A Copeptin-Based Approach in the Diagnosis of Diabetes Insipidus

Wiebke Fenske, Julie Refardt, Irina Chifu, Ingeborg Schnyder, Bettina Winzeler, Juliana Drummond, Antônio Ribeiro-Oliveira, Tilman Drescher, Stefan Bilz, Deborah R Vogt, Uwe Malzahn, Matthias Kroiss, Emanuel Christ, Christoph Henzen, Stefan Fischli, Anke Tönjes, Beat Mueller, Jochen Schopohl, Jörg Flitsch, Georg Brabant, Martin Fassnacht & Mirjam Christ-Crain

BACKGROUND
The indirect water-deprivation test is the current reference standard for the diagnosis of diabetes insipidus. However, it is technically cumbersome to administer, and the results are often inaccurate. The current study compared the indirect water-deprivation test with direct detection of plasma copeptin, a precursor-derived surrogate of arginine vasopressin.

METHODS
From 2013 to 2017, we recruited 156 patients with hypotonic polyuria at 11 medical centers to undergo both water-deprivation and hypertonic saline infusion tests. In the latter test, plasma copeptin was measured when the plasma sodium level had increased to at least 150 mmol per liter after infusion of hypertonic saline. The primary outcome was the overall diagnostic accuracy of each test as compared with the final reference diagnosis, which was determined on the basis of medical history, test results, and treatment response, with copeptin levels masked.

RESULTS
A total of 144 patients underwent both tests. The final diagnosis was primary polydipsia in 82 patients (57%), central diabetes insipidus in 59 (41%), and nephrogenic diabetes insipidus in 3 (2%). Overall, among the 141 patients included in the analysis, the indirect water-deprivation test determined the correct diagnosis in 108 patients (diagnostic accuracy, 76.6%; 95% confidence interval [CI], 68.9 to 83.2), and the hypertonic saline infusion test (with a copeptin cutoff level of >4.9 pmol per liter) determined the correct diagnosis in 136 patients (96.5%; 95% CI, 92.1 to 98.6; P<0.001). The indirect water-deprivation test correctly distinguished primary polydipsia from partial central diabetes insipidus in 77 of 105 patients (73.3%; 95% CI, 63.9 to 81.2), and the hypertonic saline infusion test distinguished between the two conditions in 99 of 104 patients (95.2%; 95% CI, 89.4 to 98.1; adjusted P<0.001). One serious adverse event (desmopressin-induced hyponatremia that resulted in
hospitalization) occurred during the water-deprivation test.

CONCLUSIONS
The direct measurement of hypertonic saline-stimulated plasma copeptin had greater diagnostic accuracy than the water-deprivation test in patients with hypotonic polyuria. (Funded by the Swiss National Foundation and others; ClinicalTrials.gov number, NCT01940614 .).