

## Combination of minimally invasive thyroid surgery and local anesthesia associated to iopanoic acid for patients with amiodarone-induced thyrotoxicosis and severe cardiac disorders: a pilot study

Piero Berti · Gabriele Materazzi · Fausto Bogazzi ·  
Carlo Enrico Ambrosini · Enio Martino · Paolo Miccoli

Received: 17 June 2006 / Accepted: 29 August 2006 / Published online: 14 November 2006  
© Springer-Verlag 2006

### Abstract

**Background and aims** Amiodarone-induced thyrotoxicosis is a life-threatening condition. A prompt control of thyrotoxicosis is obtained by thyroidectomy. Preparation with iopanoic acid proved to be very effective in reducing cardiovascular complications. Nevertheless, general anesthesia and extensive surgery may affect negatively patients also after adequate preparation. Safety and efficacy of minimally invasive video-assisted thyroidectomy performed under regional anesthesia (bilateral modified deep cervical block) in patients with amiodarone-induced thyrotoxicosis was evaluated.

**Patients and methods** Eight patients with amiodarone-induced thyrotoxicosis (three with type I and five with type II), mean age 66.2 years, were prepared with iopanoic acid. There were five men and three women. Three patients had dilatative cardiomyopathy, three had heart failure secondary to severe myocardial infarction, and two had refractory unstable rhythm disorders.

**Results** Minimally invasive video-assisted thyroidectomy was performed under regional anesthesia. Mean operative time was 55.5 min. During surgery, lung and heart function remained well and no surgical complications occurred. After surgery, all patients remained on amiodarone therapy and two patients were subsequently removed from the checklist for heart transplantation.

**Conclusion** Minimally invasive video-assisted thyroidectomy under regional anesthesia can be proposed as resolution of amiodarone-induced thyrotoxicosis in high risk patients with severe cardiac disorders, after preparation with iopanoic acid.

**Keywords** Amiodarone · Thyrotoxicosis · Minimally invasive · Thyroidectomy · Local anesthesia

### Introduction

Amiodarone-induced thyrotoxicosis (AIT) is a life-threatening condition. It occurs in about 1.5–3% of patients under chronic treatment with amiodarone. AIT may develop in patients with underlying thyroid disorders (type I) or in patients with apparently normal thyroid gland (type II) [1–4]. Medical treatment may restore euthyroidism in few weeks in patients with type II AIT; at variance, several weeks or months of therapy are necessary in type I AIT and in a subset of type II AIT [3].

However, a prompt and definitive control of thyrotoxicosis can be obtained only by means of total thyroidectomy and amiodarone may be continued for the underlying cardiac disorder.

Surgery though can be very hazardous in these patients. The cardiovascular comorbidities and high operative risk of

---

Presented at the 2nd Biennial Congress of the European Society of Endocrine Surgeons in Krakow, Poland, 18–20 May, 2006.

P. Berti · G. Materazzi · C. E. Ambrosini · P. Miccoli  
Department of General Surgery, University of Pisa,  
Pisa, Italy

F. Bogazzi · E. Martino  
Department of Endocrinology and Metabolism,  
University of Pisa,  
Pisa, Italy

G. Materazzi (✉)  
Dipartimento di Chirurgia, Ospedale S. Chiara,  
Via Roma 67,  
56126 Pisa, Italy  
e-mail: gmaterazzi@yahoo.com

this type of patients increase the complication rate and thyroidectomy has a high incidence of perioperative morbidity and mortality [5].

Preparation with iopanoic acid proved to be very effective in reducing cardiovascular complications during and shortly after operation [6–8] because iopanoic acid, an oral iodinated cholecystographic agent, is a potent inhibitor of type 1 5'-deiodinase activity, thus promptly reducing circulating T3 concentrations and likely reducing cardiovascular complications. Nevertheless, general anesthesia and extensive surgery may affect negatively patients also after adequate preparation.

