POTENTIAL BENEFIT OF ORAL CALCIUM/VITAMIN D ADMINISTRATION FOR PREVENTION OF SYMPTOMATIC HYPOCALCEMIA AFTER TOTAL THYROIDECTOMY

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Objective. To evaluate routine oral calcium and vitamin D administration for preventing symptoms of hypocalcemia after total thyroidectomy.

Subjects and methods. A total of 487 consecutive patients were prospectively randomized into two groups in terms of routine oral calcium and vitamin D supplementation: In the control group (244 patients) the treatment was not routinely started after surgery, whereas the treated group (243 patients) received routine supplementation that started on postoperative day 1.

Results. Patients of treated group had only minor hypocalcemia symptoms, whereas 7 patients of control group experienced carpopedal spasm as a major symptom ($p<0.001$). None of the patients in the treated group required intravenous calcium administration. Average hospital stay of the treated group patients was significantly shorter than that of control group ($p<0.001$).

Conclusions. Routine postoperative calcium and vitamin D supplementation therapy may be useful for the prevention of symptomatic hypocalcemia after total thyroidectomy and may allow for a safe and early discharge from the hospital.

Key words: Thyroidectomy – Hypocalcemia – Calcium - Vitamin D - Dietary supplementation

Postoperative hypocalcemia is one of the most important complications after total thyroidectomy (TT) with reported incidences ranging from 1.6 % to 50 % (Flynn et al. 1994; Szubin et al. 1996; Bergamaschi et al. 1998; Pappalardo et al. 1998; Mishra et al. 1999). Postoperative decrease of serum calcium level, whether symptomatic or not, frequently occurs within the first few days after surgery and requires close monitoring of patients and exogenous replacement therapy, if needed, which prolongs the hospital stay. The potential causes of postoperative hypocalcemia include physiological factors such as hemodilution, calcitonin release and hungry bone syndrome, the latter being seen particularly in patients with hyperthyroidism and pathological conditions such as hypoparathyroidism secondary to surgical trauma, devascularization or inadvertent excision of parathyroid glands, or autoimmune fibrosis in patients with Graves' disease (Reber and Heath 1995; Yamashita et al. 2001). In most cases the postoperative hypocalcemia is transient and serum calcium levels normalize within a few months with spontaneous recovery of parathyroid function (Bellantone et al. 2002). In few patients, however, hypoparathyroidism persists after one year and must then be considered permanent.

Routine oral calcium either with or without vitamin D has been proposed empirically and used successfully to avoid the risk of symptomatic hypocalcemia and to reduce hospital stays after TT (Moore et al. 1994; Bellantone et al. 2002; Bhattacharyya and Freid 2002).

The purpose of this study was to prospectively evaluate the efficacy of routine postoperative oral calcium and vitamin D supplementation in preventing symptomatic hypocalcemia after TT, and to examine whether supplementation can enable patients to be discharged safely in the early postoperative period.

Patients and methods

The study was performed in the Department of General Surgery at Gazi University School of Medicine, between February 2003 and February 2005. A total of 487 patients (401 women and 86 men) who underwent TT were included in the study. Patients were not enrolled in the study if they had any of the following: concomitant parathyroid disease or lymph node dissection because of thyroid malignancy; completion thyroidectomy; or use of calcium supplementation for osteoporosis before the operation. Informed consent was obtained from all patients before inclusion in the study. Age, sex, preoperative diagnosis, hormonal status, and hospital stay were recorded.

In all patients, the operations were carried out by, or under the supervision of, at least one of the authors. Suction drains were not used routinely in most of the patients.

The control group (the first consecutive 244 patients) received no routine supplementation treatment. The next 243 consecutive patients were taken as the treatment group, and were routinely given a daily dose of oral calcium 600 mg combined with vitamin D_3 400 IU (Cal-D-Vita, Bayer, Istanbul, Turkey). In the treated group, the administration was started on the first postoperative day and was terminated on postoperative day 7. All patients who had supplementation therapy were informed about the symptoms of hypocalcemia. Carpopedal spasm was defined as a major symptom whereas perioral tingling and numbness were defined as minor symptoms. If the patient had minor hypocalcemic symptoms, serum calcium levels were measured and the dose of supplementation therapy was doubled. The patients of control group were hospitalized and observed for hypocalcemia symptoms for at least 48 hours after surgery. The algorithm used for early postoperative follow-up of the patients is outlined in Figure 1.

