INVITED COMMENTARY

Non-surgical treatment of primary hyperparathyroidism

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As stated in the conclusions of a recent consensus development conference on primary hyperparathyroidism (PHP), all patients with this disease should be considered as candidates for surgery, particularly those under the age of 50, since the outcome of several decades of PHP is not known (4). Potential indications to surgery could be total plasma calcium of more than 0.25 mmol/l above the upper limit of normal range, the presence of renal stone or of a marked elevation of daily urinary calcium excretion, significantly reduced creatinine clearance or substantially decreased bone mineral density. When performed by an experienced surgeon, surgical removal of abnormal gland(s)—solitary adenoma accounting for more than 9 out of 10 cases of PHP—is usually an efficacious and definitive therapy, even leading to a partial recovery of bone mass reduction (12). If a conservative strategy is adopted, the cost of careful follow-up should also be considered, since a twice yearly investigation can be envisaged in order to detect worsening in general symptoms, aggravation of hypercalcemia, or renal impairment. Bone mass determination should be performed no more than at two-year intervals. However, several patients, particularly the elderly, in whom the incidence of PHP appears to be as high as 0.2% and 0.1% in women and men, respectively (7), could be reluctant to have an operation, or coexistent diseases may constitute contraindications to anesthesia. Various medical approaches have been reported which can be classified into agents that inhibit parathyroid hormone (PTH) secretion and those that protect bone against PTH-stimulated bone resorption (9). Among the former, propranolol or cimetidine have proven ineffective. The radioprotective organic phosphorothioate WR-2721 agent is efficient in acutely lowering PTH secretion, but it is associated with marked side effects that preclude its use. Non-hypercalcemic analogues of calcitriol, which are capable of reducing hyperparathyroidism in chronic renal failure, are promising substances that are worth testing in PHP. In an attempt to influence calcium fluxes in a PTH target organ, forced diuresis with saline and furosemide can transiently increase calcium excretion, but side effects, relatively poor and short-lasting efficacy, prevent its use as a chronic treatment (1, 8). Bisphosphonates are potent inhibitors of osteoclastic bone resorption. A variety of compounds have been tested in PHP (2). A fall in plasma calcium and in biochemical parameters of bone remodeling are observed after bisphosphonate therapy. However, plasma calcium tends to return to pretreatment values at three months despite the continuous administration of the drugs. This is accompanied by higher circulating PTH levels. Because of the potential toxicity of PTH on various organs including kidneys and brain where the presence of PTH receptors has recently been reported (10), the place, if any, of bisphosphonates in the long-term medical management of PHP remains to be established. Oral phosphate has been largely used and is capable of decreasing plasma calcium by favoring the precipitation of calcium phosphate salts in bone as well as in soft tissues, by preventing intestinal calcium absorption through the intraluminal chelation of calcium and by decreasing calcitriol production (3). However, the risk of ectopic calcifications with renal impairment as well as increases in PTH make it necessary for this treatment to be limited to very selective and carefully monitored cases.

Ultrasonography is widely applied in the localization of abnormal parathyroid glands. It can also be used for guiding the fine needle when aspirating material for PTH measurements or cytological examination, or when performing tissue biopsy for histological examination. Thanks to this technology, the efficiency of curative percutaneous ethanol injection into parathyroid adenoma of selected cases has been recognized. The efficacy of the procedure relies on the visualization and accessibility of the abnormal gland(s). One Danish group in particular has accumulated considerable experience in this technique. In the present issue of the Journal, these investigators have used their skills to address the question of the time course of plasma calcium and decreases in PTH levels after ethanol injection (6). In 6 out of the 7 patients studied, in whom this procedure was successful, the median times for the normalization of plasma calcium and PTH were 36 and 24 h, respectively, after 1 to 3 injections administered at 24-h intervals. The indication for therapy was the presence in 3 patients of severe hypercalcemic symptoms requiring a rapid intervention. Thus, the rapidity of the fall in plasma calcium could be of help in the acute care of hypercalcemic crisis within the frame of PHP. In the second paper of this issue of the Journal, the question of the long-term efficacy of ethanol injection into parathyroid adenoma is addressed (11). Thirteen symptomatic patients with a median age of 79 years were treated with 1 to 8 injections (median
2), and were followed for as long as 49 months. The success rate in terms of correction of PTH concentrations was 52%.

A major restriction in percutaneous ethanol injection is the possible difficulty in accurately localizing the adenoma and its accessibility. It should be borne in mind that the sensitivity of ultrasound to localize an adenoma is about 65%, with a false positive rate of about 12% (5). Tumors in the anterior mediastinum or the tracheo-oesophageal groove, which are not so commonly found, are poorly visualized. Thus, the precise indications for this interventional radiologic procedure, the number of injections to be required, the success rate, the prevalence of side effects, the long-term effects on the various organs susceptible to becoming damaged by an excess of PTH, remain to be clearly determined on a prospective basis and compared with operative and non-operative management of PHP. As for parathyroid surgery, the success of the intervention is likely to be highly dependent on the operator’s skill.

References
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