The aim of the study was to evaluate the safety and efficacy of a less invasive approach, such as video-assisted thyroidectomy (MIVAT) performed under regional anesthesia (RA) in patients with AIT and severe cardiac diseases, although modern general anesthesia has already proven to be quite safe also in such ill cases [9].

## Materials and methods

From June 1998 to June 2005, 22 patients underwent surgery for AIT at our Department. Fourteen patients were operated through a cervicotomy under general anesthesia, while in eight "high risk" cases, the option to perform MIVAT under regional anesthesia was chosen.

All these eight patients proved to represent the highest risk class among the cohort undergoing surgery for AIT: they were all selected for this type of treatment because they well matched both MIVAT (Table 1) and local anesthesia inclusion criteria. Three patients suffered from a dilatative cardiomyopathy, three had heart failure secondary to severe myocardial infarction, and two had refractory unstable rhythm disorder. They were all classified as American Society of Anesthesiology (ASA) class IV patients. The mean duration of amiodarone treatment was  $20.8 \pm 11$  months. A medical treatment towards hyperthyroidism was attempted in all cases. It consisted of methimazole-associated potassium perchlorate in type I AIT or glucocorticoids in type II AIT. Its duration ranged from 7 to 90 days (Table 2).

There were five men and three women. Mean age was 66.2 (62–75) years. Diagnosis of AIT [three with AIT type I (one Graves' disease and two toxic nodular goiters); five

with AIT type II] was made by clinical and laboratory findings. Mean serum FT4 was  $57 \pm 9$  pmol/l, FT3  $19 \pm 4$  pmol/l, and TSH was undetectable (normal values in our laboratory are as follows: FT4, 8.4 to 23.2 pmol/l; FT3, 3.0 to 8 pmol/l; TSH, 0.4 to 3.7 mU/l). In all patients thyroidectomy was the preferred option because all patients had unstable cardiac control after <30 days of medical therapy (potassium perchlorate and methimazole in type I and methylprednisolone in type II AIT).

They were referred to our unit after a short course of iopanoic acid preparation (1 g/day orally for a mean of 13 days). After administration of iopanoic acid, serum FT4 and FT3 levels decreased to  $43 \pm 9$  pmol/l and  $6 \pm 5$  pmol/l, respectively.

All patients underwent neck ultrasound shortly before surgery so as to check the thyroid volume which is the most important selection criterion for MIVAT eligibility (Table 1). Patients with AIT type I had a small multinodular goiter (mean thyroid volume echographically estimated was 23.4 ml), while the remaining patients with AIT type II showed a normal thyroid.

Laryngoscopy was performed in all patients before and after thyroidectomy to assess laryngeal nerve function; serum calcium and parathyroid hormone concentrations were measured after operation on the first and second postoperative day and then 1 month after operation.

All patients underwent extensive preoperative education about the type of operation (MIVAT) and type of anesthesia (bilateral deep cervical block and intravenous mild sedation).

Among the remaining 14 AIT patients, 8 had type I AIT and 6 type II AIT. All these patients, after a short course of iopanoic acid, underwent a total thyroidectomy under general anesthesia due to their acceptable general conditions. The reasons for exclusion of these patients from MIVAT were: thyroid volume exceeding 25 ml or nodule diameter larger than 3 cm in eight cases, previous neck surgery in two cases, refusal of undergoing MIVAT under local anesthesia in four cases. Iopanoic acid was of course discontinued immediately after surgery.

## Results

After informed consent, all patients underwent MIVAT under RA. Regional anesthesia was performed as previously described for minimally invasive video-assisted parathyroidectomy [10]. It was performed 15 min before the skin incision by the anesthesiologist. It comprised a bilateral deep cervical block, associated with infiltration of the upper thyroid pedicle and local infiltration along the line of incision. Twenty milliliter of a mixture of 0.25% lignocaine and 0.15% bupivacaine was used on each side to obtain the bilateral block. Some 10–15 ml was used to infiltrate the

**Table 1** Inclusion criteria for minimally invasive video-assisted thyroidectomy

Criteria
Total thyroid gland volume less than 25 ml
Nodule smaller than 30 mm in its largest diameter
No previous neck surgery or irradiation

incision site and the operative field. Remifentanyl was used to provide mild intravenous sedation.

