Do we really Need Lugol Solution in the Era of Energy Devices for the Preoperative Management of Patients with Graves’ Disease?

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**ABSTRACT**

**Introduction:** Inorganic iodide (Lugol solution) has been used for the preoperative management of patients with Graves’ disease for many years. However, some new instruments have come into the surgeons reach that can accomplish bloodless operative field without the need of preoperative treatment. The purpose of this prospective study was to evaluate the efficacy and safety in the application of two types of energy devices – SonoSurg® and Thunderbeat® in patients with and without preoperative preparation with Lugol solution.

**Material and Methods:** The study included 100 patients with Graves’ disease operated between January 2017 and December 2017. Patients were divided into four groups - 50 patients operated using SonoSurg® - 25 patients with preoperative preparation with Lugol solution and 25 without preoperative PI preparation, and 50 patients operated using Thunderbeat® - 25 patients with and 25 without preoperative Lugol preparation. We evaluated and compared the outcome between the four groups.

**Results:** The four groups had a similar distribution in the demographic features such as gender, age, and functional activity. When comparing the results, we found very similar results in the groups with preoperative preparation with PI solution. In contrast, we found significant differences in the duration of surgery, intraoperative and postoperative complications between the groups without preoperative PI preparation. Hospital stay of patients in four groups was similar - an average of 2 days stay into the clinic.

**Conclusion:** Our results showed that Lugol solution preparation has its place in the era of energy devices. Thunderbeat® can accomplish reliable hemostasis without preoperative Lugol preparation however we can achieve the same result with SonoSurg® and preoperative preparation at a much lower cost.

**Keywords:** Graves’ disease, Thunderbeat, Sonosurg, Lugol solution

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**INTRODUCTION**

The striking clinical entity of exophthalmic goiter, with its distinctive protruding eyes, tachycardia, nervousness and enlarged thyroid has been known for more than 150 years. The condition was first described in 1786 by Parry, but was not reported until after his death in 1825. The condition was also noted by other authors – von Basedow in 1840 [1] and Robert Graves in 1835 [2]. To this day, in Europe this entity is known as Basedow’s disease but in the English speaking world it is named for Robert James Graves. This disease remained clouded in mystery and despair for surgeons for another century when a ray of hope appeared. His name was Dr. Henry Plummer [3]. In 1923 he presented his results that administration of iodine preoperatively and postoperatively would prevent the crises that cause death in patients with thyrotoxicosis. One must have in mind the death rate in goiter surgery was so high that a surgeon – Samuel Gross stated – “Every stroke of a knife will be followed by a torrent of blood, and lucky will it be for him if his victim lives long enough to enable him to finish his horrid butchery.” [3] Plummer’s finding turned the deadliest operation into one of the safest in the hands of a well-

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trained surgeon. The importance of his discovery can be understand even nowadays reading the ATA recommendation guidelines for management of thyrotoxicosis [4]. Its recommendation 22 and 23 prompts the routine admission of Potassium Iodide Solution (PI) before total thyroidectomy for Graves Disease but its avoidance in toxic multinodular goiter (recommendation 39). In the last decade there has been an introduction of new class of instruments, generally better known as energy devices [5]. These instruments tend to greatly diminish blood loss and intraoperative time without any significant increase in the complications rate when making total thyroidectomy [6,7]. This fact raises the question do we need PI preoperatively [8]?

The purpose of this prospective study was to evaluate the efficacy and safety in the application of two types of energy devices – SonoSurg® and Thunderbeat® in patients with and without preoperative preparation with Lugol solution.

