Nicardipine prolonged release implant

Nicardipine prolonged release implants (NPRI) have been shown to decrease the incidence of cerebral vasospasm and infarcts significantly in patients after aneurysmal subarachnoid haemorrhage (SAH) following microsurgical clipping. Yet, the comparison with results after endovascular coiling is lacking. This study was conducted to determine the differences in the incidence of cerebral vasospasm and infarctions between those two treatment modalities

Methods: The design of this investigation reflects a case-control study; 27 patients suffering from acute SAH were treated by microsurgical clipping and received an intracisternal implantation of NPRI. Twenty-seven matching consecutive patients after microsurgical treatment without implantation of NPRI or endovascular treatment, respectively, served as controls. The incidence of angiographic vasospasm and cerebral infarctions were documented.

Results: All groups were comparable concerning demographics and severity of SAH. Twenty-four of 81 patients developed angiographic vasospasm (>33% constriction). The incidence of vasospasm was 48%, 44% and 11% for patients after endovascular treatment, microsurgical clipping without NPRI and microsurgical clipping with NPRI, respectively. New cerebral infarctions occurred in 28%, 22% and 7% of the treated patients, respectively. A good clinical recovery 1 year after the initial bleeding (modified Rankin scale 0-2) was seen in 48%, 50% and 77% of the treated patients, respectively.

Conclusion: The use of NPRI during microsurgical clipping was confirmed to be safe and effective. Patients who received intracisternally implanted NPRI during clipping after aneurysmal SAH yielded significantly lower vasospasm and infarction rates, and showed a better clinical outcome when compared with clipping without NPRI and also when compared with endovascular coiling [1)].

After aneurysm clipping, 10 NPRIs were placed next to the proximal intracranial vessels. The SDs were recorded using a subdural electrode strip. Proximal vasospasm was assessed by digital subtraction angiography (DSA). 534 SDs were recorded in 10 of 13 patients (77%). Digital subtraction angiography revealed no vasospasm in 8 of 13 patients (62%) and only mild or moderate vasospasm in the remaining. Five patients developed DCI associated with clusters of SD despite the absence of angiographic vasospasm in three of those patients. The number of SDs correlated significantly with the development of DCI. This may explain why the reduction of angiographic vasospasm alone has not been sufficient to improve outcome in some clinical studies [2)]

Bayerl et al. tested in vitro the release dynamics of a novel formulation of the calcium channel blocker nicardipine and in vivo local tolerance and tissue reaction using a chronic cranial window model in mice. To characterize the release kinetics in vitro, dissolution experiments were performed using artificial cerebrospinal fluid over a time period of 21 days. The excipients used in this formulation (NicaPlant) for sustained nicardipine release are a mixture of two completely degradable polymers. A chronic cranial window in C57BL/6 mice was prepared, and NicaPlant slices were placed in proximity to the exposed cerebral vasculature. Epifluorescence video microscopy was performed right after implantation and on days 3 and 7 after surgery. The vessel diameter of the arteries and veins, vessel permeability, vessel configuration, and leukocyte-endothelial cell interaction were quantified by computer-assisted analysis. Immunofluorescence staining was performed to analyze inflammatory reactions and neuronal alterations.

In vitro, the nicardipine release profile showed an almost linear curve with about 80% release at day 15 and full release at day 21. In vivo, epifluorescence video microscopy showed a significantly higher arterial vessel diameter in the NicaPlant group due to vessel dilatation (21.6 ± 2.6 µm vs 17.8 ± 1.5 µm in controls, $p < 0.01$) confirming vasoactivity of the implant, whereas the venous diameter was not affected. Vessel dilatation did not have any influence on the vessel permeability measured by contrast extravasation of the fluorescent dye in epifluorescence microscopy. Further, an increased leukocyte-endothelial cell interaction due to the implant could not be detected. Histological analysis did not show any microglial activation or accumulation. No structural neuronal changes were observed [3)]

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