Data from each group were analyzed and compared with Chi-square tests and t-tests by SPSS 10.0 for Windows. A *p* value less than 0.05 was considered significant.

Results

Patients' characteristics were similar in both groups (Table 1). Postoperative hypocalcemia occurred in 21 patients (11 patients of control group and 10 patients of treatment group).

In the control group, all but 11 patients had no symptoms of hypocalcemia and were discharged after 48 hours. These 11 patients had major and/or minor hypocalcemia symptoms. Their serum calcium levels were measured and these patients received parenteral calcium infusion in addition to oral calcium and vitamin D supplementation. These patients were hospitalized until they became asymptomatic, and after discharge from the hospital oral supplementation therapy was continued. Serum calcium level was checked on postoperative day 10 and at the end of the first postoperative month, and no patients required supplementation therapy beyond one month.

In the treated group, all but 10 patients had no symptoms of hypocalcemia and except in these 10 the treatment was terminated on postoperative day 7. In 10 patients with hypocalcemia, serum calcium levels were checked again on postoperative day 10 and at the end of the first postoperative month. In 9 patients, supplementation was not needed beyond the first postoperative month. The remaining one patient still required supplementation therapy after 6 months, and was diagnosed as having persistent hypocalcemia.

When the two groups were compared in terms of symptoms, it was found that 7 patients of control group, but no patients of treated group had major symptoms ($p<0.001$). Minor symptoms occurred in 4 patients of control group and in 10 patients of treated group ($p>0.05$). Intravenous calcium administration was required for 7 patients of control group, but in no patients of treated group ($p<0.001$).

Preoperative diagnoses of the patients with hypocalcemic symptoms were similar across the two groups (Table 2), and there were no statistically significant differences. Persistent hypocalcemia was seen in only one patient of treated group. No patient in the study had permanent recurrent nerve palsy.

Average hospital stay in control group was 2.9 ± 0.9 days (range 2-7 days), while in treated group it was 1.2 ± 0.4 days (range 1-2 days) ($p<0.001$).

Discussion

Postoperative hypocalcemia is still a major concern following TT, as it often extends the duration of hospital stay and increases the need for biochemical tests. Moreover, it significantly increases the overall cost of thyroidectomy, since the patient should remain hospitalized for at least 2 days to observe any changes in serum calcium concentrations. When severe, hypocal-

