Nifedipine Gastrointestinal Therapeutic System (GITS)
A Review of its Pharmacodynamic and Pharmacokinetic Properties and Therapeutic Efficacy in Hypertension and Angina Pectoris

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Summary

Nifedipine 'gastrointestinal therapeutic system' (GITS) is a recently developed formulation that slowly releases the drug into the intestinal tract over a 24-hour period. When administered once daily, it is of similar efficacy to sustained release formulations of felodipine, verapamil, and diltiazem and at least as effective as standard formulations of lisinopril and enalapril, and long-acting propranolol and atenolol in the treatment of patients with mild to moderate essential hypertension. Substitution of nifedipine GITS for conventional formulations of nifedipine, diltiazem or verapamil, maintained adequate control of anginal symptoms in patients with stable angina pectoris.

Nifedipine GITS appears to maintain quality of life and is apparently better tolerated than those formulations of nifedipine which require 2 or 3 times daily administration in both elderly and younger patients. In addition, it has minimal effect on lipid and glucose metabolism and reverses left ventricular hypertrophy, and is thus suitable for treatment of the majority of patients with mild to moderate hypertension or angina pectoris.

Pharmacodynamic Properties

The primary action of nifedipine is inhibition of the influx of calcium through cardiac and smooth muscle cell membranes by blockade of L-type voltage-operated and possibly receptor-operated calcium channels. In patients with mild to moderate essential hypertension, repeated administration of nifedipine GITS decreased systolic blood pressure (SBP) and diastolic blood pressure (DBP) by 8 to 14% and 7 to 15%, respectively, while having minimal effect on heart rate. Principally, as a result of peripheral arterial dilatation, nifedipine causes a reduction in systemic vascular resistance and therefore, afterload. The drug has a direct negative inotropic effect (in vitro and following intracoronary administration), although this is usually not observed following oral administration.

Long term treatment with nifedipine GITS reversed left ventricular hypertrophy and was associated with improved left ventricular filling and diastolic performance. The drug also increased renal blood flow and glomerular filtration rate, induced natriuresis during increased dietary sodium intake and blunted the response of the renin-aldosterone axis to changes in dietary sodium intake. Treatment with nifedipine GITS for periods of up to 12 weeks had no consistent effect on either lipid or glucose metabolism.

Pharmacokinetic Properties

The nifedipine GITS two-layered tablet utilises an osmotically driven 'push-pull' mechanism whereby nifedipine particles contained in an osmotic drug core become suspended in solution and are pushed into the intestinal tract by expanding active polymers. The oral bioavailability, relative to that of conventional nifedipine formulations, is 75 to 85% at steady-state and the formulation has linear pharmacokinetic behaviour. Mean maximum plasma concentrations (C_{max}) were similar in healthy elderly (67 µg/L) and younger volunteers (62 µg/L) following repeated administration of nifedipine GITS 60mg once daily. Compared with the twice daily sustained release formulation of nifedipine, the GITS formulation had a lower C_{max}, a longer time to C_{max}, a higher trough concentration and a smaller peak-trough fluctuation. However, the area under the plasma concentration-time curve was similar with both formulations, indicating that the rate, but not the extent, of drug absorption differed between the 2 formulations.

The mean steady-state volume of distribution of nifedipine is 1.3 L/kg and protein binding, principally to albumin, is about 98% at therapeutic plasma con-