**Co-enzyme Q10**

**Introduction**

Co-enzyme Q10 (CoQ10) is a lipid soluble chemical ubiquitous to all cell membranes. It was first isolated in beef heart mitochondria in 1957. It plays a crucial role in energy production within cells. Low levels of CoQ10 in diseases such as maternally inherited diabetes and deafness (MIDD), Huntington’s disease, Parkinson’s disease, statin-related myopathy and myotonic dystrophy have led to postulation that the repletion of CoQ10 could improve mitochondrial respiration and cellular function leading to appreciable clinical improvement.

The importance of CoQ10 as an antioxidant and its high concentration in highly differentiated cells such as those in endocrine and cardiac tissues have led to a belief that it may be a beneficial supplement in hypertension, diabetes and cardiovascular disease.

**Pharmacology**

Figure 1 outlines the function of CoQ10 as a mobile electron carrier in mitochondrial oxidative phosphorylation which in turn synthesises ATP (adenosine triphosphate). It is synthesised in mitochondria and a small amount is absorbed from the diet. CoQ10 is present at high concentrations in tissues with high energy requirements including the nervous system, eye, muscle and endocrine organs. It also acts as an antioxidant protecting cell membranes from oxidation and preventing peroxidation of circulating lipoproteins.

CoQ10 is widely sold as a health supplement and there are many brands and formulations available. MitoQ is a mitochondria-specific antioxidant analogue of CoQ10 that is being developed for better mitochondrial CoQ10 uptake.

The inter-individual variation of CoQ10 absorption makes it difficult to predict the effect of supplementation on plasma CoQ10 levels. Absorption is also affected by the amount of fat intake taken with the supplement.

CoQ10 is transported by cholesterol and low-density lipoprotein (LDL) in the blood stream and plasma CoQ10 levels correlate to cholesterol and LDL levels. Plasma CoQ10 levels are not a direct reflection of mitochondrial...
CoQ10 levels making it difficult to interpret the clinical significance of results. At present, measuring mitochondrial CoQ10 levels would require tissue biopsy which is impractical.

CoQ10 is metabolised in the liver and excreted in bile and faeces.

Trials of safety and efficacy

Formulations used in studies vary making comparisons between trials difficult but clinical safety of CoQ10 appears good. A large trial involving 3500 patients with heart failure and a follow-up period of up to seven years noted a 0.8% incidence of minor side effects.

A meta-analysis of 362 patients from three randomised controlled trials (RCTs), one crossover study and eight open label studies found that CoQ10 reduced systolic blood pressure (BP) by a range of 11–17mmHg and diastolic BP by a range of 8–10mmHg in hypertensive patients. There are several limitations to the result of this meta-analysis. Nine of the studies stopped their subjects’ antihypertensives two weeks prior to the study. This resulted in a high pre-study BP, hence the range of BP reduction may be far lower in a clinical setting where patients are established on traditional antihypertensives. The dose of CoQ10 was variable across the studies, ranging from 34–225mg/day; with concurrent use of statins varying the dose required to achieve therapeutic serum levels. Importantly, none of the studies noted any major side effects from the use of CoQ10. Only four of the 12 studies commented on side effects. Three of the studies reported no side effects or no statistically significant side effects. One study reported side effects such as nausea, flatulence and headache in 13% (n=23).

Specific evidence for use in diabetes

Type 2 diabetes (T2DM). Several studies have looked specifically at the use of CoQ10 use in T2DM patients. In 2002, Hodgson et al. conducted a double-blind RCT investigating CoQ10 200mg/day vs placebo supplementation in 74 patients with T2DM and dyslipidaemia. After 12 weeks there was a significant decrease in HbA1c (-0.37±0.17%, p=0.032) and systolic (-6.1±2.6mmHg, p=0.021) and diastolic (-2.9±1.4mmHg, p=0.048) BPs.1

The same group also looked at the independent and combined effects of CoQ10 200mg/day and fenofibrate 200mg/day on brachial artery blood flow in patients with T2DM and dyslipidaemia. First, they demonstrated that these patients had a poorer blood flow response to endothelial and non-endothelial markers of vasodilatation as compared to a group of 18 normal patients. They then showed that only a combination of CoQ10 and fenofibrate significantly improved endothelial and non-endothelial vasodilatation (12% increase towards acetylcholine [p=0.001]; 22% increase towards bradykinin [p=0.016]; 10% increase towards sodium nitroprusside [p=0.006]; 31% increase towards acetylcholine and N^G-monomethyl-L-arginine [p<0.001]). A later crossover study by the same investigators showed that T2DM patients (n=23) treated with statins did not have any change in glycaemic control, BP or lipids when supplemented with CoQ10 200mg/day. They did demonstrate an improvement in endothelial dysfunction; brachial artery flow mediated dilatation increased by 1.0% (p=0.04).2

In contrast, a larger double-blind RCT in Singapore looked at 80 T2DM patients who did not have any major diabetic complications. It showed that CoQ10 200mg/day did not alter brachial artery flow to acetylcholine and sodium nitroprusside significantly. Additionally, systolic and diastolic BPs were not found to be significantly reduced.3

In summary, the use of CoQ10 in patients with T2DM has produced mixed results in small heterogeneous studies and is not proven to have clinically significant benefits.

Mitochondrial diabetes. MIDD is the most common form of mitochondrial diabetes and is usually associated with a 3243 (A>G) mutation of mitochondrial DNA. It is characterised by both a defect in insulin secretion, which progresses to insulin dependence, and sensorineural hearing loss. There are no specific treatments for the deafness and impaired insulin secretion of MIDD.

All trials of CoQ10 in MIDD have been small, open label, and not subject to either double-blinding or randomisation. In part this is due to the low prevalence of the diseases being studied. One open-label trial involving 28 patients with MIDD, seven patients with impaired glucose tolerance and 3243 mutation, and 15 patients with normal glucose tolerance and 3243 mutation showed that treatment with CoQ10 150mg/day for three years reduced hearing loss and improved insulin secretion and blood lactate post exercise.4

In a Cochrane review of the treatment of mitochondrial disorders, the lack of large RCTs meant that use of CoQ10 in mitochondrial disorders could not be supported. The Cochrane group has concluded that more trials with clinically relevant end-points are needed to identify effective novel therapy in mitochondrial disorders.

Discussion

There is not enough robust clinical evidence to support the routine use of CoQ10 supplementation in clinical practice in any form of diabetes. Although evidence for use of CoQ10 supplementation is lacking, it is readily available without prescription and appears to have few major reported adverse effects, and therefore its use is likely continue. In MIDD the rarity of the condition makes robust clinical studies of CoQ10 less likely to be forthcoming and, as there are no effective treatments, it is likely that some patients will continue to use CoQ10 supplementation.

Declaration of interests

There are no conflicts of interest declared.

References

References are available at www.practicaldiabetes.com.
References