MATERIALS AND METHODS

This study was conducted in the Department of endocrine surgery, CCEG, Medical University – Sofia, USBALE “Acad. Iv. Penchev” Hospital. A total of 100 patients with Graves' disease operated between January 2015 and December 2015 were included. The indications for surgery in these patients were Graves’ ophthalmopathy, patient refusal for radioactive iodine, large goitre with pressure symptoms, planning for pregnancy, young age, and intolerance to anti-thyroid drugs. In order to obtain homogenous groups, patients were randomized in equal proportions with respect to age and the size of the thyroid gland. Patients treated with corticosteroids, NSAIDs, with pathological coagulation disorders, pregnancy or recurrent thyroid disease were not included in this study. All patients were operated by the same team and the operation was total thyroidectomy. Patients were divided into four groups: 50 patients operated using SonoSurg® (Olympus) - 25 patients with preoperative preparation with Lugol solution and 25 without preoperative Lugol preparation, and 50 patients operated using Thunderbeat® (Olympus) - 25 patients with and 25 without preoperative Lugol preparation. When comparing the four groups we used the following parameters: duration of surgery, postoperative pain, hospital stay, presence of postoperative complications (hypoparathyroidism and damage to the recurrent nerve). Every patient was evaluated preoperatively with thyroid function tests – free thyroxine (FT3 and FT4) and thyroid stimulating hormone (TSH), antithyroglobulin (TAT) and antimicrosomal antibodies (MAT), ultrasonography to define the extent of the disease (thyroid volume and presence of solitary nodes), laryngoscopic examination of the vocal cords and the serum calcium concentration test. Before being scheduled for surgery every patient was rendered in euthyroid state with thyreostatic drugs (Methimazole, Propylthiouracil) and the patient were at the minimal thyreostatic dosage (1 tablet per day). The patient with preoperative preparation discontinued their thyrostatic drugs and began their Lugol solution treatment 12 days prior to surgery. During the first 5 days they received 5 drops of Lugol solution three times a day orally. Between the 5 and the 10 day they received 10 drops of Lugol solution three times a day orally and for the days before the operation they received 15 drops three times a day. Those without preoperative preparation continued the thyrostatic drugs treatment until the operation. During surgery we used two different types of energy device. The first one SonoSurg® (Olympus) is a harmonic scalpel with autoclavable reusable instruments and the second one Thunderbeat® (Olympus) a new integrated bipolar and ultrasonic energy device with single use instruments (Figure 1).
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Table 1. Distribution of patients by demographic characteristics

|                      | SST Group with Lugol Preparation | SST Group without Lugol Preparation | TT Group with Lugol Preparation | TT Group without Lugol Preparation | p    |
|----------------------|----------------------------------|-------------------------------------|----------------------------------|-------------------------------------|------|
| Number of patients   | 25                               | 25                                  | 25                               | 25                                  | NS   |
| Age (mean ± SD)(years) | 40 ± 9                           | 42 ± 8                              | 44 ± 6                           | 40 ± 10                             | NS   |
| Gender               |                                  |                                     |                                  |                                     |      |
| Male (n)             | 3                                | 3                                   | 4                                | 3                                   | NS   |
| Female (n)           | 22                               | 23                                  | 21                               | 22                                  |      |
| Duration of thyrostatic drugs treatment (mean ± SD)(months)    | 24 ± 9                           | 22 ± 10                             | 20 ± 9                           | 25 ± 7                              | NS   |
| Thyroid carcinoma (number of patients)                        | 1                               | 0                                   | 0                                | 1                                   | NS   |

SST Group - SonoSurg® Thyroidectomy Group; TT group - Thunderbeat® Thyroidectomy Group
NS – not significant

