

Pearls & Oysters: The effects of renal replacement therapy on cerebral autoregulation

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PEARLS

- Hemodialysis (HD) has been associated with increases in intracranial pressure (ICP). Osmotic shifts occurring during HD are thought to be associated with the development of this phenomenon.
- In comatose patients with acute brain injury, an elevation of ICP during HD may be associated with worse cerebral autoregulation. Continuous veno-venous hemofiltration (CVVH) may be a safer alternative in these patients.

OYSTER

- HD may increase ICP; therefore, caution should be exercised when HD is needed in patients with acute brain injury.

CASE REPORT A 59-year-old man with hypertension, type 1 diabetes, and end-stage renal disease on HD presented after head trauma from a fall while walking. Initial neurologic examination showed agitated confusion (E4 M5 V5) and a noncontrast head CT showed a nondepressed linear skull fracture in the right temporal bone with a small amount of subarachnoid hemorrhage in the left superior frontal convexity. On arrival to the neurointensive care unit (NICU), his mental status deteriorated (E1 M4 VT) and a follow-up noncontrast head CT revealed a new intracerebral hemorrhage (ICH) in the left temporal lobe (4.3 cm × 2.2 cm × 3.5 cm) with surrounding edema (figure 1A). The patient's family opted for maximal medical management. Multimodality monitoring (MMM) including an intracranial pressure (ICP) monitor (Camino, Integra Lifesciences) and a brain oxygen monitor (Licox, Integra Lifesciences) was placed in the left frontal lobe, close to the perihematomal region. HD was performed every other day via a pre-existing left groin arteriovenous fistula with a negative goal fluid balance of 2 L per each 3.5-hour session.

Initially, MMM demonstrated a mildly elevated ICP (mean 18.9 ± 7.4 mm Hg) over a wide range of

