens. The effect was lost when the dose was reduced below high dose levels (Bauer and Whybrow, 1990). Bauer et al. reviewed four studies of patients with bipolar disorder that used T4 for prophylaxis. In three of the reports that included a total of 27 patients, 19 were classified as responders, 6 were partial responders and 5 showed no response (Bauer et al., 2003). The doses ranged from 50 to 500 mcg. In the fourth study of 20 patients that used doses ranging from 200 to 600 mcg (average of 377 mcg), 52% were very much improved and 19% of patients were much improved. In a 2005 study that was primarily designed to study the effects of high dose T4 on brain function in women suffering from a bipolar disorder (nine bipolar I and one bipolar II), seven patients achieved remission and three showed a partial response (Bauer et al., 2005).

In the largest psychiatric study of HDT to date, 159 patients, (125 with bipolar I and 34 with bipolar NOS) were studied retrospectively. These patients were considered highly refractory and had failed to respond to an average of 14 prior medications. More than 84% of patients responded to T3, and one-third experienced remission. The average dose of T3 was 90 mcg, which was well tolerated by patients. Bone loss was not systematically assessed, however three cases of osteoporosis were identified, all in females (Kelly and Lieberman, 2009). While Chakrabarti (2011) in his review paper found this concern, this number represented only 3% of the females in the study were affected, which was far less than the expected 15% (Aoki et al., 2000).

No literature was found that discussed fall risks associated with HDT. No fall risk is mentioned in the package inserts of US commercially available thyroid preparations of liothyronine (T3) (Package-Insert) or levothyroxine (T4) (Package-Insert).

4. Discussion

Despite the multitude of papers, expert recommendations, and treatment algorithms recommending the use of HDT, some still consider its use outside of mainstream medicine. There appears to be no risk for osteoporosis from HDT in men and premenopausal women. This is reflected in the American Thyroid Association guidelines for the treatment of DTC, which does not warn of a risk of osteoporosis for either men or premenopausal women (Cooper et al., 2009). The majority of studies also show no risk of osteoporosis in postmenopausal women, but these findings are not as consistent as those reported for men and premenopausal women. If in fact postmenopausal women are at risk of osteoporosis with HDT treatment, the risk may be mitigated by ensuring adequate calcium intake (Tang et al., 2007; Kung and Yeung, 1996). Because 75% of psychiatric patients have low vitamin D levels (Rylander and Verhulst, 2013), ensuring adequate vitamin D levels may also be important.

4.1. Risk of osteoporosis with psychiatric medications

It is important to note that many of the commonly used treatments for the bipolar disorders do carry a risk of osteoporosis. The mood stabilizing medications carbamazepine and valproic acid (O’Connell et al., 2010) are both associated with osteoporosis. Serotonin reuptake inhibitors confer risk, while tricyclic antidepressants appear to be protective (Diem et al., 2007). Neuroleptic medications have been associated with a risk of osteoporosis (Vestergaard, 2008). Lithium is sometimes cited as being a risk for osteoporosis, but other papers report lithium use as neutral or protective to BMD (Zamani et al., 2009; Vestergaard, 2008). Many psychiatric medications carry other significant risks. There are reports of sudden death associated with neuroleptic use (Ray et al., 2001). Clozapine has been linked, in the first year of use, with seizures in 5% of patients and agranulocytosis, sometimes fatal, in 1.3% of patients. Psychotropic medications that are sedating and or disturb balance are associated with falls. Sedative/hypnotics increase fall risk by 47%; antipsychotics increase fall risk by 59%, and antidepressants increase fall risk by 68% (Woolcott et al., 2009). Failure to adequately treat bipolar disorders to euthymia carries other significant risks, both in terms of osteoporosis and other risks associated with the bipolar disorders. There is the tragedy of suicide, yet suicide is not the largest risk (Osby et al., 2001). An estimated 58% of individuals with a bipolar disorder have comorbid medical conditions (Magalhaes et al., 2012). They experience cardiovascular disease onset an average of 13 years earlier than those who did not have bipolar disorder. Arthritis, hypertension, gastritis, angina, tachycardia and other forms of heart disease, diseases of the stomach, atherosclerosis, myocardial infarction, and cirrhosis of the liver and other forms of liver disease are all more prevalent in people suffering bipolar disorder (Frye et al., 2011). Depression is often associated with repeated episodes of decreased physical activity, nutritional abnormalities and a risk for osteoporosis. Cigarette smoking and alcohol abuse are more common in patients suffering from a bipolar disorder and are associated with an increased risk of osteoporosis (Halbreich et al., 1995). Medications that increase weight can be particularly risky if diabetes, obstructive sleep apnea or other weight-related issues arise (Frye et al., 2011). Obstructive sleep apnea afflicts an estimated 47.5% of patients with bipolar disorder (Kelly et al., 2013). Treating bipolar disorder to euthymia is thought to mitigate the conditions and diseases discussed above (Frye et al., 2011).