used at a min 3 mm distance from the RLN to avoid the risk of thermal injury [9]. We used standard surgical technique for the treatment of the patients. Surgical incision was performed over the isthmus of the thyroid gland and was a size 2.5 - 4 cm. The thyroid gland was reached through the midline. Consequent mobilization of the right and left lobe of the thyroid gland was achieved by ligating the vessels of the thyroid gland. Every ligation was performed with Thunderbeat® or SonoSurg®. During the mobilization we identified four parathyroid glands and the two n laryngeus recurrences. Upon completion of thyroidectomy we stitched anatomical structures layer by layer. The skin was closed using continuous intradermal suture with 4-0 or 5-0 polyglactin. If there were no risk factors for bleeding the wounds were closed without suction drains. After surgery all patients were asked whether they detect a voice change for 24 and 48 h after surgery. If so, they were directed to the ENT specialist to conduct indirect laryngoscopy. Thus we detected the presence of recurrent nerve damage. To assess the degree of pain in the postoperative period, we used a visual analog scale – we explained to the patient that the value of 0 is equivalent to no pain, at a level 5 pain is moderate and the maximum value of 10 means that the pain is unbearable. Postoperative serum calcium levels were estimated twice (24 h and 48 h after surgery). Calcium supplementation was given if serum calcium levels dropped below 2.0 mmol/l. If the patient could be weaned from the calcium supplement within six months, hypoparathyroidism was considered transient. If there was laryngoscopic evidence of RLN recovery within six months of operation the RLN palsy was defined as transient. Oral thyroxin supplementation was started from the second day after the operation at a dose of 75-150 micrograms per day, according to body weight. Follow up was planned after a month, after three months, and after six months of discharge. The data analysis and interpretation was performed on SPSS 20.0 software package (SPSS Inc., Chicago, IL). The difference between groups was analyzed with chi square test and p < 0.05 was considered significant.

RESULTS

The study population that formed the four groups had a similar distribution in the demographic features such as gender, age and duration of thyrostatic drugs treatment. Overall, 2 patients had thyroid carcinoma: one patient of the SonoSurg Thyroidectomy Group (SST Group) with Lugol Preparation and one patients of the Thunderbeat Thyroidectomy Group (TT Group) without Lugol Preparation. The average duration of thyrostatic drugs treatment was above 20 months in all groups (Table 1).

When comparing the results, we found a reduction in the duration of surgery in patients with preoperative preparation with Lugol solution operated with SonoSurg® (SST group) (41 ± 4.8 vs 69 ± 7.9, p = 0.03). In contrast there was no statistical difference in the two groups of patients operated with Thunderbeat® (p=0.121) (Table 2).

When we analyzed the postoperative complications in the four groups we found similar results (Table 2). Statistically significant differences in transient hypoparathyroidism and transient RLN injury was found only between the two groups operated with SonoSurg® - transient hypoparathyroidism in one patient in the group with Lugol preparation and 6 patients in the group without, p= 0.042; Transient damage to the RLN in 2 patients with preparation and 8 patients in the group without, p= 0.034. We did not find statistical differences between the patients operated with Thunderbeat™. There was one patient with permanent RLN injury and one with permanent hypoparathyroidism in the group operated with Thunderbeat™ without preoperative preparation but it was with no statistical significance.

Two patients in the SST group without preoperative preparation were revised due to post-operative bleeding. In four patients in the same group we detected postoperative hematoma that did not require revision (Table 2). For the postoperative pain score we detected very similar results in the four groups.

Hospital stay of patients in four groups was similar - an average of 3 days in the SST groups and 2 days in the TT Groups.
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Table 2. Comparative table of operative and postoperative results

|                      | SST Group with Lugol Preparation | without Lugol Preparation | P Value | TT Group with Lugol Preparation | without Lugol Preparation | P value |
|----------------------|----------------------------------|---------------------------|---------|---------------------------------|---------------------------|---------|
| Operative time, minute (mean ± SD) | 41 ± 4.8                          | 69 ± 7.9                   | 0.03    | 33 ± 5                          | 35 ± 10                   | 0.121   |
| Postoperative pain   | Weak to moderate (3-4)            | Moderate (4-5)            | NS      | Weak to moderate (3-4)          | Weak to moderate (3-4)   | NS      |
| Hypoparathyroidism   | Transient, n (%)                 | 1                          | 6       | 0.042                           | 3                        | 6       | 0.269   |
| m                    | Permanent, n (%)                 | 0                          | 0       | 0.312                           | 0                        | 1       | 0.713   |
| Damage to the laryngeal nerve | Transient, n (%)                 | 2                          | 8       | 0.034                           | 4                        | 5       | 0.312   |
| m                    | Permanent, n (%)                 | 0                          | 0       | 0.149                           | 0                        | 0       | -       |
| Postoperative bleeding (reoperation), n (%) | 0                          | 2                          | 0.037   | 4                               | 0                        | 0       | -       |
| Hospital stay, days (mean ± SD) | 2.9 ±1                           | 3 ± 1                      | 0.521   | 2.1 ±0.4                       | 1.9 ± 0.3                | 0.910   |

