

## 53-Long-term treatment of normal pressure glaucoma with nimodipine

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Is impaired blood supply to the optic nerve pathogenic importance behind glaucomatous damage? This is the premise behind the study by Lutz E. Pillunat, MD, and colleagues presented in San Francisco at the 1997 AAO annual meeting, entitled "Long-term treatment of normal pressure glaucoma with nimodipine."

Co-authors on the study were Andreas G Bohm, MD and Gisbert W. Richard, MD, also of Hamburg, Germany.

The basis of this study is that hemodynamic factors are of pathologic importance, especially in normal tension glaucoma (NTG). An association has been found between NTG and such hemodynamic risk factors as migraine, hypotension, myocardial ischemia, and low ophthalmic artery blood flow velocities.

Carbon dioxide, a potent cerebral vasodilator, has been shown in certain studies to increase ocular pulse volumes, and can even improve the central visual field in a subset patients with NTG. These findings suggested to Dr. Pillunat that in some patients with NTG, carbon dioxide may be used to reverse a vasospastic glaucomatous response.

This hypothesis was confirmed by observing retrobulbar hemodynamics by color Doppler imaging. In 10 NTG patients, the end-diastolic velocities were increased after increasing inhaled CO<sub>2</sub>.

The aim of the current study was to investigate whether a medical therapy might prolong these previously-observed carbon dioxide vasodilatory effects. A class of drug which could potentially relax pre-constricted ocular vessels was chosen -- namely, calcium channel blockers.

Nimodipine, a centrally-acting calcium channel blocker, was chosen to test this hypothesis, since it had the advantage of having minimal systemic arterial blood pressure effects. Nimodipine easily crosses the blood-brain barrier, and has a stronger vasodilatory effect on ciliary arteries compared to nifedipine, a more commonly used calcium-channel blocker.

31 patients with bilateral NTG with typical glaucomatous nerve cupping and corresponding visual field deficits were included in the study. All patients were experienced in performing automated visual fields, and all had previously completed at least two Humphrey 30-2 central visual fields as a baseline. No patient was under systemic antihypertensives or calcium channel blockers, or was receiving topical glaucoma therapy. All patients received 30 mg of nimodipine BID.

Oculocillodynamography was used to assess ocular pulse amplitudes. Patients were studied with normal tension glaucoma.

Ocular pulse amplitudes were measured and Humphrey 30-2 fields were assessed in all patients under both ambient air and high CO<sub>2</sub> conditions, in random order. Based on these results, patients were then divided into CO<sub>2</sub>-responder and non-responder subgroups. CO<sub>2</sub> responders were defined as those NTG patients that had a statistically significant increase in ocular pulse volumes as measured by color Doppler after stimulation with CO<sub>2</sub>.

There were 13 responders, and 18 non-responders.

Visual fields and ocular pulse amplitudes were reassessed every 3 months.

Mean follow-up was 18 months.

The acute increase in ocular pulse volume after CO<sub>2</sub> exposure in the responder group was able to be maintained on nimodipine throughout the 18 month follow-up period.

The mean defect in central visual field significantly decreased by 3.8 dB in the responder group, but remained unchanged in the non-responder group ( $p < 0.01$ ).

To Dr. Pillunat, these results suggest that their CO<sub>2</sub> test can be used to determine which NTG patients may respond to calcium channel blockers such as nimodipine. These results indicate that nimodipine may have both “neuroprotective” and “vasoactive” effects which may be useful in the treatment of patients with NTG.

This paper was discussed by Douglas R. Anderson, MD, of Miami, FL. Dr. Anderson stated that Dr. Pillunat's results seem to indicate that carbon dioxide improves ocular blood flow and visual function in a subgroup of patients with normal tension glaucoma.

Presumably, CO<sub>2</sub> might work by improving blood flow to retinal ganglion cell axons, thereby improving visual function in this subgroup of NTG. Nimodipine may mimic this effect of CO<sub>2</sub> in that subset of NTG patients who are “responders.” Even if this is true, we still do not know the basis for why some NTG patients respond, and others do not.

Finally, 18 months follow-up is probably too short to indicate definitively that nimodipine is indeed neuroprotective. Glaucomatous visual field progression is typically slow, and often measured in years rather than months. We, therefore, may be unable to tell whether the visual fields of the NTG patients in the “responder” group would have progressed even off of nimodipine. Nevertheless, this early work by Dr. Pillunat and colleagues is extremely interesting, and does provide open the door for an exciting path of clinical research.