Intraventricular nimodipine

The objective of a study of Macdonald et al. was to measure the concentration of nimodipine in CSF and plasma after intraventricular injection of a sustained-release formulation of nimodipine (EG-1962) in patients with aneurysmal subarachnoid hemorrhage (SAH).

Patients with SAH repaired by clip placement or coil embolization were randomized to EG-1962 or oral nimodipine. Patients were classified as grade 2-4 on the [World Federation of Neurosurgical Societies grading]] for SAH and had an external ventricular drain inserted as part of their standard of care. Cohorts of 12 patients received 100-1200 mg of EG-1962 as a single intraventricular injection (9 per cohort) or they remained on oral nimodipine (3 per cohort). Plasma and CSF were collected from each patient for measurement of nimodipine concentrations and calculation of maximum plasma and CSF concentration, area under the concentration-time curve from day 0 to 14, and steady-state concentration.

Fifty-four patients in North America were randomized to EG-1962 and 18 to oral nimodipine. Plasma concentrations increased with escalating doses of EG-1962, remained stable for 14 to 21 days, and were detectable at day 30. Plasma concentrations in the oral nimodipine group were more variable than for EG-1962 and were approximately equal to those occurring at the EG-1962 800-mg dose. CSF concentrations of nimodipine in the EG-1962 groups were 2-3 orders of magnitude higher than in the oral nimodipine group, in which nimodipine was only detected at low concentrations in 10% (21/213) of samples. In the EG-1962 groups, CSF nimodipine concentrations were 1000 times higher than plasma concentrations.

Plasma concentrations of nimodipine similar to those achieved with oral nimodipine and lasting for 21 days could be achieved after a single intraventricular injection of EG-1962. The CSF concentrations from EG-1962, however, were at least 2 orders of magnitude higher than those with oral nimodipine. These results supported a phase 3 study that demonstrated a favorable safety profile for EG-1962 but yielded inconclusive efficacy results due to notable differences in clinical outcome based on baseline disease severity. Clinical trial registration no.: NCT01893190 (ClinicalTrials.gov) [1)].

Unclassified

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