

## NO CHANGE OF THYROID HORMONES FOLLOWING INHALATION THERAPY WITH ALKALINE SALINE-SULFATE SPA WATER

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### Abstract

The benefits of spa therapy on different medical diseases are known since ancient times, as well its positive effects on some psychiatric symptoms. In the last decades different studies have been carried out in order to elucidate some of the possible biological mechanisms underlying spa treatment effectiveness, which include thermal, mechanical, immunomodulatory and chemical effects. It is still an open question whether or not spa waters may or not modify thyroid functions. Therefore, the aim of this study was to explore the possible influence of alkaline saline-sulfate spa waters on thyroid functions, as assessed by the FT3, FT4 and TSH levels, in a group of 12 healthy women. All subjects were recruited amongst administrative and nursing staff at the Montecatini spa (Italy), on the basis of absence of hormonal dysfunctions, medical illness and psychiatric disorders. The thyroid hormones were measured by common chemiluminescent immunoassays before (t0) and 24 hours after (t1) inhalation therapy with alkaline saline-sulfate spa waters (Leopoldina water of Montecatini Terme Spa, Italy).

The results, while showing a stability of thyroid hormone levels at t0 and t1, suggest that treatment with alkaline saline-sulfate spa waters may be safely used in patients with different thyroid disturbances.

**Key words:** spa therapy, thyroid, alkaline saline-sulfate spa waters, inhalation therapy, healthy women

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### Introduction

The use of water for medical treatment is probably as old as mankind. Since the Roman age, spa or thermal therapy has been used as a non-conventional medical treatment first in Europe and Middle-East countries rich in mineral waters and then in USA. Balneotherapy involves the immersion of the subject in mineral baths or pools and shows beneficial properties in different disorders with no risk or side-effects, particularly, in pain relief and change of the intraarticular temperature in rheumatologic disorders, such as fibromyalgia, rheumatoid arthritis and osteoarthritis. Thermal therapy has also been employed in the treatment of psoriasis and atopic dermatitis with high rates of response (Matz et al. 2003), and in chronic obstructive pulmonary

diseases, for its vasodilating effects on vessels of bronchial mucosa which can improve its trophic state and increase the number of secretory IgA and the mucociliary activity (Petraccia et al. 2005). Interestingly, thermal treatment seems to improve heart-failure-related symptoms and quality of life in patients with mild chronic heart failure by enhancing cardiac and endothelial functions (Michalsen et al. 2003). Furthermore, in subjects with the so-called lifestyle-related diseases, such as hypertension, hyperlipidemia, diabetes mellitus, obesity, and smoking, where the vascular endothelial function is impaired, thermal therapy seem to be promising (Biro et al. 2003). However, the mechanisms by which this broad range of diseases are improved have not been fully clarified, although they probably include thermal, mechanical,

immunomodulatory and chemical effects. Similarly, no comprehensive explanation is given for the subjective effects of spa therapy which include relaxation, a sense of well-being and a decrease of stress sensations, which have been related to changes of different hormones, cortisol or endogenous opiates (Laatikainen et al. 1988, Pizzoferrato et al. 2000, Toda et al. 2005, Marazziti et al. 2007).

