

estrogen administration were not associated with a marked increase in the risk of breast cancer in postmenopausal women.

Original article Lyytinen H *et al.* (2006) Breast cancer risk in postmenopausal women using estrogen-only therapy. *Obstet Gynecol* **108**: 1354–1360

Topiramate improves weight loss and glycemic control in obese patients with diabetes

The anticonvulsant topiramate causes dose-dependent weight loss in humans and in animal models of diabetes. Toplak and colleagues, therefore, investigated the efficacy and safety of topiramate as an antiobesity medication in patients with diabetes.

This international, randomized, double-blind, placebo-controlled trial included 640 obese patients (BMI 27–50 kg/m²) with type 2 diabetes. All patients continued metformin monotherapy and participated in a lifestyle-intervention program (hypocaloric diet, exercise and advice). After a 6 week placebo treatment period, patients were randomly allocated to receive placebo ($n=208$), topiramate 96 mg ($n=219$), or topiramate 192 mg ($n=213$) daily. About 80% of participants reached the target doses. The study was terminated early because the sponsor switched funding to development of controlled-release topiramate.

After 24 weeks, weight losses of 4.5% and 6.5% were achieved in patients who received 96 mg and 192 mg topiramate daily, respectively, compared with 1.7% in placebo-treated patients ($P<0.001$ for both comparisons). Glycated hemoglobin levels and systolic blood pressure improved in topiramate-treated patients. Weight loss continued in patients who continued topiramate therapy beyond 24 weeks. More topiramate-treated than placebo-treated patients withdrew owing to intolerable adverse events (13% versus 7%); most withdrawals were related to cognitive or neurological symptoms and fatigue, and occurred in patients given the highest topiramate dose.

The authors assert that topiramate is an effective antiobesity medication in obese patients with diabetes, and also improves patients'

glycemic control; however, these results require confirmation.

Original article Toplak H *et al.* (2007) Efficacy and safety of topiramate in combination with metformin in the treatment of obese subjects with type 2 diabetes: a randomized, double-blind, placebo-controlled study. *Int J Obes (Lond)* **31**: 138–146

C-peptide replacement: a possible treatment for diabetic neuropathy

Chronic hyperglycemia can lead to microvascular injuries, which subsequently cause damage to peripheral nerve fibers. Ekberg and colleagues proposed that in type 1 diabetes a deficiency of C peptide, a subunit of the proinsulin molecule, also contributes to nerve damage; their animal studies showed that C-peptide administration ameliorated structural and functional symptoms of diabetes-induced neuropathy. The same authors have now investigated whether C-peptide treatment improves peripheral nerve function in patients with type 1 diabetes and peripheral neuropathy.

In total, 139 patients (mean age 44.2 ± 0.6 years), who had had type 1 diabetes for 30.6 ± 0.8 years and had manifest neuropathy, completed the protocol. Patients were randomly assigned to receive daily subcutaneous injections of replacement-dose C peptide (1.5 mg), high-dose C peptide (4.5 mg), or placebo, for 6 months.

At baseline, sensory nerve conduction velocity (SCV) in the sural nerve was reduced in all participants compared with normal values. After 6 months, the proportion of patients whose SCV improved by >1 m/s was greater in the C-peptide-treated groups than in the placebo-treated group (37% versus 19%, $P<0.032$). This improvement, which was independent of the C-peptide dose and changes in glycemic control, was particularly evident in those patients who had the least-impaired SCV at baseline. The authors conclude that C-peptide treatment at a replacement dose for 6 months improves early neuropathic symptoms of type 1 diabetes, and they stress the importance of early intervention.

Original article Ekberg K *et al.* (2007) C-peptide replacement therapy and sensory nerve function in type 1 diabetic neuropathy. *Diabetes Care* **30**: 71–76