Nimodipine
A Review of its Pharmacodynamic and Pharmacokinetic Properties, and Therapeutic Potential in Cerebrovascular Disease

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Summary

Nimodipine is a dihydropyridine calcium antagonist which has been shown to dilate cerebral arterioles and increase cerebral blood flow in animals and humans. It has potential in the treatment of a range of cerebrovascular disorders. Major interest to date, however, has focused on its use in the prevention and treatment of the delayed ischaemic neurological deficits that frequently occur in patients with subarachnoid haemorrhages as a result of sustained cerebral vasospasm.

Initial studies in which patients were treated with an intravenous infusion of nimodipine for up to 2 weeks, followed by oral treatment for 7 days, indicated that a higher proportion of patients than would normally be expected recovered with little or no permanent neurological damage. In a number of controlled studies oral nimodipine treatment for 3 weeks significantly decreased mortality rates and increased the number of patients who had a ‘good’ neurological outcome as compared with placebo treatment. In some of these trials fewer of the nimodipine-treated patients developed neurological deficits during the treatment period, but in none was there a significant effect on the incidence of angiographic vasospasm. It would seem that other pharmacological actions, such as increasing collateral blood flow to underperfused regions or a direct anti-ischaemic effect at the cellular level, may contribute to the clinical benefits obtained with nimodipine treatment. Preliminary results suggest that nimodipine is potentially useful in other cerebrovascular disorders, particularly ischaemic stroke.

To date, nimodipine has been well-tolerated, the only adverse effects of any significance being reductions in the blood pressure of some patients and reversible increases in liver enzymes during intravenous therapy. Thus, nimodipine has significant potential in the treatment of patients with subarachnoid haemorrhage. Wider clinical use should confirm its value as a significant addition to the very limited range of therapeutic choices currently available for patients with this disorder.

Pharmacodynamic Studies

Nimodipine is a dihydropyridine calcium antagonist which relaxes arterial smooth muscle in the presence of agonist-induced increased tone. In in vitro preparations it demonstrates a marked specificity for cerebral vessels. Following intravenous and intraperitoneal doses of nimodipine, dilation of cerebral arterioles has been demonstrated in vivo in animals, and similar results have been reported following the topical application of a nimodipine solution to exposed vessels. Several studies have shown that there is a preferential effect of nimodipine on arterioles with a diameter < 70 to 100μm. Direct observations of cerebral arteriole dilation have also been made in patients undergoing cranial surgery who received nimodipine 10 μg/kg as an intravenous infusion over 10 minutes. In animal studies intravenous or intracortical doses of nimodipine up to 0.1 μg/kg/min increased cerebral blood flow (CBF) by between 18 and 170% without significantly decreasing arterial blood pressure, although it would seem that this effect is only seen when cerebrovascular resistance is raised. Oral doses of nimodipine 40 to 80mg and intraven-