The thyroid is the regulator of metabolism and energy. It is intimately intertwined with all the other hormone systems of the body. The thyroid gland produces the hormones L-thyroxine (T4) and L-triiodothyronine (T3), which regulate metabolic body processes, cellular respiration, total energy expenditure, growth and maturation of tissues, and turnover of hormones, substrates, and vitamins (Wartofsky 1994, Dumont et al. 2002, 2011). Iodine is a critical component of thyroid hormones and composes 65% of T4 weight and 58% of T3 weight. T3 is the active hormone (3 times the metabolic potency of T4), and T4 is the prohormone. Release of the hormones into the bloodstream involves the negative feedback system of the hypothalamic-pituitary-thyroid axis. (Wartofsky 1994). A low metabolic rate or a decrease in serum T3 and/or T4 levels signals the hypothalamus to secrete thyrotropin releasing hormone (TRH), which travels to the anterior pituitary gland and stimulates secretion of thyroid-stimulating hormone (TSH). An elevated T3 serum level inhibits release of TRH and TSH (Rousset and Dunn 2004). TSH, in turn, stimulates the thyroid gland to manufacture and release stored T3 and T4 until the metabolic rate is normalized (Wartofsky 1994). The most common thyroid dysfunctions involve abnormal production of thyroid hormones. Too much thyroid hormone results in a condition known as hyperthyroidism, insufficient hormone production leads to hypothyroidism. Hyperthyroidism condition can occur in several ways such as the production of too much thyroid hormone (i. e. Graves' disease), hyperfunctioning thyroid nodules (toxic adenoma or toxic multinodular goiter) and subacute thyroiditis. Hypothyroidism, by contrast, stems from an underproduction of thyroid hormones. Although the too little iodine in the diet is the most common cause of hypothyroidism, exposure to excessive amounts of iodide may cause hypothyroidism in vulnerable subjects (Leung and Braverman 2014). In areas of the world with sufficient dietary iodine, hypothyroidism is most commonly caused by Hashimoto's thyroiditis, an autoimmune disease in which the thyroid gland is attacked by a variety of cell- and antibody-mediated immune processes.

What is unique about the thyroid is its vulnerability to environmental toxins, pollutants and chemicals, all of which the thyroid quickly absorbs, disturbing its ability to regulate metabolism.

It is still an open question whether or not spa waters may or not modify thyroid functions.

Therefore, the aim of this study was to explore the possible influence of alkaline saline-sulfate spa waters (Leopoldina water of Montecatini Terme Spa, Italy) on thyroid functions, as assessed by the FT3, FT4 and TSH levels, in a group of healthy women.

## Methods

### Subjects

Twelve healthy drug-free women between 27 and

54 years of age (mean  $\pm$  SD: 44.5  $\pm$  7.6), recruited amongst administrative and nursing staff at the Montecatini Terme spa (Italy), were included in the study. They had no family nor personal history of any major psychiatric disorder, as assessed by a psychiatric interview, carried out by a senior psychiatrist.

All subjects were free of any physical illness, in particular no thyroid dysfunction, as documented by a general check-up. All were psychotropic drug-free, none were heavy smokers and none belonged to HIV-risk groups. All subjects gave their informed written consent to participating in the study which was approved by the Ethics Committee of Pisa University.

### Inhalation Therapy

All individuals were subjected to direct vapor-jet inhalation and aerosol therapy treatment with alkaline saline-sulfate spa water (Leopoldina water of Montecatini Terme Spa, Italy), which contains the following components: sodium (5680 mg/L), potassium (138 mg/L), magnesium (104 mg/L), calcium (543 mg/L), chlorides (9110 mg/L), sulfates (1205 mg/L), bicarbonates (543 mg/L), iodine (0.5 mg/L), Br (0.80 mg/L); pH = 6.4, solid residue = 17770 mg/L.

The ionic components of alkaline saline-sulfate spa water exert several specific effects. In particular, NaCl acts as antiseptic and antimycotic, iodine increases metabolic and cellular activity, Br and Ca shows analgesic and sedative effects on mucosae, and sulfates increase activity of secretory IgA. Direct vapor-jet inhalation therapy is an effective treatment for diseases of the upper respiratory tract (chronic pharyngitis and laryngitis). The largest particles of the inhalation (100 microns) exert a mechanical detergent action on the respiratory mucosa. Aerosol (particles under 2 microns in diameter) delivers the active components of the water to the lower respiratory tract, as far as the alveoli, and is therefore indicated in chronic bronchitis and chronic obstructive pulmonary disease (COPD). Generally speaking, inhalation treatments stimulate the immune defense mechanisms (secretory IgA), and are particularly indicated in the treatment of childhood diseases (G.O.S.T. 1990, Galassi 2009).

This session was followed by a rest period in a relaxing room at a temperature of 20° C.

### Thyroid hormone measurements

Venous blood (12 ml) was collected from all subjects 10 minutes before (t0) and after 24 hours (t1) from the inhalation therapy.

