

Morbus Diureticus in the Elderly (MDE)—Inappropriate Application of Diuretics Four Case Reports

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Rec date: June 12, 2014, Acc date: July 17, 2014, Pub date: July 26, 2014

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Abstract

Background: Diuretics still enjoy continued popularity for elderly patients, both in terms of effectiveness in reliably lowering blood pressure and cost considerations. Due to the frequency not only of the indications prompting prescription of diuretics, but also the high rate of drug prescription itself in this context, attempts have been made to quantify their overall toxicity and their contribution to adverse drug events and cases of hospitalization in elderly patients, particularly those with multiple illnesses and polypharmacy. Adverse drug reactions (ADRs) commonly observed and recorded which may specifically be attributed to diuretics during visits to the emergency ward and during hospital stays include: dehydration, dizziness, falls, electrolyte disturbances potentially culminating in delirium, and thrombosis.

Case presentation: Four cases of diuretic toxicity in the elderly are reported in this paper, representing variable features of a complex, but typical syndrome for which the term Morbus diureticus in the elderly has been proposed. The clinical picture, treatment and outcome of four patients displaying varying symptoms and degrees of severity as described above have been recorded and assessed according to our definition of Morbus diureticus.

Conclusion: These cases are by no means extraordinary or uncommon. They have been selected to illustrate the array of challenges associated with the prescribing and monitoring of diuretic use. The compromising use of diuretics could be amended in all the cases described here, resulting in the patients' satisfactory to excellent recovery.

Keywords: Morbus diureticus; Inappropriate use; Toxicity

Introduction

Diuretics represent well-established and commonly prescribed drugs for chronic illnesses such as arterial hypertension, heart failure and renal disease. The prevalence of these conditions is known to rise dramatically with age [1-3]. While substances under this general heading still enjoy continued popularity for elderly patients, both in terms of effectiveness in reliably lowering blood pressure and cost considerations, studies demonstrate that they are also a leading cause of adverse drug reactions (ADRs), joining oral anticoagulants in forming the most significant drug group causing ADRs and hospitalization [4,5]. The most frequently prescribed drugs in the U.S. are thiazides, with over 134 million prescriptions for the year 2008 [6].

ADRs commonly observed and recorded which may specifically be attributed to diuretics during visits to the emergency ward and during hospital stays include: dehydration, dizziness, falls, electrolyte disturbances potentially culminating in delirium, and thrombosis [5-8]. The following case studies should serve to illustrate a few examples of these key symptoms and clinical pictures in connection with the use of diuretics under the aspect of a new term proposed earlier to describe this particular constellation as a syndrome: Morbus diureticus in the elderly (MDE) [8]. These four cases were observed in

a single geriatric ward over a period of 6 months. By no means extraordinary or unusual, they are meant to illustrate the varying clinical pictures of MDE; the beneficial outcome of discontinuation of diuretics should encourage doctors to critically assess the use and dosage of diuretics in the elderly.

Case 1

An 84-year-old female patient presented in the emergency ward reporting severe pain in her right leg around the knee which had increased over a period of three weeks, now so severe as to render walking nearly impossible. The patient also reported a bout of bronchitis approximately 2 weeks previously which had required prolonged bedrest. Fluid intake amounted to approximately 1-1 ½ liters per day. History of falls was positive: the patient described dizziness and collapse one-half year previously which had had no severe sequelae. Duplex sonography revealed deep venous thrombosis of the popliteal vein extending to the calf. The patient was admitted to the geriatric ward and anticoagulation with low molecular weight heparin was initiated and later switched to phenprocoumon. The patient's blood pressure initially showed values around 115/70 (Table 1). After the removal of 3 of 5 antihypertensive medications (ACE inhibitor, a combination of ACE inhibitor and thiazide diuretic, and the loop diuretic), her blood pressure (sitting and standing) maintained stable values prior to discharge. The knee pain subsided.

The patient was informed about the importance of increasing fluid intake; she was discharged after 14 days in good general condition.

