Osteopontin in subarachnoid hemorrhage

Experimental studies reported that osteopontin (OPN), is induced in the brain after subarachnoid hemorrhage (SAH).

OPN may increase MAPK phosphatase-1 that inactivates MAPKs, upstream and downstream of vascular endothelial growth factor A, by binding to L-arginyl-glycyl-L-aspartate-dependent integrin receptors, suggesting a novel mechanism of OPN-induced post-SAH BBB protection [1].

The relationships between osteopontin (OPN) expression and chronic shunt-dependent hydrocephalus (SDHC) have never been investigated. In 166 SAH patients (derivation and validation cohorts, 110 and 56, respectively), plasma OPN levels were serially measured at days 1-3, 4-6, 7-9, and 10-12 after aneurysmal obliteration. The OPN levels and clinical factors were compared between patients with and without subsequent development of chronic SDHC. Plasma OPN levels in the SDHC patients increased from days 1-3 to days 4-6 and remained high thereafter, while those in the non-SDHC patients peaked at days 4-6 and then decreased over time. Plasma OPN levels had no correlation with serum levels of C-reactive protein (CRP), a systemic inflammatory marker. Univariate analyses showed that age, modified Fisher scale, acute hydrocephalus, cerebrospinal fluid drainage, and OPN and CRP levels at days 10-12 were significantly different between patients with and without SDHC. Multivariate analyses revealed that higher plasma OPN levels at days 10-12 were an independent factor associated with the development of SDHC, in addition to the more frequent use of cerebrospinal fluid drainage and higher modified Fisher grade at admission. Plasma OPN levels at days 10-12 maintained similar discrimination power in the validation cohort and had good calibration on the Hosmer-Lemeshow goodness-of-fit test. Prolonged higher expression of OPN may contribute to the development of post-SAH SDHC, possibly by excessive repairing effects promoting fibrosis in the subarachnoid space [2].

Abate et al. included 44 patients with the following criteria: (1) age 18 and 80 years, (2) diagnosis of SAH from cerebral aneurysm rupture, (3) insertion of an external ventricular drain. Plasma and CSF were sampled at day 1, 4, and 8. OPN levels, in CSF and plasma, displayed a weak correlation on day 1 and were higher, in CSF, in all time points. Only in poor prognosis patients, OPN levels in CSF significantly increased at day 4 and day 8. Plasma OPN at day 1 and 4 was predictor of poor outcome. In conclusion, plasma and CSF OPN displays a weak correlation, on day 1. The higher levels of OPN found in the CSF compared to plasma, suggest OPN production within the CNS after SAH. Furthermore, plasma OPN, at day 1 and 4, seems to be an independent predictor of poor outcome [3].

The aim of the study was to investigate the relationships between plasma OPN levels and outcome after aneurysmal SAH in a clinical setting. This is a prospective study consisting of 109 aneurysmal SAH patients who underwent aneurysmal obliteration within 48 h of SAH. Plasma OPN concentrations were serially determined at days 1-3, 4-6, 7-9, and 10-12 after onset. Various clinical factors as well as OPN values were compared between patients with 90-day good and poor outcomes. Plasma OPN levels were significantly higher in SAH patients compared with control patients and peaked at days 4-6. Poor-outcome patients had significantly higher plasma OPN levels through all sampling points.

Receiver-operating characteristic curves demonstrated that OPN levels at days 10-12 were the most useful predictor of poor outcome at cutoff values of 915.9 pmol/L (sensitivity, 0.694; specificity, 0.845). Multivariate analyses using the significant variables identified by day 3 showed that plasma OPN ≥ 955.1 pmol/L at days 1-3 (odds ratio, 10.336; 95% confidence interval, 2.563-56.077; $p < 0.001$) was an independent predictor of poor outcome, in addition to increasing age, preoperative World Federation of Neurological Surgeons grades IV-V, and modified Fisher grade 4. Post hoc analyses revealed no correlation between OPN levels and serum levels of C-reactive protein, a non-specific inflammatory parameter, at days 1-3. Acute-phase plasma OPN could be used as a useful prognostic biomarker in SAH [4].

References

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