Plasma thyroid hormones FT3 FT4 were analyzed using competitive chemiluminescent immunoassays; thyroid-stimulating hormone (TSH) levels were analyzed by the ultra-sensitive sandwich chemiluminescent immunoassay method. The normal values of thyroid hormones ranged between 2.7 and 5.7 pg/mL for FT3, between 0.7 and 1.7 ng/dL for FT4, and between 0.4 to 3.4 mIU/L for TSH.

### Data Analysis

The differences between the thyroid parameters at the two assessment times were assessed by paired Student t-test. All analyses were carried out by the SPSS, version 12.1 (Nie et al. 1998).

## Results

All subjects had normal-range plasma levels of thyroid hormones (FT3, FT4, and TSH) both at baseline (t0) and after the inhalation therapy (t1). FT3 values (mean  $\pm$  SD) were  $3.74 \pm 0.27$  and  $3.74 \pm 0.34$  pg/mL at t0 and t1, respectively. FT4 values (mean  $\pm$  SD) were  $1.11 \pm 0.12$  and  $1.09 \pm 0.14$  ng/dL, at t0 and t1, respectively. TSH values (mean  $\pm$  SD) were  $0.88 \pm 0.32$  and  $0.89 \pm 0.34$  mIU/L at t0 and t1, respectively (table 1).

No significant differences were observed between FT3, FT4 and TSH levels at t0 and t1.

jet and aerosol inhalation therapy with alkaline saline-sulfate spa waters (Leopoldina water of Montecatini Spa, Italy), which is commonly used in the treatment of pulmonary diseases (Tanizaki et al. 1993), does not provoke any change of thyroid hormones, can be considered safe in patients with concomitant thyroid disorders and also in psychiatric patients.

The main limitations of our study were that the sample size was small and composed exclusively by healthy women belonging to the same setting and with similar life style. Therefore, future study should be replicated in large samples of individuals of both sexes and in patients with different thyroid disorders.

**Table 1.** FT3, FT4, and TSH plasma levels (mean  $\pm$  SD) at baseline (t0) and after the inhalation therapy (t1)

	t0	t1
FT3 (pg/mL)	$3.74 \pm 0.27$	$3.74 \pm 0.34$
FT4 (ng/dL)	$1.11 \pm 0.12$	$1.09 \pm 0.14$
TSH (mIU/L)	$0.88 \pm 0.32$	$0.89 \pm 0.34$

t-test: not significant

## Discussion

The results of the present study showed that direct vapor-jet inhalation and aerosol therapy with alkaline saline-sulfate spa waters (Leopoldina water of Montecatini Spa, Italy) does not modify the main thyroid hormones (T3, T4, and TSH) in a group of healthy women. The thyroid gland is a key element and a main regulator of body metabolism and energy, through a direct effect on target organs, as well as through its interactions with other hormone systems (Wartofsky 1994, Dumont et al. 2002). Not surprisingly, thyroid is fundamental even for the functioning of the brain and thyroid dysfunctions may be accompanied by psychiatric symptoms and disorders (Bunovicus et al. 2010, 2014). People with an overactive thyroid may exhibit marked anxiety and tension, emotional lability, impatience and irritability, distractible overactivity, exaggerated sensitivity to noise, and fluctuating depression with sadness and problems with sleep and the appetite. In extreme cases, they may appear psychotic losing touch with reality and showing delusions and hallucinations. An hypoactive thyroid can lead to progressive loss of interest and initiative, slowing of mental processes, poor memory for recent events, fading of the personality's colour and vivacity, general intellectual deterioration, depression with a paranoid flavour, and eventually, if not checked, to dementia and permanent harmful effects on the brain (Placidi et al. 1998, Fountoulakis et al. 2006). Detection of the thyroid problem is complicated by the fact that everyone feels anxiety and tension to some degree, that many thyroid symptoms are similar to those of other diseases, and that hypothyroidism in particular often develops insidiously over a considerable time. For these reasons, thyroid hormones have been used and/or proposed for the treatment of depression and other psychiatric conditions. Some drugs, in particular lithium, used for the treatment of bipolar disorders can produce hypothyroidism in long-term use.

Our findings, while showing that the direct vapor-

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