2013

Should Coenzyme Q10 Be Used to Lower Blood Pressure in Asymptomatic Patients?

Daniella Barker and José Rodríguez

What is the best way to diagnose clinically suspected prolactinomas of the pituitary?

Evidence-Based Answer

In patients with a single elevated serum prolactin level (SPL), the test should be confirmed with a repeat morning measurement followed by a clinical evaluation for secondary causes (SOR: **C**, consensus guidelines). Patients with persistently elevated SPL and no clear cause should undergo gadolinium-enhanced magnetic resonance imaging (MRI) to identify possible pituitary adenomas, regardless of the degree of SPL elevation (SOR: **B**, retrospective cohort study).

Consensus guidelines by the Endocrine Society and the Pituitary Society Expert Committee recommend that patients with repeatedly elevated, appropriately obtained morning SPL should be evaluated by ruling out secondary causes with a careful history and physical examination; pregnancy test; and kidney, liver, and thyroid function analyses.[1,2] Drugs associated with hyperprolactinemia (eg, antipsychotics, neuroleptics, monamine-oxidase inhibitors, selective serotonin reuptake inhibitors, opiates, verapamil, methyldopa, reserpine, metoclopramide, domperidone, H2-blockers, estrogen, etc) should be withdrawn if possible and re-measurement of SPL performed. After excluding possible secondary causes of an elevated SPL, gadolinium-enhanced MRI should be performed to evaluate for pituitary adenoma.

A retrospective cohort study of 104 consecutive female patients (mean age 30 years) with hyperprolactinemia evaluated in a university hospital reproductive endocrinology clinic over a 5-year period sought to establish guidelines for the minimum SPL for which pituitary imaging is indicated.[3] Pregnancy, lactation, and medications associated with hyperprolactinemia were exclusion criteria. Initial evaluation included measurements of thyroid-stimulating hormone, estradiol, luteinizing hormone, and follicle-stimulating hormone. SPL measurements were repeated at the endocrinology clinic initial evaluation to confirm persistent elevation (ie, >25 ng/mL). The median SPL was 82.6 ng/mL. A diagnosis of polycystic ovarian syndrome was made in 8 patients, premature ovarian failure in 2, and hypothyroidism in 2. The remaining 86 underwent gadolinium-enhanced MRI testing.

Twenty-three patients (26%) had normal MRI findings, 47 (55%) had microadenomas <10 mm, and 16 (19%) had macroadenomas >10 mm. A SPL level >100 ng/mL was associated with a diagnosis of macroadenoma (OR 7.6; 95% CI, 1.39–55.02; P<.01). For patients with microadenomas, 52% had SPL <100 ng/mL. But 11% of microadenoma patients had SPL levels >200 ng/mL and 44% had a SPL level between 25 and 200 ng/mL. These investigators recommended imaging all patients with persistent elevations of SPL regardless of the value.[3]

Brandon M. Thurow, MD
Darrell R. Over, MD, MSc
UAMS, AHEC (South Central) FMRP
Pine Bluff, AR

1. Melmed S, et al. *J Clin Endocrinol Metab.* 2011; 96(2):273–288. **[LOE 5]**
2. Casanueva FF, et al. *Clin Endocrinol.* 2006; 65(2):265–273. **[LOE 5]**
3. Bayrak A, et al. *Fertil Steril.* 2005; 84(1):181–185. **[LOE 1b]**

Should coenzyme Q10 be used to lower blood pressure in asymptomatic patients?

Evidence-Based Answer

Coenzyme Q10 (CoQ10) may lower systolic and diastolic blood pressures in patients with primary hypertension, but is not recommended as an antihypertensive treatment (SOR: **C**, systematic review of low-quality RCTs using disease-oriented outcomes).

A 2009 systematic review identified 3 RCTs with a total of 96 patients that evaluated the effects of CoQ10 (100–120 mg/d) on heart rate and blood pressure for at least 3 weeks.[1] Each study evaluated adult patients with primary hypertension (systolic blood pressure [SBP] >140 mmHg or diastolic blood pressure [DBP] >90 mmHg). In some cases the patients used CoQ10 alone as an antihypertensive treatment, while in others the patient paired CoQ10 with additional antihypertensive treatments. Patients with creatinine levels >1.5 times normal were excluded. All studies had a mandatory washout period of at least 2 weeks before treatment with CoQ10.