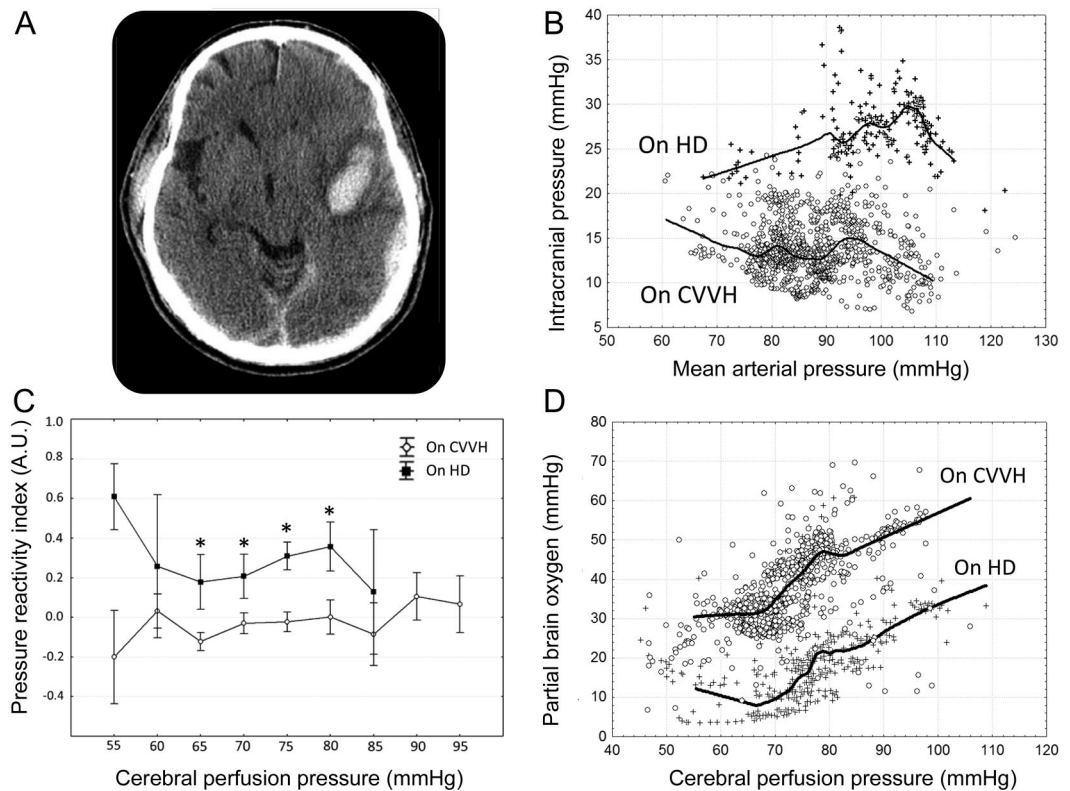
mean arterial pressures (MAPs) (60–120 mm Hg) and ICP increase was not directly proportional to MAP changes, suggesting intact autoregulation. Pressure reactivity index (PRx), a Pearson moving correlation coefficient between MAP and mean ICP, which is accepted as a surrogate for autoregulation status, was also stable at 0.18 ± 0.05 (mean \pm SD), implying intact pressure autoregulation. Partial brain oxygen tension ($P_{bt}O_2$) was directly proportional to the cerebral perfusion pressure (CPP) up to 80 mm Hg. Oxygen reactivity index, a moving correlation coefficient between $P_{bt}O_2$ and CPP, was 0.19 ± 0.11 . The mean $P_{bt}O_2$ value was 43.1 ± 11.2 mm Hg. Over the initial 2 weeks, the ICP trended up, requiring hyperosmotic agents to maintain an ICP below 20 mm Hg. Glasgow Coma Scale score deteriorated to E1, M2, VT. Follow-up brain CT scan showed increased perihematomal vasogenic edema with aggravated midline shift (figure 2). On hospital day 16, while receiving his regularly scheduled HD, the ICP surged up to 38 mm Hg just after initiating HD and remained elevated during the entire session. ICP was directly dependent on MAP, suggesting a loss of autoregulation (figure 1B). Additionally, PRx values were elevated more than 0.2, which also suggested autoregulatory failure (figure 1C). Mean $P_{bt}O_2$ values decreased to 14.7 ± 7.1 mmHg and ORx value was 0.21 ± 0.10 , suggesting loss of oxygen autoregulation. After observing this phenomenon during repeated HD treatments, a decision was made to switch the patient to CVVH with an ultrafiltration rate of 50 mL/h. CVVH was initiated on day 20. During CVVH, his ICP remained under control, and ICP change was not directly proportional to MAP fluctuation, suggesting intact autoregulation (figure 1B). PRx was stable over the all ranges of CPP, which verified intact autoregulation (figure 1C). While on CVVH, the mean $P_{bt}O_2$ value was 28.5 ± 7.0 mm Hg, which was significantly higher than when the patient was on HD. There was a similar degree of $P_{bt}O_2$ responsiveness to CPP compared to while on HD (figure 1D). In addition, ORx was

Supplemental data at
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Figure 1 Brain CT and physiologic data of the patient



A noncontrast brain CT 1 day after admission showed an intracerebral hemorrhage in the left frontal and temporal lobes with focal subdural hematoma (A). When the patient was on hemodialysis (HD), an increase in mean arterial pressure resulted in intracranial pressure elevation, suggesting autoregulation failure (B), while it is not on continuous venovenous hemofiltration (CVVH) (B). Pressure reactivity index plot confirms the status of autoregulation failure while on HD (C) (error bars represent 95% confidence interval, $*p < 0.05$) (AU = arbitrary unit). Brain partial oxygen tension was directly proportional to cerebral perfusion pressure, but the curve was shifted downward when the patient was on HD (D).

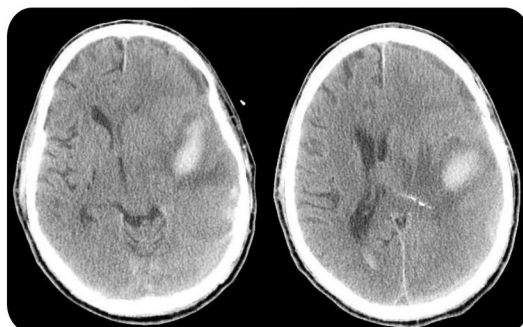
0.19 ± 0.40 , which was statistically not different from that while on HD. Other physiologic variables that did not differ on HD or CVVH were body temperature (36.7 ± 0.3 vs $36.8 \pm 0.2^\circ\text{C}$), end tidal CO (29.7 ± 2.6 vs 30.2 ± 1.3), minute ventilation (7.3 ± 0.2 L/min vs 7.4 ± 0.3 L/min), and PaCO₂ (31 vs 32 mm Hg). Moreover, the PaO₂ was higher on HD compared with CVVH (219 vs 198 mm

Hg). The patient remained stable after he was switched to CVVH. Despite improvement in monitored variables, there was no change in Glasgow Coma Scale scores. After 32 days in the NICU, he remained in a vegetative state.

