



## Original research

# The effect of preoperative Lugol's iodine on intraoperative bleeding in patients with hyperthyroidism



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## HIGHLIGHTS

- Preoperative Lugol solution treatment decreased the rate of blood flow, and intraoperative blood loss during thyroidectomy.
- Preoperative Lugol solution treatment was found to be a significant independent determinant of intraoperative blood loss.
- The reduction of intraoperative bleeding allows better visualization and preservation of the surrounding nerves, vasculature, and parathyroid glands.

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## ABSTRACT

**Aim:** To investigate the effect of preoperative Lugol's iodine on intraoperative bleeding in patients with hyperthyroidism.

**Material and methods:** This controlled, randomized, prospective cohort was carried out on 40 patients who admitted for surgery due to hyperthyroidism. Cases were randomly assigned to receive either preoperative treatment with Lugol solution (**Group 1**) or no preoperative treatment with Lugol solution (**Group 2**). **Group 3** (n = 10) consisted of healthy adults with no known history and signs of hyperthyroidism. Blood flow through the thyroid arteries of patients was measured by color flow Doppler ultrasonography. Free T3, free T4, TSH, thyroid volume and the resistance index of the four main thyroid arteries were measured in all patients.

**Results:** There was not a significant difference between gender, preoperative serum thyroid hormone levels, or thyroid gland volumes between groups 1 and 2. The mean blood flow of the patients in Group 1 was significantly lower than values in Group 2. When age, gender, thyroid hormone, TSH, thyroid volume, blood flow, and Lugol solution treatment were included as independent variables, Lugol solution treatment (OR, 7.40; 95% CI, 1.02–58.46; p = 0.001) was found to be the only significant independent determinant of intraoperative blood loss. Lugol solution treatment resulted in a 7.40-fold decrease in the rate of intraoperative blood loss.

**Conclusion:** Preoperative Lugol solution treatment was found to be a significant independent determinant of intraoperative blood loss. Moreover, preoperative Lugol solution treatment decreased the rate of blood flow, and intraoperative blood loss during thyroidectomy.

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## 1. Introduction

Hyperthyroidism is related with hemodynamic variations, including increased heart rate and cardiac contractility, and decreased peripheral resistance due to serum thyroid hormone excess [1]. Preoperative preparation of the patient is crucial to avoid

intraoperative or postoperative complications and to decrease the vascularity of the gland [2]. The incidence of complications is low in experienced hands; however, a small amount of intraoperative bleeding can reduce the visualization and preservation of the surrounding nerves, vasculature, and parathyroid glands.

Color Doppler examination has become an established imaging technique for assessing thyroid gland vascularity. Several studies revealed that thyroid vascularity has been increased in patients with hyperthyroidism [3]. Hodgson et al. reported that thyroid arterial blood flow correlated remarkably with the levels of free T3, whereas Bogazzi et al. did not find a correlation between Doppler

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findings and serum thyroid hormone levels [4,5].

Lugol solution (inorganic iodide) has been given preoperatively to patients to limit intraoperative bleeding and related complications resulting from thyroid gland vascularization [6]. It is commonly used in the preparation of patients for thyroidectomy [7]. This effect transiently blocks thyroid hormone generation, with thyroid hormone synthesis recovering in a few days or weeks. Although the practice has widespread use, there is still no agreement on its effectiveness. The main reason for this lack of consensus stems from the variety of treatment protocols in terms of drug dosage and concurrent management of antithyroid therapy [8]. Most studies related to the effects of Lugol solution are based on indirect evaluations, such as the impression of the surgeon [9].

The aim of the present study was to investigate the effect of preoperative Lugol's iodine on intraoperative bleeding in patients with hyperthyroidism.

## 2. Materials & methods

### 2.1. Study design

This randomized, controlled, prospective cohort has been performed in accordance with the principles of the Helsinki Declaration and approved by the local Institutional Review Board. Written informed consent was obtained from all subjects.

Initially, a total of 48 patients have admitted to the *Department of General Surgery* of our tertiary care center for surgery with the diagnosis of hyperthyroidism. Six patients did not meet the inclusion criteria whereas two patients declined to participate in the current study. Forty patients (Graves' disease or multinodular goiter) were considered as eligible for the study. A parallel trial design was applied and allocation ratio for Groups 1, 2 and 3 were 2:2:1.