Case 2

A 77-year old female patient presented in the emergency ward with bilateral orbita hematoma from a fall approximately two days ago. The patient reported pain in the facial area but had no other complaints. Dementia, sleep disorder and restlessness were treated with galantamine, risperidone and zolpidem. The patient was found to be in reduced general condition and good nutritional status with poor temporal and spatial orientation. Apart from the hematoma, initial neurological examination revealed no significant neurological deficits. The patient was admitted to the geriatric ward, where, upon questioning, she reported daily fluid intake of a maximum of 1 liter. Apart from mucosal swelling in the left maxillary sinus and ethmoidal cells and galea hematoma, the CT scan proved unremarkable. A pathological orthostatic stress (Schellong) test showed a drop in standing systolic blood pressure to values <100 mmHg, thus pointing to orthostatic blood pressure changes as the most probable cause of the patient's falls. The patient was taking 3 antihypertensive medications, 2 of which were diuretics (loop and thiazide). Both diuretics were discontinued, one at a time, and fluids supplemented. The patient's blood pressure, including standing blood pressure, rose and stabilized over the course of the hospital stay (Table 1). The patient experienced no further bouts of dizziness or syncope and was discharged after 10 days in improved general condition.

Case 3

An 87-year-old male patient presented in the emergency ward with a painful head injury. He reported having been greatly startled, which precipitated the fall from a sitting position. He had been unconscious briefly following the incident and was unresponsive during this time. A CT scan showed no signs of ischemia or bleeding. On the geriatric ward, the patient was found to be spatially and temporally oriented, somnolent and in markedly reduced general condition, dehydrated and in poor nutritional condition. ECG readings revealed atrial fibrillation, right bundle branch block and echocardiography showed a mild reduction in left ventricular function. Other chronic conditions included arterial hypertension, for which the patient was taking a thiazide, atrial fibrillation, for which the patient was taking phenprocoumon and digitoxin, diabetes mellitus type II (diet sufficient) and presbycusis. When specifically questioned, the patient reported a fluid intake of less than 1 liter per day. Due to the patient's elevated temperatures and increased inflammatory parameters in plasma and urine, the physician team opted to initiate calculated antibiotics, during which course of treatment these parameters returned to normal. Following extensive fluid substitution and discontinuation of the thiazide, the patient's general condition improved greatly; he experienced no further falls and could be mobilized successfully. Digitoxin was discontinued and replaced by a beta blocker. An ACE inhibitor was also added during the further course of treatment, which proved adequate for managing both the patient's hypertension as well as the cardiac insufficiency. The patient was discharged in stable condition after 9 days.

Case 4

An 83-year-old female patient presented in the emergency ward with acute nausea. The patient had reported severe nausea as a

possible reaction to a medication, which she was unable to name. Laboratory findings revealed hyponatremia (Table 1) and elevated renal retention parameters pointed to acute renal failure. On the geriatric ward, she was found to be alert and responsive and spatially as well as temporally well-oriented. General condition was good, as was her nutritional status. Physical examination revealed no pathological findings. The patient's total fluid consumption appeared to be adequate, at approximately 1 ½ liters per day. The patient was found to be taking 4 antihypertensive drugs, among them a thiazide. Normal blood pressure values were recorded on admission. The AT1 inhibitor (candesartan) and the thiazide were discontinued. As the patient's blood pressure values remained normal and stable, no further adjustment of hypertension treatment proved necessary. Plasma sodium levels returned to normal after fluids were administered. While renal clearance remained impaired, creatinine clearance improved slightly over the further course of the hospital stay. The patient's nausea disappeared quickly and completely, and she was discharged in good condition without nausea after 7 days.

Discussion

Case 1

On the basis of the following laboratory and clinical findings, the diagnosis of MDE is plausible:

- Deep venous thrombosis, presumably by hemoconcentration
- Hyponatremia and hypokalemia
- Acute, reversible renal failure as indicated by GFR values
- Chronic dehydration as indicated by inadequate fluid and food intake and prior respiratory infection and immobilization
- History of dizziness and falls, indicating possible overtreatment of hypertension (5 antihypertensive drugs, including 2 diuretics)
- Long-term, chronic use of diuretics
- Elimination of the diuretics coincides with the patient's excellent recovery

Case 2

The patient's fall risk was presumably increased by the multiple use of antihypertensives, two of which were diuretics, and possibly amplified by concomitant use of psychoactive substances prescribed to treat dementia and related syndromes.

On the basis of the following laboratory and clinical findings, the diagnosis of MDE is plausible:

- Initial low blood pressure values
- Pathological Schellong test (orthostatic drop in blood pressure)
- Chronic dehydration may be precipitated by inadequate fluid intake
- History of dizziness and falls, indicating overtreatment of hypertension (3 antihypertensive substances, including 2 diuretics)
- Long-term, chronic use of diuretics combined with other antihypertensives and psychoactive drugs, with questionable adherence
- Absence of other contributing factors
- Elimination of the diuretics coincides with the patient's satisfactory recovery

Case 3

The patient’s state of extreme dehydration, precipitated in part by a gastrointestinal infection, may have been maintained by the use of diuretics. Due to the patient’s inadequate fluid intake and poor medication adherence, the diuretic may have exacerbated this situation. An infection with elevated temperatures contributed to rapid deterioration of the patient’s hydration and general health status.

