How Does High-Concentration Supplemental Perioperative Oxygen Influence Surgical Outcomes after Thyroid Surgery? A Prospective, Randomized, Double-Blind, Controlled, Monocentric Trial

Mario Schietroma, MD, Federica Piccione, MD, Emanuela Marina Cecilia, MD, Francesco Carlei, MD, Giuseppe De Santis, MD, Federico Sista, MD, Gianfranco Amicucci, MD

BACKGROUND: Recurrent laryngeal nerve palsy (RLNP) and hypoparathyroidism are complications of thyroid surgery. The convalescence can depend on several factors (ie, pain, fatigue, nausea, and vomiting). Supplemental oxygen improves inflammatory and immune function and decreases nausea and vomiting after surgical procedures. We have investigated whether supplemental perioperative oxygen administration could improve surgical outcomes in patients undergoing thyroid surgery.

STUDY DESIGN: Three hundred and sixty patients were randomized to an oxygen/air mixture with a fraction of inspired oxygen (FiO_2) of 30% (n = 179) or 80% (n = 181). Administration was commenced after induction of anesthesia and maintained for 6 hours after surgery. The primary end points were temporary or permanent RLNP and transient or definitive hypoparathyroidism. Pain and fatigue scores, nausea, and the number of vomiting episodes were also registered. Preoperatively and at several times during the first 24 postoperative hours, we measured C-reactive protein, interleukin (IL)-6, and IL1β levels.

RESULTS: In the 80% FiO_2 group, the rate of temporary RLNP (4.4%) was significantly lower compared with the 30% FiO_2 group (9.4%) ($p = 0.040$). In addition, postoperative transient biochemical hypoparathyroidism occurred more frequently in the 30% FiO_2 group (48.5%) than in the 80% FiO_2 group (16.3%) ($p = 0.046$). Supplemental 80% FiO_2 significantly reduced postoperative levels of C-reactive protein ($p < 0.01$), IL6 and IL1β ($p < 0.05$), fatigue ($p < 0.01$), and overall pain during the first 24 postoperative hours ($p < 0.01$). Supplemental 80% FiO_2 also reduced nausea and vomiting on the day of operation ($p = 0.058$).

CONCLUSIONS: Supplemental 80% FiO_2 reduced postoperative temporary RLNP and hypoparathyroidism rates and reduced pain, fatigue, nausea, and vomiting after thyroid surgery. (J Am Coll Surg 2015;220:921−933. © 2015 by the American College of Surgeons)

Total thyroidectomy or thyroid lobectomy has been accepted as the current surgical therapy for benign and malignant thyroidal disorders,[1-5] but extensive resection might increase the risk of postoperative complications.[6,7] Recurrent laryngeal nerve (RLN) dysfunction and hypoparathyroidism are well-recognized important complications of thyroid surgery.[8] Complication rates of thyroidectomy have a varying range for permanent (0.1% to 8.85%) or transient (0.2% to 14%) RLN injury[9] and for permanent (1% to 11%) or transient (1.6% to 68%) hypoparathyroidism.[9-11] Paralysis of vocal cords can cause serious phonatory, respiratory, and psychological problems that limit working capacities and quality of life for patients.[5] Hypocalcemia is associated with the risk of developing serious postoperative clinical manifestations, ranging from paresthesias and carpopedal muscle spasms to lethargy, seizures, and electrocardiogram QT interval prolongation.[12,13] Intensive effort should be spent to prevent the complications especially related to

Disclosure Information: Nothing to disclose.

Received August 2, 2014; Revised January 13, 2015; Accepted January 26, 2015.

From the Department of Surgery, University of L'Aquila, L'Aquila, Italy.
Correspondence address: Mario Schietroma, MD, Department of Surgery, University of L'Aquila, Presso Ospedale S Salvatore, Edificio Delta 6, 67100 Coppito (AQ), Italy. email: schietroma2001@yahoo.it

http://dx.doi.org/10.1016/j.jamcollsurg.2015.01.046
ISSN 1072-7515/15

Abbreviations and Acronyms

CRP = C-reactive protein
FiO_2 = fraction of inspired oxygen
IL = interleukin
RLN = recurrent laryngeal nerve
RLNP = recurrent laryngeal nerve palsy
VAS = visual analog scale

RLN and parathyroid glands, because they can be prevented with the appropriate surgical technique during total thyroidectomy.