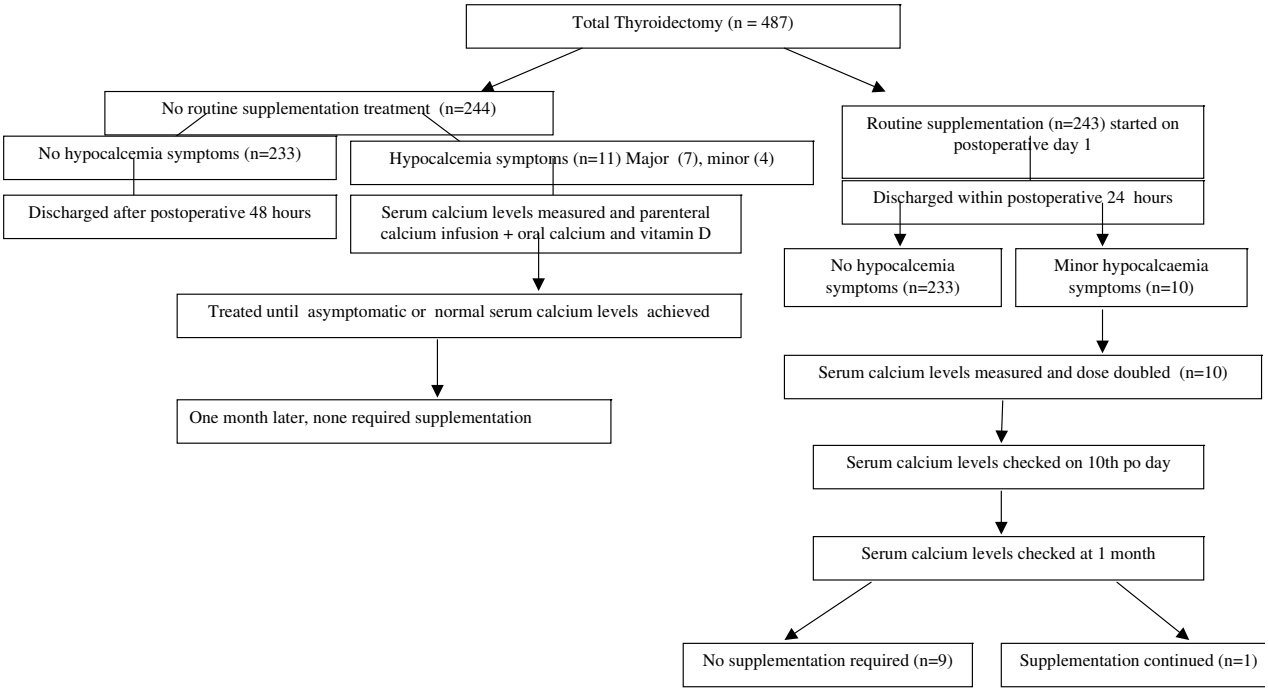

Figure 1 Treatment algorithm after total thyroidectomy

Table 1
Patient characteristics and results of statistical analysis

	Control group	Treatment group	P value
Age	47.21 ± 12.592	47.58 ± 11.256	NS
Sex (F/M)	205/39	196/47	NS
Preoperative diagnosis			
Carcinoma	39	37	NS
Benign disease	153	157	NS
Thyrotoxicosis	52	49	NS
Hospital stay (days)	2.90 ± 0.915	1.20 ± 0.399	P<0.001

Table 2
Preoperative diagnoses of patients with postoperative hypocalcemia

	Control group	Treatment group	Total
Carcinoma	3	3	6
Benign disease	6	6	12
Thyrotoxicosis	2	1	3

cemia can cause serious complications and require close monitoring of the patient and intravenous Ca infusion to alleviate the clinical symptoms. In most cases, hypocalcemia resolves spontaneously, but it can remain persistent when the parathyroid glands are irreversibly injured.

If the symptoms of hypocalcemia occur after TT, they usually do so in the first 24 to 48 hours (Bellantone et al. 2002). Carpopedal spasm is an acute symptom of hypocalcemia and requires treatment with parenteral calcium that continues with oral calcium and the active form of vitamin D. Perioral tingling

indicates mild hypocalcemia, which may be treated with only oral calcium and vitamin D supplementation (Pallotti et al 2002). It is difficult to predict which patients will experience postoperative hypocalcemia, because its pathogenesis is multifactorial. Physiological factors such as hemodilution, calcitonin release and hungry bone syndrome (the latter being seen particularly in patients with hyperthyroidism) have been implicated in postoperative hypocalcemia after TT. Extent of resection, reoperation for completion and patient volume per surgeon are other factors that may play a role in the pathogenesis of persistent hypocalcemia (Bergamaschi et al. 1998). Recently, Lombardi et al.(2004) have shown that one single measurement of intact parathyroid hormone can reliably predict in the early postoperative period (4 hours after surgery) which patients are prone to symptomatic hypocalcemia.

In order to minimize the symptoms of postoperative hypocalcemia, some surgeons prefer to give calcium treatment empirically, while others prefer to educate patients about symptoms so that patients can return to the hospital if these arise (Moore et al. 1994; Bellantone et al. 2002; Bhattacharyya and Freid 2002). We prefer the first approach, and we combine this with vitamin D therapy, because deficiency of 1,25-dihydroxyvitamin D is worsening the symptoms of hypocalcemia (Pallotti et al. 2002). Moreover, it has been reported that administration of oral calcium with vitamin D did not appear to inhibit the function of normal parathyroid glands (Fardellone et al. 1998).

Whether TT can be done safely on an outpatient basis is still under discussion in the literature (Lo Gerfo et al. 1995; Mowschenson et al. 1995; McHenry et al. 1997; Schwartz et al. 1998). Hypocalcemia is one of the major problems that can occur after TT (McHenry et al. 1997). Its detection requires observation and biochemical testing, and therefore if it cannot be predicted or reliably prevented, the possibility that hypocalcemia will develop is often a reason for extending a patient's hospital stay after surgery. Postoperative therapy with calcium and vitamin D may provide an alternative approach to postoperative treatment.

In conclusion, the present results suggest that routine administration of oral calcium and vitamin D soon after TT can significantly reduce the occurrence of the major symptoms of hypocalcemia and can permit earlier discharge from the hospital after surgery.

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