Despite the direct evidence presented here, the risk for osteoporosis has historically been directly attributed to high levels of circulating thyroid hormone. Early studies of HDT included a mixture of DTC patients treated with HDT and hyperthyroid patents. Biomarkers indicating an increase in osteoblasts activity and decrease in osteoclasts activity are present in hyperthyroidism, and in DTC patients treated with HDT (Belaya et al., 2007). Still, the association between high circulating thyroid hormone levels and osteoporosis is only a correlation. Why does hyperthyroidism cause osteoporosis while HDT treatment does not? Grave’s disease which accounts for 80% of hyperthyroid cases, is an autoimmune disease caused by TSH receptor (TSHr) antibodies that mimic TSH. The TSHr antibodies stimulate TSH receptors causing the high circulating levels of thyroid hormone in the absence of TSH (Bahn et al., 2011). These TSHr antibodies are now accepted as the cause of exophthalmos (Wall and Lahooti, 2010) and Grave’s dermopathy (pretibial myxedema) (Topliss and Eastman, 2004). There is growing evidence that the osteoporosis associated with hyperthyroidism is mediated by TSHr antibodies (Schett and David, 2010). A major difference may be the presence of thyrotoxic symptoms present in hyperthyroidism. In psychiatry, thyrotoxic symptoms are considered a side effect and are minimized or entirely absent. The thyroid physiology of individuals who suffer from a bipolar disorder appears different than those who do not suffer a bipolar disorder. There is in fact support for this statement. Any disturbance of the hypothalamic–pituitary–thyroid (HPT) axis can worsen the course of bipolar disorders (Chakrabarti, 2011). Bipolar I patients respond better to non-thyroid treatments when thyroid levels are in the upper range of normal compared to patients in the lower normal ranges (Cole et al., 2002). Depression, concentration difficulties, psychomotor slowing, psychosis, anxiety, memory impairment, intellectual slowness, paranoia, visual hallucinations, auditory distortions, and delusions are recognized symptoms of both hypothyroidism...
and bipolar disorders. In the case of hypothyroidism, these symptoms are reversible with thyroid replacement alone (Petris et al., 2007). Normal thyroid laboratory values are based on large population studies, but normal thyroid levels for patients with a bipolar disorder have never been established. Evidence suggests that patients are closer to a normal physiologic state in the presence of elevated thyroid hormone levels, no thyrotoxic symptoms and the absence of bipolar symptoms, compared to the presence of bipolar symptoms and normal thyroid levels. Brain imaging studies of patients with bipolar disorder show abnormal function in prefrontal and limbic brain areas, specifically increased activity compared to controls in the left thalamus, right amygdala, right hippocampus, and right dorsal and ventral striatum including the nucleus accumbens and putamen. In one study, women who received HDT therapy showed a decrease in brain activity in the right subgenual cingulate cortex, left thalamus, right amygdala, right hippocampus, right ventral striatum, and cerebellar vermis. Following these changes, their imaging data were indistinguishable from those collected in controls (Bauer et al., 2005).

Multiple studies have remarked on how well patients tolerate HDT treatment (Bauer et al., 2005; Kelly and Lieberman, 2009; Bauer et al., 2002). Bauer et al. compared a 400 mcg dose of T4 given to depressed patients and normal controls. The depressed patients suffered from a bipolar disorder or major depression, while the controls had no psychiatric or thyroid related illnesses. Both groups had normal thyroid laboratory values. HDT was well-tolerated in affective patients, with none dropping out of the study. Conversely, HDT is not well-tolerated in non-affective disordered individuals, 38% of the control group dropped out due to thyrotoxic side effects (Bauer et al., 2002). Even in the setting of overt hyperthyroidism, the levels of T3 and T4 are only moderately correlated with thyrotoxic symptoms (Bahn et al., 2011). The terms high dose thyroid, supraphysiologic, augmentation, and TSH suppressive therapy are all problematic and overlap to a certain degree. Clinical experience indicates that HDT therapy does not necessarily lead to T3 or T4 levels outside the normal ranges and that augmentation doses occasionally result in low TSH and or high T3 or T4 levels. Until the underlying mechanism of action of thyroid hormone on affective disorders is identified, our current terms remain unsatisfactory. Given the great improvement seen with HDT in the bipolar disorders and the general lack of side effects the idea that HDT restores normal physiologic balance is intriguing and warrants further exploration.

5. Limitations

This review only considered the risk of osteoporosis and did not address other possible risks of HDT. Most of the studies examined involved high dose T4. The terms remission and response were defined differently in the various studies of bipolar disorders. Some of the psychiatric studies also included patients with major depression. The types of bipolar disorders studied also varied. No systematic evaluation of fall risks with psychiatric medications was examined. The nomenclature describing the use of HDT varied and is a potential source of confusion. Studies of the use of HDT to treat DTC employed different methodologies. Case control matching studies did not account for every factor, including but not limited to, alcohol intake, smoking, physical activity, calcium intake, vitamin D intake, race, and exposure to sunlight (for endogenous vitamin D production). Thyroid doses and the degree of TSH suppression varied between studies, as did the length of HDT treatment. Finally, the number of women studied was greater than the number of men.

6. Conclusion

The existing evidence indicates that high dose thyroid is not a risk factor for osteoporosis in men or premenopausal women. The majority of articles report little or no risk for postmenopausal women, but a minority of articles does indicate a risk. This risk, if present, may be mitigated or prevented by ensuring adequate calcium intake. HDT cannot, by the definition put forth by the American Thyroid Association and the American Association of Clinical Endocrinologists, be considered hyperthyroidism even if T3 or T4 are elevated and cannot even be considered thyrotoxic if no symptoms are present. The risk of osteoporosis is present with many commonly used psychiatric medications. HDT treatment does not appear to increase the risk of falling. So even if HDT poses a small risk of osteoporosis, it may still be preferable to use it in postmenopausal women when compared to other commonly used psychiatric medications that pose a significant fall risk or a greater risk of osteoporosis. Ultimately, the decision to employ HDT hinges on its comparison to the risks and benefits of other medications or the risk of failing to treat patients to euthymia. A risk benefit analysis must be individualized for each patient. As psychiatrists, we cannot delegate the decision to prescribe high-dose thyroid to treat bipolar disorders to other specialists. Endocrinologists and other non-psychiatric specialists lack the requisite knowledge regarding the morbidity and mortality of bipolar disorders and the risk of alternative medications to make an adequate risk benefit assessment.

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Conflict of interest

The author has no conflicts of interest.

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