Continuous Intraarterial Nimodipine Infusion

Rescue treatment for delayed cerebral ischemia (DCI) after subarachnoid hemorrhage can include induced hypertension (iHTN) and, in refractory cases, endovascular approaches, of which selective, continuous intraarterial nimodipine (IAN) is one variant. The combination of iHTN and IAN can dramatically increase vasopressor demand. In case of unsustainable doses, iHTN is often prioritized over IAN. Assuming the potential of iHTN to be exhausted in case of refractory hypoperfusion, additional IAN may serve as a last-resort measure to bridge hypoperfusion in the DCI phase. With close monitoring, preemptive lowering of pressure target after induction of intraarterial nimodipine may be a safe alternative to alleviate total noradrenaline load and potentially reduce complication rate [1].

IAN treatment appears to be effective in reversing angiographic CV. However, it is not always effective in reversing clinical deterioration, as several other factors including treatment delay affect the clinical course [2].

Vasospasmolysis consist of 3.2 mg intra-arterial nimodipine, injected in the internal carotid artery of the pathological side [3].

An intraarterial application of nimodipine has been shown to increase the vessel diameter, although this effect is transient. The feasibility of long-term, continuous, intra-arterial nimodipine (CIN) treatment and its effects on macrovasospasm, autoregulation parameters and outcome were evaluated in patients with refractory severe macrovasospasm.

Case series

Continuous Intraarterial Nimodipine Infusion was initiated and ended based on the clinical evaluation and transcranial Doppler (TCD), CT-angiography, CT-perfusion (PCT), and digital subtraction angiography (DSA). Nimodipine (0.5-2.0 mg/h) was administered continuously through microcatheters placed in the extracranial internal carotid and/or vertebral artery. Primary outcome measures were Glasgow Outcome Scale (GOS) at discharge and within 1 year after aSAH, and the occurrence of minor and major (<⅓ and >⅓ of LVV-affected territory) DCI-related infarctions in subsequent CT/MRI-scans. Secondary outcome measures were CIAN-associated complications.

Results: A total of 17 patients underwent CIAN. Median onset of CIAN was 9 (3-13) days after aSAH, median duration was 5 (1-13) days. A favorable outcome (GOS 4-5) was achieved in 9 patients (53%) at discharge and in 13 patients within 1 year (76%). One patient died of posthemorrhagic cerebral edema. Minor cerebral infarctions occurred in five and major infarctions in three patients. One patient developed cerebral edema possibly due to CIAN. Normalization of PCT parameters within 2 days was observed in 9/17 patients. Six patients showed clinical response and thus did not require PCT imaging.

The favorable outcome in 76% of patients after 1 year is in line with previous studies. CIAN thus may

be used to treat patients with severe therapy-refractory DCI [4].

Three different patient groups were compared: group 1 had only been treated with oral nimodipine and hypervolemic hypertensive therapy (HHT) (2006-2010), group 2 with a single shot of intra-arterial nimodipine (SSN) in addition to oral conservative treatment (2006-2010), and group 3 with continuous intra-arterial nimodipine (CIAN) (2011-2017). The incidence of cerebral infarction was significantly lower in CIAN group ($p = 0.005$) than in conservative and SSN group. The indication for consecutive decompressive craniectomy was significantly lower in CIAN group in comparison with the conservative group ($p = 0.018$). The rates of VP shunting and tracheotomy were significantly higher in the CIAN group than in the conservative group ($p = 0.028$ for VP, and $p = 0.003$ for tracheotomy). The significantly lower rate of craniectomy in the CIAN group was most probably attributable to the significantly lower rate of CV-induced infarction. The higher rate of tracheotomy reflects more extensive sedation and the need of longer stays on the intensive care unit. Thus, the effect on long-term neurological outcome and quality of life has to be evaluated separately [5].

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Twenty-one patients received 28 intra-arterial nimodipine infusions. Six months after discharge, the occurrence of cerebral infarctions was significantly lower (42.6 %) in the nimodipine group than in the control group (75.0 %). This result was reflected by a significantly higher proportion (76.0 %) of patients with good outcomes in the nimodipine-treated group when compared to 10.0 % good outcomes in the control group. Median GOS was 4 in the nimodipine group and 2 in the control group ($p = 0.001$).

Continuous intra-arterial nimodipine infusion is an effective treatment for patients with severe cerebral vasospasm who fail to respond to HHT and oral nimodipine alone. Key to the effective administration of continuous intra-arterial nimodipine is multimodal neuromonitoring and the individual adaptation of dosage and time of infusion for each patient [6].

Ten patients were included with refractory macrovasospasm despite bolus nimodipine application (n=4) or with primary severe vasospasm (n=6). The patients were assessed with continuous multimodal neuromonitoring (MAP, ICP, CPP, pbrO2), daily TCD exams and CT angiography/perfusion (CTA, CTP). Autoregulation indices, the pressure reactivity index (PRx) and oxygen reactivity index (ORx) were calculated. Indwelling microcatheters were placed in the extracranial internal carotid arteries and 0.4 mg nimodipine was continuously infused at 50 ml/hour.

The duration of CIN treatment ranged from 9-15 days. During treatment ICP remained stable, TCD flow velocity decreased and pbrO2 improved by 37%. Macrovasospasm, as assessed via CTA, had improved (n=5) or disappeared (n=5) at the end of treatment. Cerebrovascular autoregulation according to the PRx and ORx significantly worsened during treatment. All patients showed a favorable outcome (median GOS 5) at 3 months.

In well-selected patients with prolonged severe macrovasospasm, continuous intra-arterial nimodipine treatment can be applied as a rescue therapy with relative safety for more than 2 weeks to prevent

secondary cerebral ischemia. The induced impairment of cerebrovascular autoregulation during treatment seems to have no negative effects [7].

2011

10 patients received IA nimodipine in 15 procedures. The decision to perform angiography and endovascular treatment was based on the neurological examination, brain computed tomography (CT) and CT-angiography. The procedure reports, anesthesia records, neurological examination before and after the procedure, brain imaging and short- and long-term outcome were studied.

The average dose of nimodipine was 2 mg. The median change in mean arterial pressure at 10 min was -10 mmHg. No significant change of heart rate was observed at 10 min. There was radiological improvement in 80% of the procedures. Neurological improvement was noted after eight out of 12 procedures when nimodipine was used as the sole treatment and after 10 out of 15, overall. Six patients clinically improved after the treatment and had good outcome. In one patient, an embolus caused fatal anterior and middle cerebral arteries infarction. There was no other neurological deficit or radiological abnormality due to the nimodipine treatment itself.

Low-dose IA nimodipine is a valid adjunct for the endovascular treatment of cerebral vasospasm. Beneficial effects are achieved in some patients, prompting a prospective control study [8].

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