MIVAT was performed, as previously described [11], through a 1.5-cm skin incision 2 cm above the sternal notch. The neck was not hyperextended. The midline was divided as much as possible. The operative space was maintained by external retraction. Visualization of recurrent nerve and parathyroids was magnified by endoscopic vision. Hemostasis was achieved by ultrasonic scissors (Harmonic® Johnson and Johnson, Cincinnati, OH, USA). After removing the endoscope and the retractors, the upper pole of the gland was pulled out using conventional forceps and gentle traction allowed the complete exteriorization of the lobe. The lobe was freed from the trachea by ligating the small vessels and dissecting the Berry ligament. The same procedure was utilized for the contralateral lobe.

Mean operative time was 55.5 min (range 45–73). Conversion to conventional cervicotomy, or to general anesthesia was never required. During surgery, lung and heart function remained well, no surgical complications occurred. Patients tolerated well the procedure and were able to speak to the surgeon during the operation. All patients were discharged from the surgical ward on the second postoperative day. Postoperative calcemia remained between the normal range (8–10 mg/dl) in all patients and none of them required calcium supplementation. One month after surgery, no patient showed vocal cord paralysis at direct laryngoscopy. Mean calcium value was 8.4 mg/dl and no wound infection or hematoma was registered. Mean follow up after thyroidectomy was 4 months (range 2–6).

After surgery, all patients remained on amiodarone therapy. Thyroid hormone replacement was started shortly, none expired and all demonstrated improvement in their cardiac disease, so that two of them were subsequently removed from the checklist for heart transplantation.

Among the 14 patients who underwent “standard” open thyroidectomy, surgery was complicated in three cases (two transient hypocalcemia and one transient laryngeal nerve palsy; in this latter case, a delayed extubation (1 day) was also registered. Postoperative course was also complicated by pneumonia in one case. Mean postoperative stay in this group was 5 days (mean 3–14).

## Discussion

Amiodarone causes thyroid dysfunction in a substantial proportion of patients, hypothyroidism in about 6% and thyrotoxicosis in 1.5 to 3% [1, 3]. AIT may develop in normal (type II) or abnormal (type I) thyroid glands. Although thyrotoxicosis poses a serious risk in patients with underlying cardiac disorders, thyrotoxicosis associated with a iodine load is often refractory to conventional

antithyroid drug treatment [1] and usually cannot be treated by radioiodine therapy because of low RAIU values [12]. Thus, surgery may represent the only alternative therapy in these patients and paradoxically might be remarkably successful. Total or near total thyroidectomy is the most effective and fastest treatment of AIT but has high incidence of perioperative morbidity and mortality even in specialized centers [5]. When comparing our results with others' [5] though, some considerations should be stressed: even though AIT is a well-defined clinical condition, not all patients are seriously ill up to the same level. Both the severity of cardiac conditions and of the underlying thyroid pathology can play an important role in the outcome of the surgical procedure. Our patients in fact were all able to tolerate a cessation of amiodarone therapy, short though the interruption was. Moreover, the eight cases of our series all presented small volume thyroid glands and this might be considered a bias when evaluating the results of a total thyroidectomy in AIT patients. On the other hand, thyroidectomy is not more risky or demanding in these patients than in others from a surgical standpoint. But general anesthesia can be associated with serious arrhythmias, hypotension, and congestive heart failure [13–16] so as to induce AIT patients to refrain from surgery or to delay it. Several options of general anesthetic techniques are proposed to minimize risks [13–16] but these patients still undergo cardiac stress from induction of the general anesthesia, hemodynamic variability during the procedure, and difficulty to be extubated postoperatively [17–19].