CoQ10 lowered SBP by an average of 10 mmHg (95% CI, 7.7–14) and DBP by 6.6 mmHg (95% CI, 5.2–8.1) compared with placebo. In 1 of the reviewed trials (N=58), CoQ10 reduced patients' heart rate by 12 beats per minute (95% CI, 8.8–15) compared with placebo. The studies did not provide sufficient data to

construct a dose–response curve, nor did they provide data on patients who dropped out.[1]

The authors concluded that because of the inherent bias in each of the reviewed studies, they would not recommend CoQ10 as an antihypertensive agent. The authors were also unable to find any studies that showed that CoQ10 was ineffective, or any head-to-head trials against other hypertensive medications.[1]

Daniella Barker, MS
José E. Rodríguez, MD
FSU College of Medicine
Tallahassee, FL

1. Ho MJ, et al. *Cochrane Database Syst Rev.* 2009; (4):CD007435. **[LOE 2a]**

How does the intensity of therapy to lower HbA1c affect long-term cardiovascular risk in patients with type 2 diabetes mellitus?

Evidence-Based Answer

Intensive glycemic control (glycosylated hemoglobin [HbA1c] <6%) is associated with significantly lower rates of nonfatal myocardial infarction (MI) and coronary heart disease (CHD) compared with standard glycemic control; however, there does not appear to be a benefit on all-cause mortality (SOR: **A**, meta-analysis of RCTs).

A 2009 meta-analysis of 5 prospective RCTs (UKPDS, ADVANCE, VADT, ACCORD, and PROactive trials) compared the rates of nonfatal MI, CHD, cerebrovascular accident, and all-cause mortality in patients with type 2 diabetes mellitus assigned to intensive glycemic control (HbA1c <6%) or standard glycemic control (HbA1c 7%–7.9%).[1] There were a total of 33,040 participants, with 17,267 participants receiving intensive glycemic control followed over 5 years.

A 17% reduction (OR 0.83; 95% CI, 0.73–0.93) in nonfatal MI and a 15% reduction (OR 0.85; 95% CI, 0.77–0.93) in CHD events was noted in the intensive glycemic control group. There was no significant change in stroke events (OR 0.93; 95% CI, 0.81–1.1) or all-cause mortality (OR 0.93; CI, 0.87–1.2).[1]

A subsequent prospective cohort study in the Zwolle region of the Netherlands followed 1,145 patients with type 2 diabetes mellitus in a primary care setting for a median of 5.8 years.[2] The patients achieving a mean HbA1c of <6.5% did not have a reduction in all-cause mortality (HR 1.1; 95% CI, 0.71–1.7) or cardiovascular mortality (HR 0.94; 95% CI, 0.47–1.9).

Robert Uniszkiewicz, MD
Elias Banuelos, MD
Brian Schmidt, DO
Naval Hospital Pensacola FMR
Pensacola, FL

1. Ray KK, et al. *Lancet.* 2009; 373(9677):1765–1772. **[LOE 1a]**
2. Landman GW, et al. *Br J Gen Pract.* 2010; 60(572):172–175. **[LOE 2b]**

How do you treat perioral dermatitis?

Evidence-Based Answer

Treatment with oral tetracycline and discontinuation of any cosmetics or topical corticosteroids are effective management strategies for perioral dermatitis (POD) (SOR: **A**, systematic review). The use of pimecrolimus cream 1% applied twice daily for up to 4 weeks is also effective (SOR: **A**, consistent RCTs).

In a systematic review of 30 RCTs on the treatment of POD, 2 studies (207 patients) were of medium-range quality and the remaining 28 studies (1,261 patients) were of low quality.[1] The authors were unable to combine the data. However, the authors concluded there was "consistent evidence" of effectiveness with oral tetracycline and, to a lesser extent, with the discontinuation of any cosmetics or topical corticosteroids.

Two subsequent RCTs evaluated pimecrolimus for POD. The first study compared pimecrolimus cream 1% applied twice daily for 1 month with placebo in 40 adults.[2] The disease severity was assessed by the Perioral Dermatitis Severity Index (PODSI) score (the sum of individual scores [0–3] for erythema, papules, and scaling).

The reduction in PODSI score for the pimecrolimus group was significantly greater than that of the placebo group over the entire treatment period (pimecrolimus 4.5 to 1.6; placebo 4.6 to 2.6; P=.02). Four weeks after completion of therapy, no significant differences were observed between the pimecrolimus group and placebo. The median time until 50% of patients attained at least a 50% reduction of PODSI from baseline was 1 week with pimecrolimus treatment and 4 weeks with placebo (P=.02).[2]