Original Article

Therapeutic approach in patients with dysnatraemias

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Abstract

Background. Rapid correction of dysnatraemias is frequently associated with increased morbidity and mortality. Therefore, it is important to estimate the proper volume and type of infusate required to change the serum sodium concentration predictably. The aim of this study is to evaluate the utility of the Adrogue–Madias formula in managing patients with hyponatraemia and hypernatraemia.

Methods. Among the 317 patients who either on admission to our internal medicine clinic or during their hospitalization were found to have hyponatraemia or hypernatraemia, we studied 189 patients (59.6%) in whom the administration of intravenous solutions was required for the correction of dysnatraemias.

Results. Twelve hours after starting the administration of intravenous solutions the anticipated as well as the achieved serum sodium concentration were as follows: in volume depleted patients 130.2±4.1 vs 131.3±5.2 meq/l (n = 45; P = NS), in syndrome of inappropriate antidiuretic hormone secretion (SIADH) patients 127.4±5.7 vs 128.9±5.9 meq/l (n = 10; P = NS), in patients with diuretic-induced hyponatraemia 123.8±6 vs 125.5±5.6 meq/l (n = 29; P = NS), in patients with primary polydipsia 122.5±0.7 vs 129±1.4 meq/l (n = 2; P = 0.02), while in patients with hypernatraemia 153.6±7.5 vs 156.5±8.9 meq/l (n = 92; P = 0.021). Furthermore, 24 h from the initiation of the therapeutic intervention the expected and the achieved serum sodium concentrations were 130±4 vs 135.6±3.3 meq/l (n = 15; P = 0.002) in patients with volume depletion, 128.1±4.8 vs 130±4.5 meq/l (n = 15; P = NS) in patients with diuretic-induced hyponatraemia and 151.5±6.4 vs 153.3±8.3 meq/l (n = 67; P = NS) in patients with hypernatraemia.

Conclusions. The formula that has been proposed by Adrogue and Madias predicted with relative accuracy the changes in serum sodium concentration in almost all patients. Thus, it should be considered as a very useful tool for the management of dysnatraemias. However, special attention should be paid when this equation is used in patients with hyponatraemia due to extracellular volume depletion after euvalaemia’s restoration and primary polydipsia in order to avoid rapid correction of hyponatraemia.

Keywords: adrogue–madias formula; hypernatraemia; hyponatraemia

Introduction

Dysnatraemias are frequent electrolyte abnormalities occurring in a broad spectrum of patients. Such patients are exposed to major neurologic complications [1–3]. Hyponatraemia and hypernatraemia produce brain oedema and dehydration, respectively, which potentially lead to subsequent neuropathological sequelae or death. On the other hand, rapid correction of dysnatraemias is associated with increased morbidity and mortality. Specifically, excessive treatment for hyponatraemia could be followed by development of central demyelinating lesions, particularly in the pons (a disorder called central pontine myelinolysis or osmotic demyelination) with major disability or even fatal outcome [4–9]. Likewise, overcorrection of hypernatraemia can induce cerebral oedema, seizures, permanent neurologic damage and death [10–11]. So, the treatment for hyponatraemia/hypernatraemia is focused mainly on how to avoid the devastating neurologic complications, which can potentially occur either during the course of untreated dysnatraemias or after inappropriate correction of these disorders. Consequently, formulas that accurately predict the change in serum sodium concentration as a result of a given course of therapy are of paramount importance. Recently, Adrogue and Madias proposed a new formula for the management of both hyponatraemia and hypernatraemia [12–14]. According to this formula, the anticipated change in the patient’s serum sodium concentration as a result of administration of 1 l of any
In this setting, the corrected serum sodium concentration was evaluated.

In hyperglycaemic patients, more than 148 meq/l that was verified by a repeat measurement, cortisol and thyroid-stimulating hormone (TSH). Calcium, magnesium, phosphorus, triglycerides, osmolality (\(\text{Os}_{\text{std}}\)) and hydration of mucous membranes. Orthostatic hypotension and orthostatic changes in the pulse rate and blood pressure, decreased skin turgour or axillary dryness and clinical symptoms (e.g. seizures) were treated in an aggressive but controlled manner.

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A fresh urine specimen was tested for osmolality (\(\text{U}_{\text{osm}}\)), creatinine and sodium. A standard formula was used for the determination of the fractional excretion of sodium (\(\text{FENa}^+\)).