Thus, thyroidectomy performed under local anesthesia minimizes potential hemodynamic and autonomic nervous system changes during operation. It has been reported by several authors for the treatment of AIT and revealed to be safe and effective in the described series [20–22].

To our knowledge, a minimally invasive approach to remove the thyroid in AIT patients was never used, in particular under local anesthesia.

MIVAT, already proved to be feasible under local anesthesia [23] as long as patients are compliant with it. AIT patients besides, showing usually small glands (small nodular goiter in type I and normal thyroid in type II), tend to match the inclusion criteria (Table 1) described for MIVAT [24]. Furthermore, RA proved not to be particularly uncomfortable when performing the minimally invasive approach because the procedure avoids the hyperextension of the neck, a position not well tolerated by patients if not under general anesthesia.

Surgery was completely uneventful in these eight patients. Neither conversion to open surgery nor to general anesthesia were necessary in this small series. We did not record any intraoperative or postoperative complication. Mean operative time (55 min) was comparable with that reported in larger series of MIVAT [24] and comparable to

large series of open thyroidectomy performed under local anesthesia by experienced surgeons [25]. We had some concerns due to the knowledge that AIT type II is characterized by destructive thyroiditis, which is considered a partial contraindication for MIVAT [11], but our intra-operative findings in patients with AIT type II were reassuring and similar to those reported by others [21]. There was only a slight inflammatory response around the gland. It was not difficult to access the operative space, endoscopic identification, and dissection of the inferior laryngeal nerve and parathyroid glands was easy and the parenchyma was solid enough to be retrieved safely from the wound without disrupting the gland.

## Conclusions

AIT can be quickly and definitively cured only by total or near total thyroidectomy, but general anesthesia might carry further risks to already critically ill patients. Combination of preparation with iopanoic acid, to restore quickly and temporarily euthyroidism, and a less invasive approach characterized by a less painful postoperative course [26, 27] seemed to be effective and safe particularly when performed under regional anesthesia. Of course our data need to be confirmed in a larger series of patients.