DISCUSSION Renal replacement therapy (RRT) helps substitute for deteriorating kidney function and treats volume overload. Although intermittent or continuous RRT are equally effective in regards to mortality or dialysis dependency,¹ a few anecdotal reports exist showing a different effect of HD and CVVH on ICP in patients with acute brain injury.²⁻⁵ Though the exact mechanism remains unclear, several theories, including the reverse urea effect, increase in idiogenic osmolar products, or a paradoxical intracellular acidosis, exist.²⁻⁴

Our case shows a close relationship between initiation of HD and surges of ICP together with a decline in P_{bt}O₂. Moreover, a direct relationship between ICP and MAP suggests a failure in autoregulation. PRx, a moving correlation coefficient between ICP and MAP, is a surrogate for the status of

Figure 2 Follow-up brain CT scan of the patient



Follow-up brain CT on day 14 shows an increased perihematomal vasogenic edema with aggravated midline shift.

autoregulation.⁶ The PRx was elevated in CPP ranges from 65 mm Hg to 80 mm Hg ($p < 0.05$) during HD compared to during CVVH. In order to maintain a similar CPP, the MAP was maintained at a slightly higher level when the patient was on HD compared to when the patient was on CVVH or not on any RRT. This was because the ICP was significantly elevated even with similar MAP ranges during HD.

The brain oxygen response to the CPP curve confirmed that there is a general direct correlation between $P_{bt}O_2$ and CPP, regardless of dialysis condition. However, when the patient was on HD, the absolute $P_{bt}O_2$ level was lower than when on CVVH with a relative apparent downward shift in the $P_{bt}O_2$ -CPP curve overall. It is unclear why $P_{bt}O_2$ values decreased during HD. However, limited brain oxygen diffusion due to increased brain water content might be a possible explanation.^{7,8} Another possible mechanism is increased oxygen consumption secondary to the ICP surges. $P_{bt}O_2$ values are regarded as a surrogate of tissue oxygen balance between supply and demand.⁹ ICP elevation is associated with brain hypermetabolism and increased oxygen consumption.¹⁰ Therefore, an ICP surge may represent increased metabolism leading to an increase in oxygen consumption, resulting in a decrease in brain oxygen tension.

This case illustrates that HD may be associated with autoregulatory disturbance. However, it is not clear why HD did not aggravate ICP until hospital day 15. One possibility is the degree of difference in plasma osmolality before and after HD. A previous report showed that rapid decrease in plasma osmolality during HD was associated with an increase in ICP.¹¹ Our patient had a dramatic decrease in serum osmolality on day 16 after HD, compared to previous days on HD (figure e-1 on the *Neurology*[®] Web site at www.neurology.org). Rapid falls in serum osmolality is thought to be responsible for increases in brain edema and ICP crisis, invoking the reverse urea effect. In line with this, the change in serum osmolality was minimal while on CVVH. Taken together, we think that the rapid decrease in serum osmolality on day 16 during dialysis might be the reason that ICP crisis was observed on day 16 and not before.

HD may aggravate ICP and is associated with autoregulatory failure where elevated ICPs promote brain hypoxia in a CPP-dependent way. Thus, more continuous forms of RRT, such as CVVH, might be better tolerated in patients at risk for ICP crisis due to brain injury.

AUTHOR CONTRIBUTIONS

Dr. Ko was involved in drafting the manuscript, data acquisition, and analysis of data. Dr. Choi was involved in drafting the manuscript

and analysis of data. Dr. Gilmore was involved in revising the manuscript and analysis of data. Dr. Schmidt was involved in data acquisition and analysis of data. Dr. Lee was involved in revising the manuscript and analysis of data. Dr. Claassen was involved in revising the manuscript and analysis of data. Dr. Mayer was involved in revising the manuscript and analysis of data. Dr. Badjatia was involved in revising the manuscript, concept of study, analysis of data, and supervising study.

DISCLOSURE

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