All patients were treated with antithyroid drugs until they were euthyroid. Subsequent to randomisation, the patients received either Lugol's iodine, 0.8 mg/kg for 10 days (**Group 1**,  $n = 20$ ), or did not receive Lugol's iodine (**Group 2**,  $n = 20$ ). The patients in Group 1 immediately underwent surgery after treatment with Lugol's iodine for 10 days. Antithyroid drugs were continued throughout the study. **Group 3** ( $n = 10$ ) consisted of healthy adults with no known history and signs of hyperthyroidism.

Exclusion criteria consisted of a solitary toxic nodule, fine-needle aspiration biopsy result indicating cancer or suspicious cytology, anticoagulant usage, a previous thyroid operation, pregnancy and refusal to participate in this study. Follow-up and management of patients was made in collaboration with radiology and endocrinology departments of our institution.

### 2.2. Surgical procedure

In all patients, indirect laryngoscopic examination was used to evaluate vocal cord motility before and after surgery. Total thyroidectomies were performed by the same surgeon in all patients. The duration of surgery, the volume of blood loss measured as the amount of blood in the suction bottle were recorded for each patient.

Persistent nerve palsy was defined as persistent dysfunction and clinical dysphonia that lasted for 6 months postoperatively. Hypocalcemia was defined as a serum calcium level less than 8 mg/dl after the operation. Persistent hypoparathyroidism was defined as serum PTH levels less than 10 pg/ml in patients that need treatment for longer than 3 months to achieve and maintain normocalcemia.

#### 2.2.1. Primary and secondary outcome measures

Thyroid volume, thyroid glandular blood flow features and

thyroid hormone levels were the main parameters investigated in this trial.

### 2.3. Doppler ultrasonography

Color flow Doppler ultrasonography using a high frequency wideband linear transducer (frequency range, 7.3–11.4 MHz) was performed before treatment of Group 1 patients with Lugol solution. Vascular studies were implemented routinely 24 h before surgery. Ten healthy medical staff volunteers were included as healthy controls (**Group 3**). The same investigator who was unaware of the laboratory values at the time of the examination performed each color Doppler examination blindly.

Thyroid volume was measured by ultrasound and calculated using the ellipsoid model (width x length x thickness x 0.5233 for each lobe) [10]. The superior and inferior thyroid arteries on each side of the neck were initially identified, followed by peak systolic and diastolic velocities, vessel diameter, and the flow volumes were calculated using measurement tools installed within the Doppler unit. The study evaluated the resistance index (RI) of the four main thyroid arteries, sampled near their entrance into the gland. The RI was evaluated according to the following formula: (peak systolic velocity/end diastolic velocity)/peak systolic velocity [11,12]. A mean thyroid RI and blood flow rate were calculated from 12 measurements, with four for each artery.

### 2.4. Biochemical analysis

Normal ranges of the parameters under investigation were as follows: free T3 (FT3), 2.3–4.2 pg/mL; free T4 (FT4), 0.74–1.52 ng/dL; TSH, 0.35–5.50 uIU/liter.

No changes have been made to trial outcomes after the trial commenced. The sample size was determined on the basis of inclusion of all volunteer patients diagnosed in the study period. Random allocation sequence was provided using a computer program. Any restriction such as blocking was not performed. Determination of the random allocation sequence, enrolment of participants and assignment of participants for interventions were made by the primary investigator (YY). Care providers and participants were blinded to interventions.

### 2.5. Statistical analysis

Data were analyzed using the IBM Statistical Package for Social Sciences v21 (SPSS Inc., Chicago, IL, USA). A normal distribution of the quantitative data was checked using Kolmogorov-Smirnov test. Parametric tests (Students *t* and chi-square tests) were applied to data of normal distribution and non-parametric tests (Mann-Whitney *U* test) were applied to data of questionably normal distribution. Logistic regression was performed to find the risk factors (age gender, FT4, TSH, lugol's solution use, thyroid volume, blood flow) for intraoperative bleeding. Correlations between continuous variables were determined nonparametrically using Spearman's rho. Continuous data were presented as mean  $\pm$  standard deviation. All differences associated with a chance probability of 0.05 or less were considered statistically significant.

## 3. Results

**Fig. 1** demonstrates the flow chart of the present study and the current study was performed. Baseline descriptive, clinical and radiological characteristics of study groups are presented in **Table 1**. The mean age of the whole study group was  $43.97 \pm 9.25$  (range, 25–63) years. The female/male ratio was 31:9. The mean serum FT3, FT4, and TSH levels were  $2.89 \pm 0.62$  pg/mL,  $1.04 \pm 0.37$  ng/dL,

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