Letter: Cerebrospinal fluid shunting for idiopathic intracranial hypertension

Mollan, Susan; Sinclair, Alex; Tsermoulas, Georgios

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To the Editor:

Salih et al[1] recently published a meta-analysis on cerebrospinal fluid (CSF) shunting in Idiopathic Intracranial Hypertension (IIH). This publication amongst others[2] are important in highlighting the lack of detail provided in common data points and the need for uniformity in reporting outcome measures when assessing the success of any intervention. IIH is a condition managed by neurologists, ophthalmologists, neurosurgeons and more recently interventional radiologists. Each specialist sees a different angle of the condition however the contemporary literature is there to guide us in the advances in our understanding of the disease and how to manage it.

IIH is a systemic metabolic disease and comes under the classification of pseudotumour cerebri syndrome (PTSC).[3] This distinction is important as PTCS may be primary (IIH) or arise from an identifiable secondary cause such as anaemia, medication use or indeed cerebral venous sinus thrombosis (CVST).[3-5] Outcomes from shunting in secondary pseudotumor versus IIH can be expectantly different, and why classifying the underlying pathology in this context is essential. The authors have not detailed this nuance for readers nor provided an assessment of quality of the studies specifically against any version of the diagnostic criteria. The 2002 Friedman and Jacobson criteria[6] are cited as useful for diagnosis, which is in part true but for the time frame when the majority of the included studies performed data capture. However in modern practice these have been superseded by the revised diagnostic criteria for PTSC which were published in 2013.[3]

A key concern we have is the discussion detailing management strategies which was not the focus of the meta-analysis. Papilloedema is a key single point of entry to the investigational pathway,[3-5] which has been omitted in their discussion. We agree that establishing the diagnosis of IIH early is important but this is not based on symptoms of headache, visual loss or visual changes and tinnitus, which are nonspecific. Yri and Jensen[7] eloquently showed that in a control population one third reported transient visual obscurations, one quarter had pulsatile tinnitus, and one quarter experienced double vision. Indeed the controls' headache phenotype had features of a raised ICP headache. More intriguing still was that one quarter of those without IIH had

improvement of their headache following lumbar puncture. We, and a multidisciplinary group, therefore strongly discourage the use of symptoms to guide surgical management in IIH.[4,5]

We agree that venography is absolutely critical in the assessment of papilledema to exclude CVST which has devasting consequences if missed.[4,5] We would be concerned about this over emphasis on DVSS in the absence of randomized control trial evidence. The tsunami of institutional based case series in stenting is challenging to unpick the indications for the intervention and indeed the heterogenous outcomes that have been reported.[8] We agree there is a role for DVSS in IIH and to address this gap in the literature we are spearheading a randomized control trial in the United Kingdom for the evaluation of CSF diversion and DVSS in those with visual failure in IIH.

We are encouraged by the reducing complication rate reported.[1] This too has been our local experience which we believe is due to a dedicated CSF shunt pathway, CSF specialist surgeons, and a standardized protocol: where there is a preference for a frontal ventriculoperitoneal shunt; use of adjustable gravitational valves; an implantable ICP monitoring device in line with the shunt to optimize CSF drainage and identify possible future malfunction; frameless stereotactic image-guidance for insertion of the ventricular catheter; and laparoscopic placement of the peritoneal end in patients with high body mass index.[9,10]

Horizon scanning in IIH reveals an avenue where the need for surgical intervention could be reduced. This has been the translation of Glucagon-like peptide-1 receptor (GLP-1R) agonists from an animal model with raised ICP (hydrocephalic)[11] to the first phase 2 study assessing the biological effect of the GLP-1R agonist Exenatide on ICP utilising highly accurate telemetric ICP monitors. Exentide was successful in reducing ICP at 2.5hours, 24 hours and 12 weeks.[12]

To our final point there is firm evidence that IIH is a metabolic disease encompassing a spectrum of systemic manifestations. There is twofold risk of cardiovascular disease, presence of insulin resistance, increased truncal adiposity, hyperleptinemia, fertility and pregnancy complications.[13-15] These features are in excess than that driven by the presence of obesity. Adipose tissue in IIH has a unique profile of transcription and metabolic dysregulation driving lipogenesis and

promoting increased adipose deposition.[15] Hormonal perturbations have been identified with patients noted to have a unique phenotype of serum and CSF androgen excess and a dysregulated glucocorticoid phenotype.[16,17] Weight loss is now established as the only disease modifying therapy with bariatric surgery producing long term control of ICP.[18] While venous sinus stenosis is almost universally observed in active IIH, we strongly believe this reflects a consequence of the disease rather than the casual driver in the majority.