SST Group - SonoSurg® Thyroidectomy Group; TT group - Thunderbeat® Thyroidectomy Group
NS – not significant

DISCUSSION

Graves’ disease is the most common reason for hyperthyroidism [10]. It is associated with hemodynamic changes – decreased peripheral resistance, increased heart rate and cardiac contractility [11]. On the other hand, the massive stimulation of the thyroid gland leads to its enlargement and the increase of its blood supply. These facts necessitate the need for a preoperative preparation to avoid intraoperative or postoperative thyroid storms and to decrease the vascularity of the gland [12]. Lugol solution (Inorganic iodide) is known to decreases the synthesis of thyroid hormone and their release from the thyroid in the short term (Wolff–Chaikoff effect) [13]. However one must have in mind the major flaw of this preoperative preparation - the Wolff-Chaikoff effect lasts 10–14 days and the escape phenomenon is possible [14]. It has been proven that it also decreases the rate of blood flow, thyroid vascularity, and thus intraoperative blood loss during thyroidectomy [15]. In the past these effects were proved subjectively - on the impressions of the surgeons, but nowadays they are supported by a large number of studies using Doppler techniques [16,17].

From a surgical point of view, the thyroid is distinguished from other parenchymal organs by the strong vascularity and the extremely sensitive location. These two characteristics indicate the importance of perfect hemostasis with minimal damage to surrounding tissues. Failure to achieve this goal can lead to severe complications: postoperative hemorrhage, asphyxia, vocal cord paralysis, hypoparathyroidism, death. For this reasons we have witnessed the emergence of a new class of instruments to achieve hemostasis - energy devices. SonoSurg® is an ultrasonic scalpel which provides hemostasis by applying mechanical energy for both cutting and coagulation. The low temperature is a factor that ensures minimal lateral thermal spread [18]. In our study we found better short time result in the group with preoperative preparation. The explanation for this might be the diminished blood supply after preoperative preparation [13]. However, we found no patients with permanent complications in the two groups. In a study consisting of a large number of patients it would be possible to have different results. The other energy device, Thunderbeat® is a combination of bipolar and ultrasonic energy device. This combination is theory provides better outcome in terms of hemostasis [19,20]. Our study showed no statistically significant difference in the frequency of postoperative complications between the two groups operated using Thunderbeat. However, in the TT group without preoperative preparation there was one patient with permanent hypoparathyroidism and one with permanent RLN palsy. These two patients cannot be of statistical significance but we must have in mind that, as with any kind of electrosurgery Thunderbeat has a hot tip which bears the risk of potentially fatal thermal injuries. We must have in mind that during an operation there cannot be any certainty about the duration of the Thunderbeats use. Experimental studies have shown that the use of Thunderbeat for more than 8 s near the RLN might cause its thermal injury [9]. This concerns have been also expressed by other authors [9,19].

The main criticism of the energy devices is their price [21]. This criticism is fully justified in cases where disposable instruments are used. Unlike other ultrasonic scalpels on the market “SonoSurg” uses autoclavable reusable instruments. So the cost of use is drastically reduced. When we compared the result of the groups with preoperative preparation operated with the different energy devices we found similar results with no statistical significance.

CONCLUSION

Our results showed that Lugol solution preparation has its place in the era of energy devices. Thunderbeat® might accomplish reliable hemostasis without preoperative Lugol preparation however we can achieve the same result with SonoSurg® and preoperative preparation at a much lower cost.

Declaration of interest: The authors report no conflicts of interest.

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Compliance with Ethical Standards: Although SonoSurg® and Thunderbeat® are registered for thyroid operations in Bulgaria and there is no legal need for ethics committee approval all patients included in this study completed informed consent.

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