



CME Digest

CONSERVATIVE VS SURGICAL TREATMENT OF HYPERPARATHYROIDISM: WHICH TO CHOOSE, AND WHEN?

In asymptomatic patients with hyperparathyroidism and mild hypercalcemia, what is the best approach to management?

On the side of surgical management, the following four arguments can be made. First, when carefully investigated, most patients actually have symptoms (eg, fatigue, weakness, depression, nonspecific abdominal pain, and constipation). Second, osteopenia may improve with parathyroidectomy, and older women may be at significant risk of accelerated bone disease with medical therapy alone. Third, the usual operation takes 2 hours, requires no blood transfusions, is associated with a success rate of over 95%, a complication rate of 5% to 6%, and rare mortality, and, in patients with no complications, hospitalization should not exceed 3 days. Fourth, the morbidity associated with medical therapy is unknown because many patients are “lost to follow-up” after 5 to 10 years.

On the other hand, the following case can be made for medical management. First, there is no evidence that prolonged elevated levels of parathyroid hormone are associated with clinically significant osteoporosis. Second, although randomized, controlled studies have not been done and many patients are lost to follow-up, there is little evidence of disease progression or deterioration of renal function in patients who have been followed. Third, long-term studies indicate that a substantial number of surgically treated patients with both adenomas and hyperplasia have recurrent disease after an interval of 10 years or more. And fourth, many of these patients are elderly and have cardiovascular disease, and so may be poor candidates for surgery.

In general, when hyperparathyroidism is diagnosed, the following patients should be considered candidates for surgical management: (1) all patients with a serum calcium greater than 12 mg/dL; (2) all patients, regardless of age, who have complications of the disease—bone disease, nephrocalcinosis, nephrolithiasis, peptic ulcer disease, pancreatitis; (3) all patients with significant symptoms (weakness, depression, gout, unexplained anemia) if that symptom interferes with quality of life (remember that “quality” varies with age); and (4) all patients below age 50 after excluding familial benign hypercalcemia in asymptomatic cases.

A conservative approach is recommended in patients over age 50 who are totally asymptomatic and have a serum calcium level less than 12 mg/dL, and in patients medically unfit for surgery for whatever reason. Thiazide diuretics, dehydration and volume contraction, prolonged bed rest or inactivity, and a high-calcium diet should all be avoided, since they tend to aggravate hypercalcemia. Moderate physical activity should be promoted. In addition, adequate hydration (six to eight glasses of water per day) and moderate calcium intake (600 to 800 mg every 24 hours) are to be encouraged. When selecting from among available agents, keep in mind that propranolol and cimetidine are ineffective, and that oral phosphates may be dangerous. Estrogens and progestins are useful in postmenopausal women. Unfortunately, oral diphosphonates, which may be the therapy of the future, are currently not well tolerated.

ZALMAN S. AGUS, MD
Renal and Electrolyte Section
University of Pennsylvania, Philadelphia

SUGGESTED READING

- Bilezikian JP. Surgery or no surgery for primary hyperparathyroidism. *Ann Intern Med* 1985; 102:402.
- Goldman L, Tosteson ANA. Uncertainty about postmenopausal estrogen—time for action, not debate. *N Engl J Med* 1991; 325:800.

Palmer M, Adami HO, Bergstrom R, et al. Survival and renal function in persons with untreated hypercalcemia. Population-based cohort study with 14 years of follow-up. *Lancet* 1987; 1:59.

Rao DS, Wilson RJ, Kleerekoper M, et al. Lack of biochemical progression or continuation of accelerated bone loss in mild asymptomatic primary hyperparathyroidism: evidence for biphasic disease course. *J Clin Endocrinol* 1988; 109:959.

Scholz DA, Purnell DC. Asymptomatic primary hyperparathyroidism. Ten-year prospective study. *Mayo Clin Proc* 1981; 56:473.

TREATING SLE NEPHRITIS: SOME GUIDELINES

While data concerning the use of total lymphoid radiation and cyclosporine show promise in the treatment of lupus nephritis, evidence is still anecdotal. A conservative approach that combines vigorous early treatment with long-term low-dose therapy is still the preferred method of treatment. The following points outline the basic tenets of this approach:

- Ideally, early treatment of lupus nephritis should start when the patient has diffuse proliferative lupus glomerulonephritis and a serum creatinine ≤ 1.2 .

- An accurate renal biopsy will help avoid over-treatment. Patients with mild involvement will respond well to a relatively modest therapeutic regimen.

- Short-term oral cyclophosphamide has proven to be as efficacious as other immunosuppressive regimens that have been added to prednisone.

- Intravenous cyclophosphamide should be used instead of oral cyclophosphamide if there is a possibility of poor patient compliance.

- Early treatment (for the first 4 to 8 weeks) should be as vigorous as possible, followed by a judicious tapering of prednisone with a long-term goal of alternate-day steroid therapy.

- The induction of a remission of glomerulonephritis, with a serum creatinine ≤ 1.4 mg/dL and a 24-hour urine protein ≤ 300 mg, is an important determinant of long-term prognosis.

- Prednisone may be required indefinitely for patients who have had severe lupus nephritis. Such patients should be followed closely, both systemically and nephrologically, since they are susceptible to recurrence.

