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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

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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).

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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
In the second RCT, 124 adult patients with POD were randomized to pimecrolimus 1% twice daily for 1 month or placebo. After treatment, the pimecrolimus group had an average PODSI score of 2.6 versus 3.5 for the placebo group (between-group difference 0.9; 95% CI, 0.4–1.4; \(P=0.001\)). The subgroup of patients (n=35) with topical corticosteroid-associated POD had a mean PODSI score of 5.4 at baseline and 2.3 on day 29 with pimecrolimus. Patients with steroid-associated POD receiving placebo had a PODSI score of 5.4 at baseline and 4.2 on day 29 (between-group difference 1.9; 95% CI, 0.6–3.1; \(P=0.007\)).

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What is the optimum frequency for corticosteroid injections of the knee?

**Evidence-Based Answer**

The evidence is limited on the optimum frequency of intra-articular corticosteroid (ICS) injections of the knee for treatment of osteoarthritis (OA). Current guidelines recommend ICS injections be performed no more frequently than every 3 months (SOR: C, expert opinion).

A randomized, double-blind, placebo-controlled trial of 66 patients between 40 and 80 years of age with radiologic evidence of OA compared the efficacy (pain) and safety (joint space width) of a scheduled ICS injection with placebo. The ICS group received injections (triamcinolone acetonide, 1 cc of 40 mg/mL) every 3 months over the course of 2 years while the placebo group received saline injections over the same period. Outcomes measured were improvement in subjective pain indices as well as joint space width (JSW) on X-ray.

The radiologic evaluation of JSW performed at study entry (ICS 4.1 mm vs placebo 3.9 mm), year 1 (ICS 4.0 mm vs placebo 3.9 mm), and year 2 (ICS 4.0 mm vs placebo 3.9 mm), revealed no significant differences between treatment groups and no signs of disease progression. At 1 year, the ICS group had significant improvement in range of motion (ICS 4.4° vs placebo 2.7°; \(P<0.05\)). At 2 years the area under the curve analysis for differences in scores on the WOMAC VA 3.0 (visual analog scale, measuring 0–100, with 0 being no pain or stiffness) from baseline to month 24 showed significant differences between groups favoring ICS for night pain (ICS −0.66 vs −0.31 placebo; \(P=0.0047\)) and joint stiffness (ICS −0.636 vs −0.320 placebo; \(P=0.05\)).

A retrospective cohort analysis over a 20-year period studied 65 patients (35 rheumatoid arthritis and 30 OA) receiving ICS injections of varying frequency (interval not less than every 4 weeks) over a period of 4 to 15 years. The total injection count varied from 15 injections in 4 years to 167 injections over 12 years. Post hoc radiographs compared with earlier films did not reveal any correlation between frequency or total injection count and joint deterioration.

A consensus guideline from the American College of Rheumatology states that ICS injections should be given no more than every 3 months per joint for a maximum of 4 per year. This recommendation is based on concerns for steroid and crystal arthropathy, which have been variably reported in the human and animal literature.

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What is the utility of imaging studies in adult patients after a first-time seizure?

**Evidence-Based Answer**

Neuroimaging with computed tomography (CT) is abnormal in up to half of unselected adult patients with a first-time seizure, resulting in a change in diagnosis in 44%, change in disposition in 26%, and change in acute management in 9%–17%. (SOR: B, systematic reviews of cohorts studies).

An American Academy of Neurology (AAN) subcommittee conducted a systematic review to examine the effects of neuroimaging on the management of the adult emergency patient presenting with a first-time seizure. The authors searched for English-language