On the basis of the following laboratory and clinical findings, the diagnosis of MDE is plausible:

- Chronic use of diuretics
- Chronic dehydration as indicated by inadequate fluid intake (<1 liter/day) and use of diuretics (overtreatment), compounding fluid loss
- Overtreatment of hypertension
- Elimination of the diuretics coincides with the patient’s satisfactory recovery

Case 4

On the basis of clinical and laboratory findings and by the patient’s rapid response to discontinuation of the diuretics (in this case overtreatment) and simultaneous fluid substitution, and quick and excellent recovery, the patient’s hyponatremia and chronic dehydration are likely to be caused by the regular use of a diuretic, thus representing another example of MDE.

Practical Conclusions

MDE is a common condition which manifests itself in various forms and degrees of severity. If present, diuretics should be suspected as potential cause of the following (non-exhaustive) list of key symptoms: dehydration, orthostasis with falls, thrombosis, electrolyte disturbances (hypokalemia, hyponatremia), confusion and delirium [for review see ref. 6]. “Hidden” diuretics in combination preparations are particularly dangerous, as they may precipitate severe symptoms if sequential nephron blockade is unintentionally instituted [7].

If diuretics prove to be necessary, patients need to be educated on the importance of fluid intake/balance and regular monitoring of electrolytes, with the aim of improving communication and optimizing patient adherence.

The critical assessment of diuretic prescription in the elderly should be routinely performed, aiming at restrictive use; dosage should be lowered if clinically tolerated. In this short case series, diuretic withdrawal coincided with clinical improvement as also documented by measures typically recorded in geriatrics. The results of the locomotion (Tinetti) and Timed-up-and-go tests, the Activities of Daily Life (ADL) improved in all patients, as did renal function and electrolyte disorders (Table 1); this should encourage physicians further to take MDE into account if treating elderly patients on diuretics.

	Case 1	Case 2	Case 3	Case 4
Blood pressure (systolic/diastolic) admission /discharge (mmHg)	115/70; 125/65	115/55; 130/70	120/70; 140/70	110/60; 135/70
Plasma sodium admission/discharge (mmol/l)	132 (-) / 138	138 / 135	138 / 142	128 (-) / 137
Plasma potassium admission/discharge (mmol/l)	3.60 / 3.90	3.70 / 3.70	4.15 / 3.70	3.69 / 3.60
MDRD-GFR admission/discharge (ml/min)	33 (-) / >60	>60 / >60	59 / >60	23 (-) / 26 (-)
Activities of Daily Living (ADL) Scale admission/discharge (max. 100)	70/ 90	65/70	35/75	70/100
Tinetti Test (locomotion) admission/discharge (max. 27)	15/27	18/27	16/18	27/27
Timed up and go Test (s)	25/20	20/15	40/27	13/12
Number/names of diuretics prescribed admission/discharge	2/0 hydrochlorothiazide, torasemide	2/0 hydrochlorothiazide, torasemide	1/0 hydrochlorothiazide	1/0 hydrochlorothiazide

Table 1: Laboratory findings and test scores

Acknowledgements

Cases are anonymous and do not contain any information which could lead back to the individual.

We would like to acknowledge financial support provided by the German research Foundation (Deutsche Forschungsgesellschaft) and the Ruprecht-Karls-Universität Heidelberg within the funding program “Open Access Publishing”.

Competing Interests

AK-T and HB declare that they have no competing interests. MW The author was employed by AstraZeneca R&D, Mölndal, as director of discovery medicine (= translational medicine) from 2004-2006, while on sabbatical leave from his professorship at the University of Heidelberg. After return to this position in January 2007, he received lecturing, reporting and/or consulting fees from Sanofi-Aventis, Novartis, Takeda, Roche, Pfizer, Bristol-Myers Squibb, Daichii-

Sankyo, Lilly, LEO Pharma, Novo-Nordisk, Shire and Pro Bono Bio Entrepreneur Ltd.

Authors' contribution

AK-T reviewed the data and prepared and drafted the manuscript. HB and MW oversaw the procedure and made major contributions to the manuscript.

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