



# RAPID GOAL DIRECTED PRE-OPERATIVE PREPARATION OF MEDICALLY REFRACTORY UNCONTROLLED GRAVES' DISEASE PATIENTS FOR SURGERY

CASE SERIES AND SYSTEMATIC REVIEW OF THE LITERATURE Dr. Shelley Stokes, Dr. Ian Kuo, A/Prof. Senarath Edirimanne. Nepean Hospital Clinical School of the University of Sydney Contact: Shelley.Stokes@health.nsw.gov.au



## INTRODUCTION

Graves' disease, named after the physician Robert Graves at the 1862 French Academy<sup>1</sup> classically described the triad of goitre, exophthalmos and tachycardia to describe a syndrome that is the most common cause of autoimmune hyperthyroidism resulting from a complex interaction of genetics and environmental exposures<sup>2,3</sup>.

Preoperative management in Graves' is crucial for successful surgical outcomes. Patients at risk of developing hyperthyroid complications such as severe thyrotoxicosis (thyrotoxic storm) are managed through early admission to our facility in order to ameliorate hyperthyroid symptoms and aim to achieve preoperative euthyroidism. Although thyroid storm is rare in the range of 1-5%<sup>4</sup> of patients with hyperthyroidism, the mortality is high from 10-20%<sup>5</sup>.

Prior to commencing preoperative therapy baseline bloodwork is obtained including full blood count, liver function testing, electrolytes, vitamin D and thyroid and parathyroid hormone levels to allow tailoring of treatment and to set baseline for serial monitoring. Prior to admission patients are placed on propranolol for beta blockade, antithyroid medications belong to the thiamazole group, carbimazole (active metabolite methimazole) or propylthiouracil (PTU) in the first trimester of pregnancy or allergy<sup>6</sup> in addition to cholestyramine for enteric sequestration of iodothronines<sup>7</sup>. Once admitted patients are commenced on a short course of potassium iodide solution (Lugol's iodine - LI) in concordance with the 2016 recommended by the American Thyroid Association<sup>6</sup> however use of Lugol's iodine has recently been challenged<sup>8</sup>.

### THE CASES

Two females aged 25 and 39 years of age were admitted 5 days prior to elective total thyroidectomy for symptomatic hyperthyroidism related to Graves' disease including thyroid ophthalmopathy, tremor, pretibial myxoedema, restlessness and tremor. Prior to admission both patients were placed on our routine medical management but one of the patients was unable to tolerate medical management. Both patients were administered Lugol's iodine with resultant drops in triiodothyronine dropping 28.7pmol/L down to 7.6 pmol/L and 20.1pmol/L to 6.7pmol/L and free thyroxine reducing from 28.7pmol/L to 24.1pmol/L and 47.2pmol/L to 21.9pmol/L as charted below.

Clinically both patients improved with tachycardia, diaphoresis and tremor resolving pre-operatively. Operative courses were uncomplicated with one patient experiencing transient hypocalcaemia which resolved within 24 hours. Trending of their thyroxin and trijodothyronine levels are presented below.

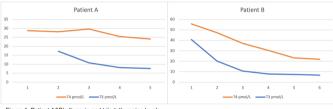


Figure 1. Patient A&B's thyroxin and triiodothyronine levels.

### DISCUSSION

In the preoperative phase a short term course of potassium iodide solution is recommended<sup>6</sup> and has been used since Plummer demonstrated a 75% reduction in mortality with the use of LI in 1924<sup>9</sup>. Wolff-Chaikoff first described if the thyroid is bombarded with excess iodine resulting in increased iodine uptake and acute inhibition of thyroperoxidase<sup>10</sup> leading to reduced T3 and T4 which typically takes effect in 2-3 days<sup>11</sup> in order to induce a euthyroid state.

LI reduces thyroid microvascularity as was demonstrated by in 2007<sup>12</sup> by Erbil et al resulting in a reduction in surgical haemorrhage<sup>13</sup>. In a 2017 randomised controlled trial (RCT) demonstrated in addition to reduced haemorrhage there was a reduction of surgical time in those treated with LI14 despite having no effect on the difficulty of surgery. Lower rates of transient hypoparathyroidism and transient hoarseness have been reported post operatively<sup>15</sup> with the administration of LI.

Typical administration is 0.5ml every 8 hours but clinical practice dosing varies<sup>16</sup>, although many of the studies that have explored the use of Lugol's iodine utilising this product for 10-14 days preoperatively<sup>17</sup> however there have been no studies looking at optimal duration of therapy so this is

unknown and in the reported literature there is variation from 10 days to 1 vear<sup>11</sup>. It should be noted that LI should not be started without antithvroid drugs systemically for at least an hour as this may potentiate hyperthyroidism<sup>6</sup>.

In Hope et al.'s 2017 literature review they examine the available studies that describe the use of LI. They found high level evidence lacking on the clinical relevance of this medication in ameliorating post operative complications<sup>8</sup>. They do however concede that the scientific basis for the use of LI has merit<sup>8</sup> in reduction of haemorrhage and reduction of microvasculature. Their recommendations include a large, prospective RCT to further assess the use of this medication on a population basis.

#### CONCLUSION

On pre surgical administration Lugol's iodine has demonstrated utility in reducing surgical bleeding and in conjunction with other agents may assist in achieving a preoperative euthyroid state however further research is required to clearly elucidate the clinical utility of this agent.

The authors of this poster have no conflicts of interest to declare.

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