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ALZHEIMER DISEASE

Peripheral Aβ clearance — a therapeutic strategy for AD?

Peripheral clearance of amyloid-β (Aβ) by peritoneal dialysis could help to reduce the amyloid plaque burden in the brain, and might, therefore, represent a new therapeutic approach for Alzheimer disease (AD), according to new research published in *Acta Neuropathologica*.

"Previous studies from our group and others have shown that removal of Aβ from the blood can reduce brain Aβ levels," explains study leader Yan-Jiang Wang. "We found that peritoneal dialysis can remove Aβ from the blood, and another group recently showed that patients who have undergone haemodialysis exhibit lower amyloid deposition in the brain."

In the new study, Wang and colleagues measured plasma Aβ levels before and immediately after peritoneal dialysis in patients with chronic kidney disease and in APP/PS1 mice — a standard animal model of AD. In both cases, plasma $Aβ_{40}$ and $Aβ_{42}$ levels were significantly reduced after dialysis, consistent with the earlier findings.

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To examine the effects of peripheral Aβ depletion on the brain, the investigators conducted in-depth analyses in the APP/PS1 mice. In these animals, peritoneal dialysis resulted in a decrease in Aβ levels in the interstitial fluid of the brain, mirroring the effects on blood Aβ. Moreover, mice that underwent dialysis exhibited reduced Aβ deposition in the brain, even if the intervention was administered once plaque formation was well underway.

The mouse experiments suggested beneficial effects of dialysis on other aspects of AD pathology and disease progression. The dialysis-treated mice showed reduced levels of hyperphosphorylated tau in the brain, suggesting a slowing of neurodegeneration. Dialysis was also associated with decreased neuroinflammation and increased phagocytosis of Aβ by microglia in the brain. In addition, the treated mice showed evidence of attenuation of cognitive decline, as indicated by improved performance on the Y-maze and open-field tests.

"The most significant findings are that peritoneal dialysis can reduce brain Aβ deposition, attenuate the brain inflammatory microenvironment, and improve the phagocytosis of Aβ by microglia," concludes Wang. "These findings are important, as they provide proof-of-concept evidence that restoration of the AD brain microenvironment and clearance of brain Aβ could be achieved via peripheral approaches."

The researchers hope that this approach can eventually be translated into the clinic. "In the future, we plan to conduct clinical trials to see whether dialysis is able to reduce brain pathologies and improve cognition in patients with AD," says Wang.

Heather Wood

ORIGINAL ARTICLES Jin, W.-S. *et al.* Peritoneal dialysis reduces amyloid-beta plasma levels in humans and attenuates Alzheimer-associated phenotypes in an APP/PS1 mouse model. *Acta Neuropathol.* http://dx.doi.org/10.1007/s00401-017-1721-y (2017)

FURTHER READING Sakai, K. *et al.* Patients that have undergone hemodialysis exhibit lower amyloid deposition in the brain: evidence supporting a therapeutic strategy for Alzheimer's disease by removal of blood amyloid. *J. Alzheimers Dis.* **51**, 997–1002 (2016)