## References

- Martino E, Bartalena L, Bogazzi F, Braverman LE (2001) Amiodarone and the thyroid. *Endocr Rev* 22:240–254
- Trip MD, Wiersinga W (1991) Incidence, predictability, and pathogenesis of amiodarone-induced thyrotoxicosis and hypothyroidism. *Am J Med* 91:507–511
- Bartalena L, Bogazzi F, Braverman LE, Martino E (2001) Effects of amiodarone administration during pregnancy on neonatal thyroid function and subsequent neurodevelopment. *J Endocrinol Invest* 24:116–130
- Daniels GH (2001) Amiodarone-induced thyrotoxicosis. *J Clin Endocrinol Metab* 86:3–8
- Houghton SG, Farley DR, Brennan MD, van Heerden JA, Thompson GB, Grant CS (2004) Surgical management of amiodarone-associated thyrotoxicosis: Mayo Clinic experience. *World J Surg* 28(11):1083–1087 (Nov)
- Bogazzi F, Miccoli P, Berti P, Cosci C, Brogioni S, Aghini-Lombardi F, Materazzi G, Bartalena L, Pinchera A, Braverman LE, Martino E (2002) Preparation with iopanoic acid rapidly controls thyrotoxicosis in patients with amiodarone-induced thyrotoxicosis before thyroidectomy. *Surgery* 132(6):1114–1117 (Discussion 1118, Dec)
- Bogazzi F, Aghini-Lombardi F, Cosci C, Lupi I, Santini F, Tanda ML et al (2002) Iopanoic acid rapidly controls Type I amiodarone-induced thyrotoxicosis prior to thyroidectomy. *J Endocrinol Invest* 25:176–179
- Panzer C, Beazley R, Braverman L (2004) Rapid preoperative preparation for severe hyperthyroid graves' disease. *J Clin Endocrinol Metab* 89(5):2142–2144 (May)
- Sutherland J, Robinson B, Delbridge L (2001) Anaesthesia for amiodarone-induced thyrotoxicosis: a case review. *Anaesth Intensive Care* 29:24–29
- Miccoli P, Barellini L, Monchik JM, Rago R, Berti PF (2005) Randomized clinical trial comparing regional and general anaesthesia in minimally invasive video-assisted parathyroidectomy. *Br J Surg* 92(7):814–818 (Jul)
- Miccoli P, Materazzi G (2004) Minimally invasive, video-assisted thyroidectomy (MIVAT). *Surg Clin North Am* 84(3):735–741 (Jun)
- Bartalena L, Bogazzi F, Martino E (2002) Amiodarone-induced thyrotoxicosis: a difficult diagnostic and therapeutic challenge. *Clin Endocrinol* 56:23–24
- Wilson JS, Pdrif PJ (1991) Side effects from amiodarone. *Am Heart J* 121:158–171
- Perkins MW, Dasta JF, Reilley TE, Halpern P (1989) Intra-operative complications in patients receiving amiodarone: characteristics and risk factors. *DICP* 23:757–763
- Stoelting RK, Dierdorf SF (1993) *Anesthesia and co-existing disease*, 3rd edn. Churchill Livingstone, New York
- Hamoir E, Meurisse M, Defechereux T, Joris J, Vivario J, Hennen G (1998) Surgical management of amiodarone-associated thyrotoxicosis: too risky or too effective? *World J Surg* 22:537–542
- Lehman A, Boldt J, Zeitler C, Thaler E, Werling C (1999) Total intravenous anaesthesia with remifentanyl and propofol for implantation of cardioverter-defibrillators in patients with severely reduced left ventricular function. *J Cardiothorac Vasc Anesth* 13:15–19
- Tsubokawa T, Yamamoto K, Koyabashi T (1998) Propofol clearance and distribution volume increase in patients with hyperthyroidism. *Anesth Analg* 87:195–199
- Barbier GH, Hettigar UR, Appunn DO (1995) Clinical rationale for the use of ultra-short acting beta-blocker, esmolol. *Int J Clin Pharmacol Ther* 33:212–218
- Klein SM, Greengrass RA, Knudsen N, Leight G, Warner DS (1997) Regional anesthesia for thyroidectomy in two patients with amiodarone-induced hyperthyroidism. *Anesth Analg* 85:222–224
- Williams M, Lo Gerfo P (2002) Thyroidectomy using local anesthesia in critically ill patients with amiodarone-induced thyrotoxicosis: a review and description of the technique. *Thyroid* 12(6):523–525
- Mehra A, Widerhorn J, Lopresti J, Rahimtoola SH (2001) Amiodarone-induced hyperthyroidism: thyroidectomy under local anesthesia. *Am Heart J* 122:1160–1161
- Lombardi CP, Raffaelli M, Modesti C, Boscherini M, Bellantone R (2004) Video-assisted thyroidectomy under local anesthesia. *Am J Surg* 187(4):515–518 (Apr)
- Miccoli P, Berti P, Materazzi G, Minuto M, Barellini L (2004) Minimally invasive video-assisted thyroidectomy: five years of experience. *J Am Coll Surg* 199:243–248
- Spanknebel K, Chabot JA, DiGiorgi M, Cheung K, Lee S, Allendorf J, Lo Gerfo P (2005) Thyroidectomy using local anesthesia: a report of 1,025 cases over 16 years. *J Am Coll Surg* 201(3):375–385 (Sep)
- Miccoli P, Berti P, Raffaelli M, Materazzi G, Baldacci S, Rossi G (2001) Comparison between minimally invasive video-assisted thyroidectomy and conventional thyroidectomy: a prospective randomized study. *Surgery* 130(6):1039–1043 (Dec)
- Ikeda Y, Takami H, Sasaki Y, Takayama J, Niimi M, Kan S (2002) Comparative studies of thyroidectomies: endoscopic surgery vs conventional open surgery. *Surg Endosc* 16:1741–1745