- Systemic arterial hypertension and drug-associated renal damage and dysfunction are as much a

concern among these patients as in any population with chronic renal disease.

EDMUND J. LEWIS, MD
Section of Nephrology
Rush Presbyterian St. Luke's Medical Center
Chicago, Ill

SUGGESTED READING

Lewis EJ, Hunsicker LG, et al. Collaborative Study Group. A controlled trial of plasmapheresis therapy in severe lupus nephritis. *N Engl J Med* 1992; 326:1373-1379.

Schwartz MM, Bernstein J, Hill G, et al. Predictive value of renal pathology in diffuse proliferative lupus nephritis. *Kidney Int* 1989; 36:891-896.

Schwartz MM, Lan SP, Bonsib SM, Gephart GN, Sharma HM. Clinical outcome of three distinct histologic patterns of injury in severe lupus glomerulonephritis. *Kidney Int* 1989; 36:891-896.

HEMODIALYSIS-INDUCED HYPOTENSION: THE SEARCH FOR A CAUSE

Often during the course of dialysis, episodes of hypotension occur that can be severe enough to require interruption of dialysis and treatment with saline infusion. Among the proposed etiologic factors in dialysis-induced hypotension are (1) excessive fluid removal; (2) venodilation with venous sequestration of blood volume; (3) autonomic neural dysfunction, with the inability to counterbalance cardiovascular instability induced by fluid removal; and (4) autonomic disequilibrium with predominant vagal stimulation induced by the reduction of left ventricular volume.

Autonomic dysfunction in hemodialysis has been extensively studied as a cause of dialysis-induced hypotension; however, evidence suggests that the pathogenesis is more related to hemodynamic and volume factors. Studies at the Cleveland Clinic have shown that although the efferent parasympathetic pathway was abnormal in hemodialysis patients, adrenergic responses were generally normal. These findings could not be linked to the occurrence of dialysis-induced hypotension and, in fact, there were no differences between dialysis patients with and without hemodialysis-related hypotension.

Echocardiographic studies of dialysis patients at the Cleveland Clinic point out the importance of

intravascular volume redistribution between the central and peripheral segments of the circulation. Since these studies have demonstrated that unloading of the cardiopulmonary receptors is associated with a normal response of heart rate and diastolic blood pressure, we concluded that this redistribution of blood volume may provoke hypotension by mechanisms unrelated to any abnormality in the cardiopulmonary afferent reflex pathway.

Studies done at The Cleveland Clinic Foundation in collaboration with Southwestern University of Dallas, Texas, have shown that the hypotension was linked to acute paradoxical withdrawal of sympathetic vasoconstrictor drive, producing vasodepressor syncope. The stimulus leading to this response can be presumed to be the central hemodynamic unloading produced by venodilation. Venodilation during dialysis has been previously suggested by the finding of a reduction in cardiac output in association with improvement of indices of cardiac performance.

Dialysis-induced hypotension is an important clinical problem, the cause of which is under investigation. At present, its pathophysiology seems more related to hemodynamic factors and volume changes than to chronic adrenergic neural hypofunction.

FETNAT M. FOUAD, MD
Department of Heart and Hypertension Research
The Cleveland Clinic Foundation

SUGGESTED READING

Chaignon M, Chen WT, Tarazi RC, Bravo EL, Nakamoto S. Effect of hemodialysis on blood volume distribution and cardiac output. *Hypertension* 1981; 3(3):327-332.

Converse RL, Jacobsen TN, Toto RD, Jost CMT, Cosentino F, Fouad-Tarazi FM. Sympathetic overactivity in patients with chronic renal failure. *N Engl J Med* 1992; 327:1912-1918.

Nakashima Y, Fouad FM, Nakamoto S, Textor SC, Bravo EL, Tarazi RC. Localization of autonomic nervous system dysfunction in dialysis patients. *Am J Nephrol* 1987; 7(5):375-381.

THE CLEVELAND CLINIC FOUNDATION

25 YEARS OF MYOCARDIAL REVASCULARIZATION

CURRENT TECHNOLOGIES AND
CLINICAL CONTROVERSIES

ON VIDEO

FOR YOUR
CONTINUING EDUCATION

- Provocative debates
- State-of-the-art reviews
- Live demonstrations

PRICE INCLUDES:

- 8 videotapes
- Original symposium syllabus
- Book: *The Challenging Dream of Heart Surgery* by Rene G. Favaloro, MD
- Category I credit (14 hours)

VIDEO

Price:

U.S. \$425

INTERNATIONAL \$525

Specify: PAL SECAM OTHER

price includes shipping and handling

- Please charge the following account:
 VISA MASTERCARD Exp date: _____

Card number _____

Signature: _____
(Not valid without signature)

Total amount to be charged: \$ _____

To expedite credit card orders, fax this form to: (216)445-9406

- Check enclosed : \$ _____ All checks must be issued in US dollars drawn on a US bank

Please make checks payable to:

The Cleveland Clinic Educational Foundation

Please print

Name _____

Address _____

City _____ State _____ Zip _____

Country _____

Fax () _____ Home phone () _____

Business phone () _____

Mail order form to:

The Cleveland Clinic Educational Foundation
Department of Continuing Education TT-31
9500 Euclid Avenue
Cleveland, OH 44195
1-800-762-8173