- studies on cerebral blood flow autoregulation and mechanisms of cerebral injury

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Abstract

Cerebral dysfunction (CD) occurs frequently after cardiac surgery with cardiopulmonary bypass (CPB). The main causes of CD are thought to be cerebral hypoperfusion, cerebral microembolisation, cerebral inflammation or disruption of the blood brain barrier (BBB). Data on the effects of the frequently used anaesthetics, isoflurane and sevoflurane, on the cerebral pressure-flow relationship and cerebral flow-metabolism coupling during CPB are scarce and inconsistent. Furthermore, the effects of cerebral microembolisation on the release of serological or cerebrospinal fluid markers of brain injury and BBB function after transcatheter - (TAVI) or surgical aortic valve replacement (SAVR) have previously not been evaluated.

Patients and methods: The effects of isoflurane and sevoflurane on cerebral blood flow velocity (CBFV), oxygen extraction (COE) and flow autoregulation were performed during cardiac surgery on CPB, using transcranial Doppler (TCD) and a right jugular bulb catheter for measurement of jugular bulb pressure and oxygen saturation. Furthermore, patients undergoing TAVI were studied with TCD for estimation of microembolic signals (MES), and postoperative serum release of S-100B, a marker of glial cell injury. Finally, the effects of SAVR on the BBB function and the release of CSF markers of neuronal and glial-cell injury and two markers of inflammation were analysed. Changes in CSF biomarkers were correlated to the microembolic load.

Results: Isoflurane and sevoflurane both decreased CBFV (27% and 17%, respectively), and COE (13% and 23%, respectively). Both isoflurane and sevoflurane increased the slope of the autoregulation curve, relating cerebral perfusion pressure to CBFV. During the TAVI procedure, 282±169 MES were recorded. Approximately 2/3 appeared during the balloon valvuloplasty of the native valve. Serum S-100B increased sharply within the first hour after the balloon valvuloplasty, and returned toward baseline levels within 4-6 hrs. There was a correlation between MES and the 24hr release of S-100B. In SAVR patients, the two markers of glial cell injury, S-100B and GFAP, increased by 35% and 25%, respectively. The CSF markers of neuronal injury, NSE, Tau and NFL, were not significantly affected postoperatively. The CSF/serum albumin ratio increased by 61%. There was a-12 and-3.5 fold increase in IL-6 and IL-8, respectively. A total of 354±79 MES were detected, but their magnitude correlated neither to the changes in CSF markers of astroglial damage, changes in cytokine levels, nor to the degree of BBB disruption.

Conclusions: Both isoflurane and sevoflurane exert a direct cerebral vasodilatory effect, which impairs the cerebral pressure-flow autoregulation, but improves the cerebral oxygen-supply demand relationship The substantial cerebral microembolic load during TAVI causes a glial cell injury. Cardiac surgery with CPB does not seem to cause neuronal damage but instead induces a substantial cerebral inflammation causing a BBB dysfunction, probably caused by astroglial cell injury. Despite the extensive microembolic load during SAVR, its magnitude does not correlate to the degrees of BBB dysfunction, glial cell injury or cerebral inflammation.

Key words: Cardiac surgery; cerebral dysfunction; cardiopulmonary bypass; anaesthetics; aortic valve replacement; transcranial Doppler; embolism; cerebrospinal fluid; blood-brain barrier.

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Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska Akademin vid Göteborgs Universitet kommer at offentligen försvaras i Hjärtats aula, Sahlgrenska Universitetssjukhuset/Sahlgrenska, tisdagen den 6 december 2011, kl 0900

> av Björn Reinsfelt Leg. läkare

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Avdelningen för Thoraxkirurgi
Karolinska Institutet

Avhandlingen baseras på följande delarbeten:

- I. Reinsfelt B, Westerlind A, Houltz E, Ederberg S, Elam M, Ricksten SE

 "The Effects of isoflurane-Induced Electroencephalographic Burst
 Suppression on Cerebral Blood Flow Velocity and Cerebral Oxygen
 Extraction During Cardiopulmonary Bypass."

 Anesthesia & Analgesia 2003;97:1246 –50
- II. Reinsfelt B, Westerlind A, Ricksten SE

 "The effects of sevoflurane on cerebral blood flow autoregulation and flow-metabolism coupling during cardiopulmonary bypass."

 Acta Anaesthesiol Scand 2011; 55: 118–123
- III. Reinsfelt B, Westerlind A, Ioanes D, Zetterberg H, Fredén-Lindqvist J, Ricksten SE
 - "Transcranial Doppler microembolic signals and serum marker evidence of neuronal injury during transcatheter aortic valve implantation."
 - Acta Anaesthesiol Scand; Accepted for publication Aug 28, 2011.
- IV. Reinsfelt B, Westerlind A, Zetterberg H, Blennow K, Fredén-Lindqvist J, Ricksten SE
 - "Cerebrospinal fluid markers of brain injury, inflammation and blood-brain barrier dysfunction and their relation to cerebral microembolism in cardiac surgery."

Manuscript submitted