

Advances in the management of asymptomatic hyperparathyroidism

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Abstract

Asymptomatic primary hyperparathyroidism (PHPT), a condition defined as hyperparathyroidism that lacks specific symptoms or signs and with calcium levels of less than 1 mg/dL above the upper limit of normal, is a common clinical problem. Two previous conferences on the management of asymptomatic PHPT (a Consensus Development Conference and a National Institutes of Health workshop) indicated that medical monitoring rather than surgery is appropriate in certain patients with this condition. The Third International Workshop on the management of PHPT reviewed evidence that has become available since the last workshop in 2002. The purpose of this report is to describe recent advances reviewed during the third workshop on asymptomatic PHPT held in 2008.

Introduction and context

Primary hyperparathyroidism (PHPT) is increasingly being diagnosed as a result of the detection of hypercalcemia by widespread use of multiphasic screening. The increased diagnosis of hyperparathyroidism by screening tests has disclosed a population of patients who have subtle or absent symptoms and mild hypercalcemia (<1 mg/dL above normal), which indicate asymptomatic PHPT [1]. The asymptomatic aspect of PHPT has raised new questions about the natural history and the management of this disorder.

To develop guidelines for the management of asymptomatic PHPT, a Consensus Development Conference and a workshop were held at the National Institutes of Health in October 1990 and in April 2002, respectively [2,3]. The summary statements generated by the two workshops represented a distillation of thoughts of participants convened to discuss how to change the recommendations for physicians who care for patients with asymptomatic PHPT. The panel of experts in the two conferences considered questions specifically concerning asymptomatic PHPT in the US; the applicability

of the guidelines regarding asymptomatic PHPT to patients in other countries is not known. The two prior reports found that medical monitoring rather than surgery is appropriate in asymptomatic PHPT. However, as surgery is considered to be the definitive therapy even in asymptomatic patients, a decision to elect medical monitoring should follow guidelines regarding the severity of the manifestations of the disease and how patients should be appropriately monitored.

A third workshop was prompted by a number of issues that have arisen over the 6 years that followed the second workshop. To address these issues, in May 2008, a panel of international experts reviewed the evidence presented by authorities in the field in order to respond to a total of 22 prespecified questions assigned to four categories: (a) diagnosis of PHPT [4], (b) presentation of PHPT [5], (c) surgery for PHPT [6], and (d) medical management of PHPT [7].

Recent advances

The major differences in the management of asymptomatic PHPT between the last workshop and the previous

consensus conferences are reported in the summary statement from the Third International Workshop (please refer to [8] for the guidelines). Growing evidence for reversible aspects of PHPT (such as improvement in bone density, reduction in fractures, reduced frequency of kidney stones, and improvements in some neurocognitive elements) supports the greater use of parathyroidectomy by surgeons who are highly experienced in this operation. The present guidelines suggest that asymptomatic patients (no kidney stones, nephrocalcinosis, fractures, or other symptoms) should undergo surgery if they are under the age of 50, if their serum calcium is >1 mg/dL above normal, if their creatinine clearance is <60 mL/minute, or if they have a bone mineral density T-score of less than -2.5 at lumbar spine, hip, or forearm (the Z-score is used in men under 50 years of age and in premenopausal women). Hypercalciuria by itself is not considered an indication for surgery. The consensus remains that asymptomatic patients who do not meet surgical guidelines can be managed safely without surgery by the monitoring of biannual serum calcium levels, annual serum creatinine levels, and bone mineral density every 1-2 years at three sites. Pharmacological interventions have not been adequately evaluated and require further study. The workshop also identified the items to be placed on the research agenda for asymptomatic PHPT over the next decade [8].

Implications for clinical practice

Besides the guidelines for surgery and medical management outlined above, the main messages for the clinical management of asymptomatic PHPT, generated from active discussion during the Third International Workshop, can be summarized as follows: First, vitamin deficiency should be assessed in all patients suspected of having PHPT, and vitamin D deficiency should be cautiously corrected at the time it is detected. Second, advances in the field clearly indicate testing for the genetic forms of PHPT, especially in young subjects. Third, the presence of a fragility fracture provides clinical confirmation of osteoporosis and represents an

indication for surgical intervention independently of bone mass measurement. There is also growing support for the increased use of parathyroidectomy for asymptomatic PHPT, especially when performed by high-volume surgeons. Finally, cinacalcet, a drug that acts as a calcimimetic, can be very effective in normalizing serum calcium in PHPT, although it is approved in these settings in only some countries and long-term studies still need to be performed.

Abbreviation

PHPT, primary hyperparathyroidism.

Competing interests

The author declares that she has no competing interests.

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