DEPARTMENT OF INTERNAL MEDICINE

SECTION OF ENDOCRINOLOGY

CLINICAL PRACTICE GUIDELINES

HYPERCALCEMIA IN PRIMARY HYPERPARATHYROIDISM

SIGNS AND SYMPTOMS

Mild Hypercalcemia

* Usually asymptomatic

More Severe Hypercalcemia

* Neurological – mild drowsiness, weakness, depression, lethargy, stupor, coma, hypotonia, hyporeflexia
* Gastrointestinal – constipation, nausea, vomiting, anorexia, peptic ulcer disiease
* Renal – Nephrogenic Diabetes Insipidus (DI), decreased GFR, nephrolithiasis, nephrocalcinosis, polyuria, nocturia, dehydration
* Cardiovascular – increased myocardial contractility, shortened ventricular systole, hypotension, syncope from arrhythmias

DIAGNOSIS

Lab tests, Physical Exam and History

Confirm hypercalcemia

* Measure total serum calcium and ionized calcium at least twice

Obtain detailed history, physical exam, review prior routine chemistry results

* Inquire about past kidney stones, fractures, weight loss, bone pain, fatigue, vitamin and mineral ingestion, lithium and diuretic use

Measure serum Parathyroid Hormone (PTH) intact

* Elevated PTH with hypercalcemia usually indicates primary hyperparathyroidism

Exceptions: Familial hypocalciuric hypercalcemia (FHH), autonomous parathyroid secretion and rarely, ectopic malignant neoplasm

* Low-undetectable PTH suggests parathyroid-independent hypercalcemia
* Evaluate patient for malignancy (most often, malignancy will already be known)
* If malignancy is not present, search for unusual causes of hypercalcemia

TREATMENT DECISION

Indications for Surgery:

Surgery is indicated for patients with primary hyperparathyroidism if any of the following are present:

* Symptoms of hypercalcemia
* Serum calcium >0.25 mmol/l (1 mg/dl) above upper limit of normal
* Creatinine clearance reduced by >30% compared to age- matched healthy individuals
* History of life-threatening hypercalcemic episode
* Patient < 50 years old

PARATHYROIDECTOMY

* An option for patients with primary hyperparathyroidism
* Controversy of medical versus surgical management of asymptomatic hypercalcemic patients
* Cost, compliance, and long-term follow-up are some arguments against medical management
* Surgery is the only permanent cure
* Routine localization is not usually necessary
* Effects: 95% of patients achieve normocalcemia, if performed by experienced surgeon and pathologist
* Complications: Vocal cord paralysis, permanent hypoparathyroidism

MEASURES TO LOWER SERUM CALCIUM

Mild Asymptomatic Hypercalcemia:

* Stop any medication that may cause hypercalcemia e.g. thiazide diuretics
* Patients should avoid diuretics
* Patients should avoid prolonged immobilization
* Maintain adequate hydration
* Patient should seek immediate medical attention for illness that may cause dehydration especially severe vomiting or diarrhea
* If patient becomes symptomatic, they should be referred to a surgeon immediately

Acute Severe Hypercalcemia:

* Monitor patient closely preferably in the ICU setting especially if with forced dieresis- monitor CVP, plasma or urine electrolytes, may need to catheterize the bladder
* Diagnostic testing should occur while aggressive calcium lowering treatment is initiated
* Primary hyperparathyroidism will benefit from immediate surgery

Fluids:

* Restore normal hydration –Patient is usually dehydrated from vomiting, or defective urinary concentrating ability
* If serum calcium >2.8 mmol/l (11.2 mg/dl), patient needs to be instructed to drink 2-3 L/day of low calcium liquids
* If serum calcium >3 mmol/l (12 mg/dl):

Infuse NaCl 0.9% at 2-6 L/day IV which will increase calciuria.

Loop diuretic may be added to improve dieresis.

Potassium and magnesium depletion needs to be prevented.

If diuresis proves unsuccessful:

* Hemodialysis is the treatment of choice. Dialysis bath should be free of or low in calcium.

PHARMACOTHERAPY

Primary Hyperparathyroidism:

* Estrogen replacement – in postmenopausal women, estrogen replacement may lower serum calcium with no effect on PTH; protects against bone loss
* Bisphophonates – further study is needed to prove usefulness in mild hypercalcemia caused by primary hyperparathyroidism

Acute Severe Hypercalcemia:

* Loop diuretics – Stimulates natriuresis which is accompanied by calciuresis
* Bisphosphonates – high affinity for bone especially in areas of increased bone turnover where they inhibit bone resorption;

Depending on agent used, may take a few days to reach normocalcemia;

Example: Pamidronate – serum calcium starts to decrease 1-2 days after administration and normocalcemia usually occurs within 1 week of single dose; hypocalcemic effects last for a month

* Calcitonin – blocks bone resorption through receptors on osteoclasts, increases urinary calcium excretion by blocking renal tubular calcium reabsorption; may be used in combination with rehydration and saline dieresis within the 1st 24 hours of treatment until bisphosphonates take effect
* Glucocorticoids – in pharmacologic doses, cause an increase in urinary calcium excretion and decrease in intestinal calcium absorption

FOLLOW-UP

Post-parathyroidectomy patient:

* Monitor serum and urine calcium to avoid hypo- or hypercalcemia
* Give calcium supplement for >/= 1 year to increase bone density

Primary Hyperparathyroidism patient managed medically:

* Follow-up patient every 6 months
* Measure BP, serum calcium and creatinine at each visit
* Perform yearly abdominal radiographs, urinary calcium and bone mineral density (BMD)tests