Fludrocortisone

Notes. Fludrocortisone binds to mineralocorticoid receptors (MR) and activates pre-existing Na⁺ channels in the early phase via complex signalling pathways. In the later phase it activates transcription and translation of proteins to increase Na⁺ transport channels and reabsorption of Na⁺ into the circulation.

Introduction

Autonomic neuropathy is a common complication of diabetes with up to 40% affected. It is often asymptomatic, but one of the most troublesome and under-appreciated features is postural hypotension. This is a consequence of cardiac and peripheral vasomotor nerve damage, leading to an inability to increase the heart rate and vasoconstrict peripheral blood vessels when changing posture. Symptoms of postural hypotension include dizziness, weakness, blurred vision, tiredness, and loss of consciousness. These are usually more marked on waking or in the early morning. The diagnosis can be made when there is a drop in the systolic blood pressure of at least 20mmHg when checked at least 1 minute after standing, and there are usually abnormalities on cardiovascular reflex testing using electrocardiography.

Once symptoms arise, the autonomic damage is likely to be irreversible and the prognosis is poor due to concurrent complications such as cardiac or renal disease. There is little in the way of causal treatment. Supportive measures such as compression stockings and giving patients advice on changing position can be used with varying degrees of success. Pharmacological treatment with fludrocortisone is one option for symptom control.

Pharmacology

Figure 1 outlines the pharmacological action of fludrocortisone. It is a mineralocorticoid belonging to the class of compounds known as 21-hydroxysteroids. It is highly potent with a half-life of 3.5 hours and is
postural hypotension caused by recom m ends gradually reducing the dose over weeks or months on efficacy data are lacking there are should carry a steroid card. The SPC well-known, predictable side effects induce expression of Na⁺ channels, ber of proteins. These proteins undergoes conformational change that assessed the use of fludrocortisone in patients with symptomatic pos- tural hypotension that was associated with Parkinson’s disease and with chronic fatigue syndrome. In 17 patients with Parkinson’s disease there was an improvement in a com- posite autonomic symptom score after three weeks of fludrocortisone 100µg, with no significant effect on blood pressure. In 100 patients with chronic fatigue randomised to nine weeks of placebo versus fludrocortisone 100µg the latter was no better than placebo on a global wellness score or measures of blood pressure.

Specific evidence for use in diabetes
There has been one small, short trial that assessed the use of fludrocorti- sone in patients with diabetes, auto- nomic neuropathy and symptomatic postural hypotension. This was a double-blind, crossover randomised control trial in six patients. Patients were given fludrocortisone 100µg or placebo twice daily for three weeks, followed by a three-week washout period, then crossover to three weeks of the alternative treatment. The results showed a statistically significant improvement in both systolic (154±29mmHg versus 110±16mmHg; p<0.005) and dias- tolic blood pressure (88±11mmHg versus 76±4mmHg; p<0.05) on both tilt table testing and with supine blood pressures (180±26mmHg versus 149±21mmHg; p<0.05) compared to placebo. In four patients there was significant improvement in symptoms. The other two patients had low albumin and developed ankle oedema. All patients had an increase in plasma blood volume but no change in serum or plasma osmolalities.

Following this trial, the same group followed up 14 patients with diabetes and postural hypotension who were using fludrocortisone for 12 months with similar effective results. It was concluded that fludrocortisone 100–300µg was effective in the treatment of postural hypotension secondary to diabetic autonomic neuropathy.

Discussion
Postural hypotension is an under-appreciated and often frustrating and debilitating symptom of auto- nomic neuropathy as a complication of diabetes. A NICE evidence summary on the use of fludrocortisone for postural hypotension from October 2013 states that any pharmacological treatment for postural hypotension needs to be given ‘off licence’ as no drug used in the UK currently has marketing authorisation for the treatment of postural hypotension. The studies described above are summarised by NICE to support decision making for an individual patient, but the summary is not NICE guidance.

Although the trials were small, short and underpowered and the long-term efficacy is uncertain, the results in two small trials in patients with diabetes demonstrate that fludrocortisone may have a role to play in orthostatic hypotension secondary to diabetic autonomic neuropathy for up to 12 months; fludrocortisone will likely remain the recommended first choice for the immediate treatment for the symptoms of postural hypotension in this patient population.

Declaration of interests
There are no conflicts of interest declared.

References
References are available in Practical Diabetes online at www.practicaldiabetes.com.
References