Keywords: Cerebrospinal fluid shunt, Dural Venous Sinus Stenting, Headache, Idiopathic Intracranial Hypertension, ICP, Papilloedema, Pseudotumour cerebri.

Abbreviations: CSF = cerebrospinal fluid; DVSS = dural venous sinus stenting; ICP = intracranial pressure; IIH = idiopathic intracranial hypertension;

REFERENCES

1. Salih M, Enriquez-Marulanda A, Khorasanizadeh M, et al. Cerebrospinal Fluid Shunting for Idiopathic Intracranial Hypertension: A Systematic Review, Meta-Analysis, and Implications for a Modern Management Protocol. *Neurosurgery*. 2022;91(4):529-540.
2. Mollan SP, Sinclair AJ. Outcomes measures in idiopathic intracranial hypertension. *Expert Review of Neurotherapeutics*. 2021;21(6):687-700.
3. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology*. 2013;81(13):1159-65.
4. Mollan SP, Davies B, Silver NC, et al. Idiopathic intracranial hypertension: consensus guidelines on management. *J Neurol Neurosurg Psychiatry*. 2018;89(10):1088-1100.
5. Hoffmann J, Mollan SP, Paemeleire K, Lampl C, Jensen RH, Sinclair AJ. European headache federation guideline on idiopathic intracranial hypertension. *J Headache Pain*. 2018;19(1):93.
6. Friedman DI, Jacobson DM. Diagnostic criteria for idiopathic intracranial hypertension. *Neurology*. 2002;59(10):1492-1495.
7. Yri HM, Jensen RH. Idiopathic intracranial hypertension: Clinical nosography and field-testing of the ICHD diagnostic criteria. A case-control study. *Cephalalgia*. 2015;35(7):553-562.

8. Gurney SP, Ramalingam S, Thomas A, et al. Exploring The Current Management Idiopathic Intracranial Hypertension, And Understanding The Role Of Dural Venous Sinus Stenting. *Eye Brain*. 2020;14(12):1-13.
9. Galloway L, Karia K, White AM, et al. Cerebrospinal fluid shunting protocol for idiopathic intracranial hypertension for an improved revision rate. *J Neurosurg*. 2021;8:1-6.
10. Tsermoulas G, Thant KZ, Byrne ME, et al. The Birmingham Standardised Idiopathic Intracranial Hypertension Shunt Protocol: technical note. *World Neurosurg*. 2022:S1878-8750(22)01283-9.
11. Botfield HF, Uldall MS, Westgate CSJ, Mitchell JL, Hagen SM, Gonzalez AM, Hodson DJ, Jensen RH, Sinclair AJ. A glucagon-like peptide-1 receptor agonist reduces ICP in a rat model of hydrocephalus. *Sci Transl Med*. 2017;9(404):eaan0972.
12. Mitchel JL, Lyons H, Walker J et al. The effect of exenatide on ICP in Idiopathic Intracranial Hypertension, IIH Pressure: A Randomised Clinical Trial. *medRxiv* 2022.05.24.22275518.
13. Adderley NJ, Subramanian A, Nirantharakumar K, et al. Association Between Idiopathic Intracranial Hypertension and Risk of Cardiovascular Diseases in Women in the United Kingdom. *JAMA Neurol*. 2019;76(9):1088-1098
14. Hornby C, Botfield H, O'Reilly MW, et al. Evaluating the Fat Distribution in Idiopathic Intracranial Hypertension Using Dual-Energy X-ray Absorptiometry Scanning. *Neuroophthalmology.* 2017;42(2):99-104.
15. Westgate CS, Botfield HF, Alimajstorovic Z, et al. Systemic and adipocyte transcriptional and metabolic dysregulation in idiopathic intracranial hypertension. *JCI Insight*. 2021;6(10):e145346
16. O'Reilly MW, Westgate CS, Hornby C, et al. A unique androgen excess signature in idiopathic intracranial hypertension is linked to cerebrospinal fluid dynamics. *JCI Insight.* 2019;4(6):e125348
17. Hardy RS, Botfield H, Markey K, et al. 11βHSD1 Inhibition with AZD4017 Improves Lipid Profiles and Lean Muscle Mass in Idiopathic Intracranial Hypertension. *J Clin Endocrinol Metab.* 2021;106(1):174-187.

18. Mollan SP, Mitchell JL, Ottridge RS, et al. Effectiveness of Bariatric Surgery vs Community Weight Management Intervention for the Treatment of Idiopathic Intracranial Hypertension: A Randomized Clinical Trial. *JAMA Neurol*. 2021;78(6):678-686.