Asymptomatic primary hyperparathyroidism: to treat or not to treat?

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BACKGROUND

Asymptomatic primary hyperparathyroidism became increasingly diagnosed in the 1970s in both North America and Europe with the introduction of readily available serum calcium measurements that were for the first time being applied to a broad range of patient groups and population samples. Indeed asymptomatic hyperparathyroidism became the commonest form of the disease to be referred to endocrine clinics. Subjects with this mild form of the disease classically had serum calcium concentrations just above the normal range and serum parathyroid hormone concentrations also just above, or in the upper half, of the normal range. Further these patients did not have the well recognized complications of primary hyperparathyroidism: urinary stone disease, high turnover parathyroid bone disease, or symptomatic hypercalcemia. Because the mass of the parathyroid gland was only just abnormally increased in these patients, surgical removal of the adenoma was often challenging and many of these asymptomatic patients ended up with having failed parathyroidectomies. At about the same time clinical investigators were following asymptomatic primary hyperparathyroid patients for biochemical and symptomatic changes at regular clinic visits. It became increasingly clear that in many of these patients, the hyperparathyroidism did not progress; the serum calcium and parathyroid hormone did not increase, and the patients did not develop the recognized complications of primary hyperparathyroidism. Because of the complication of failed parathyroidectomy and because asymptomatic hyperparathyroidism was common, a more conservative approach was taken to its management. Fewer cases were referred for surgery and more were followed medically with no therapeutic intervention.

NIH CONSENSUS DEVELOPMENT CONFERENCE IN 1991

However, with the developments in imaging which held out the hope of improving surgical success by localization of the adenoma and reports that some “asymptomatic” patients actually felt better after parathyroidectomy, there was a need to establish guide lines for the management of patients with primary hyperparathyroidism, particularly the asymptomatic or mild form of the disease. Thus, in 1991 the NIH held a Consensus Development Conference on Diagnosis and Management of Asymptomatic Primary Hyperparathyroidism the proceeding of which were published as a supplement in the Journal of Bone and Mineral Research [1]. The consensus incorporated presentations from both North America and Europe which covered the etiology and epidemiology [2, 3], biochemical diagnosis [4-6], clinical spectrum, bone mass and fracture [7-9], evaluation [10-15], medical and surgical management and parathyroid localization [16-20]. Guidelines emerged for the management of patients with primary hyperparathyroidism in general. Further, it was concluded that there was subgroup of patients with asymptomatic primary hyperparathyroidism who could be safely followed by conservative medical management.

WORKSHOP ON ASYMPTOMATIC PRIMARY HYPERPARATHYROIDISM: A PERSPECTIVE FOR THE 21ST CENTURY

During the decade following the 1991 conference long-term results of following asymptomatic primary hyperparathyroidism with conservative medical management accumulated. Over the same time a number of new issues and questions emerged. Concerns on the long-term effect on bone mass and fracture was now being assessed by longitudinal measures of bone mass at spine, hip and forearm. The use of antiresorptive agents particularly bisphosphonates and selective estrogen receptor modulators were being successfully used to manage subjects with osteoporosis and fracture. The use of lithotripsy to manage urinary stone disease was becoming widely available. Research was providing new
information on the role of the calcium receptor in the pathogenesis of the hypercalcemic disorders. Imaging and surgical techniques aimed at improving the success of parathyroidectomy were being refined. Thus a Workshop on Asymptomatic Primary Hyperparathyroidism was convened in 2002 to update the guidelines for management of patients with asymptomatic primary hyperparathyroidism the proceedings of which were published in the Journal of Bone and Mineral Research [21]. The workshop again incorporated presentations from Europe and North America, but also from other continents. It cover a wide range of topics in primary hyperparathyroidism including clinical presentation and pathophysiological aspects, differential diagnosis, bone mass and fracture, clinical spectrum, kidney stone, vitamin D, and non classical effects, surgery and medical management [22-45]. The summary statement of the workshop outlined changes in guidelines for the management of patients with asymptomatic primary hyperparathyroidism from the censuses meeting in 1991 and the workshop in 2002 [46]. The statement recommended dropping 24hour urine calcium, creatinine clearance and abdominal x-ray and including spine and hip bone mineral density measured by DXA for monitoring asymptomatic primary hyperparathyroidism. It also recommended that surgery should be considered at serum calcium greater than 0.25 mmol/l above the normal range rather than 0.4 mmol/l and a bone mineral density T-score at any skeletal site less than 2.5.

REFERENCES

42. Marcus R. The role of estrogens and related compounds in the management of primary hyperparathyroidism. J Bone Miner Res 2002 ; 17 (Suppl 2) : N146-N149.