TITLE CLONIDINE DECREASES THE SYMPATHETIC HYPERACTIVITY OCCURING AFTER HEAD INJURY

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Introduction. Severe head injury induces sympathetic hyperactivity. Alpha-2 adrenergic agonists, such as clonidine, may be of interest in this setting since they inhibit the medullary vasomotor centre (1) involved in the generation of sympathetic hyperactivity during the cerebral ischemic response (2), a setting similar to head injury. Therefore the effect of clonidine on systemic hemodynamics, common carotid blood flow (CCBF) and plasma catecholamines was assessed in patients having suffered severe head injury.

Methods and materials. Seven patients (age mean ± sd = 33±3) were studied 3 to 5 days after severe head injury as assessed by 1) Glasgow coma score between 3 and 6 2) severe brain contusion by CT scan. None of these patients had undergone craniotomy or had intracranial hematoma, hypothalamic lesions, or received any anesthetics or sedative for at least 6 h prior to study. The following variables were measured or calculated : heart rate (HR, b.p.min), arterial presure via a radial artery catheter (systolic SAP ; diastolic DAP ; mean MAP); diameter of the common carotid (D,cm), mean velocity (V,cm.s$^{-1}$) and flow (CCBF,ml.min$^{-1}$) from the common carotid using a Pulsed Doppler (8MHz) (3), carotid vascular resistances (CVR=MAP/CCBF in IU). Plasma samples were collected from the radial artery and jugular vein to measure 1) arterio-venous $O_2$ differences ($AVDO_2$) 2) epinephrine (EPI) and norepinephrine (NOR) using a radio-enzymatic technique. All patients were mechanically ventilated and had stable hemodynamics. Circulatory data were recorded at 1) baseline 2) every 5 min thereafter for 45 min following infusion of clonidine (2.5µg.kg$^{-1}$ iv over 10 min) 3) for an additional 5 min after the injection of naloxone (6µg.kg$^{-1}$ iv) given after the end of the 45 min period. Plasma samples were collected at 1) baseline 2) then 10 and 20 min after the beginning of clonidine infusion. Data were analyzed by analysis of variance followed by Newman-Keuls test.

Results. Clonidine decreased SAP and DAP (maximum decrease : -21%, $p<0.001$) from the 10 min interval up to the 45 min interval. HR decreased from 109±27 b.p.min to 97±23 ($p<0.05$). Carotid velocity was significantly reduced ($p<0.05$) while the carotid diameter slightly increased thus explaining the lack of change in CCBF. CVR, $PO_2$, $PCO_2$, $AVDO_2$ were unchanged. Plasma CA were significantly reduced as shown in the table :

| MEAN ± SD | BASELINE (B) | 10 min | 20 min | ANOVA | NEWMAN-KEULS B-10 | B-20 | 10-20 |
|---|---|---|---|---|---|---|---|
| NORa | 706<br>414 | 618<br>336 | 575<br>299 | 0.045 | NS | 0.05 | NS |
| NORv | 763<br>395 | 639<br>330 | 626<br>299 | 0.01 | 0.025 | 0.025 | NS |
| EPIa | 074<br>054 | 055<br>036 | 052<br>033 | 0.05 | 0.05 | 0.05 | NS |
| EPIv | 075<br>028 | 066<br>043 | 048<br>036 | 0.05 | 0.05 | 0.05 | NS |

NOR in pg/ml (Normal : 350-420) ; EPI in pg/ml (Normal : 35-60)
a : arterial ; v : venous

Naloxone did not produce any circulatory change.

Discussion. Low doses of iv clonidine reduced HR, arterial pressure and decreased or normalized plasma CA in patients having suffered severe head injury. Despite the reduction in arterial pressure, the common carotid blood flow, an index of cerebral perfusion which is closely related to the mean hemispheric flow (3), remained constant. In this setting, naloxone did not reverse the effect of clonidine, which is in contrast to another report obtained in patients with essential hypertension (4). This pilot study done after the acute phase of head injury shows that clonidine may be a therapeutic tool in this setting to suppress sympathetic hyperactivity.

References.

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