The surgical technique is one of the important factors affecting the outcomes of thyroidectomy.[7] In the past, most surgeons avoided dissections in close proximity to the RLN to prevent its injury. Recently, endocrine surgeons have considered this unacceptable. The identification and preservation of the RLN are essential to avoid its injury.[14] Meticulous hemostasis and delicate technique are required to prevent nerve injury. Once found, the nerve, with all the identified branches, must be followed superiorly through the entire course until it enters the larynx.[15] This surgical technique, which requires more dissections, can harm the RLN and parathyroid glands.[7] In fact, recurrent laryngeal nerve palsy (RLNP) can result from direct mechanical damage without disruption. This disparity between anatomic neural integrity and actual RLN function probably results from trauma to the intact nerve. Nerve manipulation during thyroid surgery can cause traumatic edema or vasospasm, and consequent dysfunction, resulting in anything from neurapraxia to axonotmesis (edema) and/or temporary hypoparathyroidism (vasospasm).

The duration of convalescence, after noncomplicated thyroid operation, depends on several factors, the most important of which pain are fatigue and sociocultural factors. Pain and fatigue are most intense on the day of operation and the next day. Nausea and vomiting occur mainly on the day of operation and only rarely contribute to prolonged convalescence.

During anesthesia and surgery, oxygen is routinely administered to all patients. Inspired oxygen concentrations, however, vary between 30% and 100%, and oxygen is often administered in a seemingly random manner. During the last decade, it has been shown in several randomized trials that perioperative supplemental oxygen administration might improve outcomes after certain surgical procedures.[16-18] Supplemental oxygen improves inflammatory and immune functions.[19-21] Some studies have shown that supplemental oxygen also decreases the rate of postoperative nausea and vomiting after laparoscopic and open abdominal surgical procedures.[22,23] In addition, 80% inspired oxygen fraction almost doubles subcutaneous tissue oxygen tension and halves the rate of postoperative wound infections.[24-28] Preconditioning with oxygen might improve organ function after liver transplantation[29] and outcomes after spinal ischemic insults.[30] Supplemental perioperative oxygen administration is not associated with clinically important side effects.[31]

There is little information in the literature about the use of supplemental oxygen in thyroid surgery. Only the study by Joris and colleagues[32] has evaluated the role of supplemental oxygen on nausea and vomiting after thyroidectomy.

We therefore undertook the current prospective, randomized study to investigate whether perioperative supplemental oxygen administration could improve surgical outcomes in patients undergoing either total thyroidectomy or total lobectomy with routine identification of RLN. Our primary aim was to evaluate the role of perioperative supplemental oxygen in preventing postoperative RLNP and hypoparathyroidism. We also investigated the effects of perioperative supplemental oxygen on pain, fatigue, nausea, vomiting, and the duration of convalescence.

METHODS

From February 2007 to June 2014, we included, in a prospective randomized study, 368 consecutive patients (219 women, 149 men; mean age 51.4 years) who underwent elective thyroid surgery. Exclusion criteria were American Society of Anesthesiologists physical class III or IV, age older than 75 years, and pregnancy. Patients were not included if they had chronic pain due to a disease other than thyroid disease; if they had any signs of renal, hepatic, and immunological disease; if they received opioids or tranquilizers (>1 week of treatment before thyroidectomy); if they spoke a foreign language only; if they had mental disorders; or if they had a history of alcohol or drug abuse. Finally, because the development of surgical complications might influence the chosen outcomes parameters, we decided before the start of the study to exclude these patients, and the results were analyzed according to the protocol.

Medical history was recorded, and a systematic physical examination was performed preoperatively. The patients were classified as grade I or II, according to the American Society of Anesthesiologists' classification system.[33] The study protocol was approved by the ethical committee of the Faculty of Medicine of the University of L'Aquila, and all patients gave their written informed consent to participate in the study.

Patients were followed from the day before the operation and daily during the first postoperative week. The day of operation was defined as day 0 and the first day after operation as day 1, the second day after as day 2, and so on.