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A journal breaking new ground in the understanding of cerebrovascular disorders . . .

Cerebrovascular and Brain Metabolism Reviews

Editor:
A. Murray Harper, M.D.,
Wellcome Surgical Institute and Hugh Fraser
Neuroscience Laboratories, University of Glasgow,
Glasgow, Scotland

This exciting quarterly journal for researchers and practitioners scrutinizes the clinical aspects of cerebrovascular disorders . . . evaluates methods for assessing cerebral circulatory and brain metabolism changes . . . reports on relevant progress in neuropharmacology, neurophysiology, neurochemistry, and neuropathology . . . and summarizes particularly important papers published in the three months preceding each issue.

FORTHCOMING REVIEWS

The Therapeutic Use of Gangliosides, C. Fieschi/
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Metabolism and Cerebral Function, R. W. Price/PET
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L. Friberg, et al.

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Air delivery is included for European and Asian
countries; for air service elsewhere, add $29.00.
ISSN 1040-8827

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THROUGH A CALCIUM-MODULATING MECHANISM OF ACTION

CEREBROSELECTIVE

NIMOTOP
nimodipine/Miles
CAPSULES 30 mg

REDUCES INCIDENCE OF CEREBRAL INFARCTION IN PATIENTS FOLLOWING SUBARACHNOID HEMORRHAGE

In the largest study to date, NIMOTOP demonstrated a significant reduction in incidence of cerebral infarction\(^1\)

- Twenty-two percent (61/278) of NIMOTOP-treated patients experienced cerebral infarction vs. 33% (92/276) of controls
- NIMOTOP reduced the incidence of cerebral infarction by 34%

Thirty-four percent reduction in incidence of cerebral infarction with NIMOTOP-treated patients vs. controls (n=554; p=0.003)*

![Graph showing reduction in cerebral infarction](image)

- 90% of patients in this study were Hunt and Hess Grades I-III.

**Dose:** 60 mg (two 30 mg liquid-filled capsules) every 4 hours for 21 days commencing within 96 hours of SAH.

Adapted from Pickard, et al.\(^1\)

NIMOTOP modulates calcium influx to promote cerebral perfusion, and may directly protect neurons\(^2,5\)

"[In animals] The beneficial cytoprotective effect of nimodipine, probably related to normalization of calcium homeostasis and blood-brain barrier permeability after ischemia, may reflect both vascular and cellular sites of action."\(^6\)

"[In humans] The data thus suggest that nimodipine neither prevents nor reverses cerebral vasospasm. Calcium channel blockers such as nimodipine may have an effect on cerebral arterioles that are below the limits of resolution of angiography...."\(^1\)

Please see references and Brief Summary of full prescribing information on next page.
Gastrointestinal Rash

Abnormal Liver Function Test

Decreased blood pressure in 44% of these patients. Twenty-nine of 479 (6.1%) placebo treated patients had adverse experiences reported by the patients who were given 0.25 mg q4h, 30 mg q4h or 120 mg q4h. Adverse experiences with an incidence rate less than 1% in the 60 mg q4h dose group were: headache, gastrointestinal hemorrhage; rhombencephalitis; anemia; pyrexia; somnolence; flushing; diaphoresis; wheezing; serotonin toxicity, lightheadedness; diziness; rebound vasospasm; jaundice; hypertension; hematomas.

Contra-Indications

None known.

Precautions

General: Blood Pressure: Nimodipine has the hemodynamic effects expected of a calcium channel blocker, although they are generally not marked. In patients with subarachnoid hemorrhage given Nimotop® in clinical studies, about 5% were reported to have had lowering of the blood pressure and about 1% left the study because of this (not all could be attributed to nimodipine). Nevertheless, blood pressure should be carefully monitored during treatment with Nimotop® based on its known pharmacology and the known effects of calcium channel blockers.

Hepatic Disease: The metabolism of Nimotop® is decreased in patients with impaired hepatic function. Such patients should have their blood pressure and pulse rate monitored closely and should be given a lower dose (see Dosage and Administration).

Drug Interactions: It is possible that the cardiovascular action of other calcium channel blockers could be enhanced by the addition of Nimotop®. Nevertheless, blood pressure should be carefully monitored during treatment with Nimotop® based on its known pharmacology and the known effects of calcium channel blockers.

Pregnancy: Pregnancy Category C. Nimodipine has been shown to have a teratogenic effect in hamsters. Incidences of malformations and stunted fetuses were increased at oral (by gavage) doses of 1.0 mg/kg/day but not at higher doses. Nimodipine was embryotoxic, causing resorption and stunted growth of fetuses, in Long Evans rats at 100 mg/kg/day administered by gavage. It has not been shown to be teratogenic in rats at oral doses, 60 mg/kg/day or 30 mg/kg/day nimodipine administered by gavage from day 16 of gestation and continued until sacrifice (day 20 of pregnancy or day 21 post partum) were associated with higher incidences of skeletal variation, stunted fetuses and stillbirths but no malformations. There are no adequate and well controlled studies in pregnant women to directly assess the effect on human fetuses. Nimodipine therapy should commence within 96 hours of the subarachnoid hemorrhage. Oral Nimotop® therapy should begin within 96 hours of the subarachnoid hemorrhage and continue for 21 days.

CONTRACTUAL INDICATIONS

Nimotop® (nimodipine) is indicated for the improvement of neurologic deficits due to spasm following subarachnoid hemorrhage from ruptured congenital intracranial aneurysms in patients who are in good neurological condition post-ictus (e.g. Hunt and Hess Grades I-III). Oral Nimotop® therapy should begin within 96 hours of the subarachnoid hemorrhage and continue for 21 days.

ADVERSE REACTIONS

Nimodipine should be used during pregnancy only if the potential benefit justifies the potential hazard to the fetus.

DOSE 4th Number of Patients (%)

<table>
<thead>
<tr>
<th>Sign/Symptom</th>
<th>Nimodipine</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>1 (1.2)</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (1.4)</td>
<td>0</td>
</tr>
<tr>
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<td>2 (2.4)</td>
<td>0</td>
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<tr>
<td>Other</td>
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The oral dose is 60 mg (two 30 mg capsules) every 4 hours for 21 consecutive days. Oral Nimotop® therapy should commence within 96 hours of the subarachnoid hemorrhage.

DOSAGE AND ADMINISTRATION

Nimotop® is given orally in the form of ivory colored, soft gelatin 30 mg capsules for subarachnoid hemorrhage.

A 30 mg capsule contains nimodipine hydrochloride 27 mg (0.01 mg/kg). This is the amount of nimodipine per capsule that is absorbed from the GI tract. The capsule is not scored and should be swallowed whole.

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If the capsule cannot be swallowed, e.g., at the time of surgery, or if the patient is unconscious, a hole should be made in each end of the capsule with an 18 gauge needle, and the contents of the capsule extracted into a syringe. The contents should then be emptied into the patient's sinus naso-gastric tube and washed down the tube with 30 ml of normal saline (0.9%).

Patients with hepatic failure have substantially reduced clearance and approximately doubled Cmax. Doseage should be reduced to 30 mg every 4 hours, with close monitoring of blood pressure and heart rate.

MILES

Manufactured by: Miles Inc. West Haven, CT 06516

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