CORRESPONDENCE

The Association of Hyponatremia, Risk of Confusional State, and Mortality—A Prospective Controlled Longitudinal Study in Older Patients

by Dr. med. Tania Zieschang, Dr. med. Marcia Wolf, Dr. med. Tinu Vellappallil, Lorenz Uhlmann, Prof. Dr. med. Peter Oster, and PD Dr. med. Daniel Kopf in issue 50/2016

Hyponatremia Is a Common Cause

I can only underline the study results reported by Zieschang et al. (1).

Patients in a confusional state who are mostly older and over 65 years of age are transferred by relatives, emergency physicians, but also other somatic wards to optional protected gerontopsychiatric wards because they “can’t be controlled.”

A very common cause is hyponatremia of unclear etiology. Clinically, the dominant symptoms in addition to pronounced cognitive deficits are agitation, fear/anxiety, perplexity/helplessness, and depressive symptoms.

The clientele of patients with hyponatremia is extremely heterogeneous and diagnoses at admission vary. In my opinion, however, one aspect of the etiology was not given enough room: pharmacogenic hyponatremia.

The authors did discuss that hyponatremia is often facilitated, or even triggered by (in many cases) inadequate pharmacotherapy (for example, with thiazide diuretics), but they did not provide a detailed list/explanation of the potentially risky medications. Especially antidepressants, such as selective serotonin reuptake inhibitors (SSRIs), entail a fivefold risk for hospital admission subsequent to hyponatremia (2).

Antipsychotic drugs are also associated with an increased risk for hyponatremia—and they are used particularly often in geriatric and gerontopsychiatric patients (3).

Furthermore, diverse anticonvulsive drugs, analgesics (especially non-steroidal anti-inflammatory drugs), and cytotoxic substances range among the medications associated with a high risk. Rastogi et al. (4) summarize typical at-risk patients for hyponatremia as follows:

- Receiving treatment with thiazide diuretics
- Older age
- Hypoglycemia
- Type 2 diabetes
- Receiving treatment with ACE inhibitors
- Reflux esophagitis, and
- Urinary tract infections.

If we extend the spectrum to also include gerontopsychiatric patients, who may be treated with an

SSRI or antipsychotic drug, the risk probably rises further.

For this reason, a careful risk-benefit analysis should be done in at-risk patients before initiating pharmacotherapy. DOI: 10.3238/arztebl.2017.0289a

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In Reply:

We agree with Dr. Quante that the pharmacological etiology of hyponatremia is of crucial importance, especially as iatrogenic causes can be influenced and avoided most easily.

Due to multimorbidity and polypharmacy, a multifactorial genesis of hyponatremia is common in geriatric patients.

Both in out-patients (1) as well as in hospital in-patients with severe hyponatremia (2), a multifactorial etiology was found in more than 50% of patients. Even though the etiology was not the focus of our study, we documented all medications of the included patients and compared the groups for medications that potentially induce hyponatremia. (3).

We obviously cannot confirm causality by using this method, but our study confirmed the strong association of thiazides with hyponatremia (use of thiazide diuretics in 26% of patients in the hyponatremia group versus 14% in the control group, $P=0.017$). By contrast, the use of ACE inhibitors or AT1 antagonists was identical in both groups: 67%.

In the group of patients who were being treated with thiazide diuretics (4) the proportions of patients who received concomitant treatment with ACE inhibitors or AT1 blockers did not differ (30%/36% versus 17%/19%, $P=0.70$). Antidepressants were often used (23% versus 26%, $P=0.58$) in both groups, whereas neuroleptics/antipsychotics were used less often (16% versus 15%, $P=0.74$).

We unreservedly support Dr. Quante's plea for a careful risk-benefit analysis in the pharmacotherapy of older persons.

Especially regarding the population of gerontopsychiatric patients that he mentioned, it is important to not treat the symptoms of hyponatremia—such as agitation, anxiety, confusional state, or depressiveness—with the very medications that might sustain the hyponatremia (antipsychotics/neuroleptics, SSRIs, or tricyclic antidepressants).

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Conflict of interest statement

The authors of both contributions declare that no conflict of interest exists.

CLINICAL SNAPSHOT

Look Out—A Trap in the Cardiac Cath Lab

A 76-year-old woman was referred for preoperative coronary angiography, which was performed via the right radial artery. The invasive evaluation of the severity of aortic valvular stenosis is recommended by the specialty societies in case the echocardiographic findings are inconclusive, e.g., in low-flow-low-gradient aortic valvular stenosis (evidence level Ic: strong recommendation based on expert consensus). After clinically relevant coronary heart disease had been excluded, a high gradient was surprisingly observed as the pigtail catheter was withdrawn from the left ventricle (peak-to-peak/mean gradient 147/97 mm Hg). In itself, this finding could easily have been interpreted as a consequence of severe aortic valvular stenosis, but the preceding echocardiographic Doppler study had revealed only mildly elevated gradients (Pmax/mean 29/15 mm Hg). The discrepancy was explained by aortography (*Figure*), which revealed a hemodynamically relevant stenosis of the brachiocephalic trunk. The finding arose by a summation phenomenon, in combination with radial access: because the catheter was withdrawn rapidly, only a single prestenotic aortic pressure signal was registered. Although the patient had no symptoms referable to the brachiocephalic trunk stenosis, the manometric blood pressures in her two arms differed by more than 70 mmHg (127/91 mmHg on the right, 210/80 mmHg on the left). This case underscores the fact that even an invasive study cannot be called a “gold standard” without proper attention to detail. One must always evaluate the findings critically before proceeding to treatment.

Excessively high gradient during withdrawal across the aortic valve.
Aortography reveals severe stenosis (arrow) of the brachiocephalic trunk.

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