In hyponatraemic patients, the detection of the cause of hyponatraemia was one of our primary tasks. The diagnostic approach was based on history, physical examination and laboratory tests. In particular, diuretic-induced hyponatraemia was defined as hyponatraemia in patients receiving diuretics but in the absence of heart failure, hepatic cirrhosis, nephrotic syndrome, extracellular and intracellular volume depletion unrelated to diuretics, renal insufficiency unrelated to diuretics and SIADH.

Hyponatraemia due to extracellular volume depletion was diagnosed in patients with historical (e.g. vomiting, diarrhoea), clinical (such as postural changes in blood pressure and pulse rate, decreased skin turgour) and laboratory (serum urea to creatinine ratio greater than 40, urine sodium less than 20 meq/l and \(\text{FENa}^+ <1\%\)) indications of hypovolaemia. The diagnosis of the syndrome of inappropriate antidiuretic hormone (ADH) secretion was made in patients who fulfilled the following criteria: (1) hyponatraemia and hyposmolality; (2) increased \(\text{U}_{\text{osm}}\) (greater than 100 mosmol/kg); (3) inappropriate natriuresis (greater than 40 meq/l); (4) normovolaemia; (5) normal renal, adrenal and thyroid function and (6) normal acid-base and potassium balance [16]. SIADH was also supported by the presence of hypoosmolacemia, as well as by low serum urea and phosphate levels, if present.

This report is focused on patients who received intravenous solutions for the correction of dysnatraemias. The decision to treat patients with or without infusions, as well as the determination of the rate of correction was based on the presence of symptoms directly attributed to dysnatraemias, the degree of dysnatraemias, whether the condition is acute (defined as a duration of less than 48 h) or chronic, and the presence of hypovolaemia. Given their diverse and non-specific nature, the symptoms of both hyponatraemia (headache, nausea, vomiting, muscle cramps, restlessness, followed by disorientation, seizures, respiratory arrest and coma) and hyponatraemia (laryngeal, weakness, irritability, seizures and coma) were ascribed to dysnatraemias after excluding other possible causes. In fact, only patients with symptomatic dysnatraemias or/and patients with extracellular volume depletion participated in this study. In these patients, the serum as well as the anticipated (based on Adrogue–Madias formula) sodium concentration was determined at 12, 24 and 36 h after starting the infusion.

Patients with acute, severely symptomatic hyponatraemia (e.g. seizures) were treated in an aggressive but controlled fashion (1.5–2 meq/l/h for 3–4 h or until the severe neurologic symptoms were alleviated), while less symptomatic hyponatraemia was corrected at a slow pace (<0.5 meq/l/h).

However, in all patients our therapeutic target was to limit the increase in the serum sodium concentration to less than 12 meq/l on the first day and to less than 18 meq/l in the first 2 days of treatment, as well as to avoid the overcorrection of the serum sodium concentration to above 140 meq/l within the first 2 days of treatment. The cessation of hyponatraemic symptoms and the euvolaemia’s restoration led us to stop the intravenous solutions. In patients with symptomatic hyponatraemia that was developed over a period of less

\[
\Delta [\text{Na}^+] = \left( [\text{Na}^+]_{\text{inf}} - [\text{Na}^+]_s \right) / (\text{TBW} + 1)
\]

where \(\Delta [\text{Na}^+]\), \([\text{Na}^+]_{\text{inf}}\) and \([\text{Na}^+]_s\) represent the expected change in the patient’s serum sodium concentration, the sodium concentration of the infusate and the sodium concentration of the patient’s serum, respectively, in meq/l, and TBW represents the patient’s body water, expressed in litres. When the administered solution contains potassium chloride also, the equation (1) is converted as follows:

\[
\Delta [\text{Na}^+] = \left( [\text{Na}^+]_{\text{inf}} + [\text{K}^+]_{\text{inf}} - [\text{Na}^+]_s \right) / (\text{TBW} + 1)
\]

where \([\text{K}^+]_{\text{inf}}\) represent the potassium concentration of the infusate.

However, the precision of this equation has not been verified in large series of patients with dysnatraemias of various origins. The aim of this prospective study was the evaluation of the utility of and/or the accuracy of the Adrogue–Madias formula for the proper management of patients with hyponatraemia and hypernatraemia.

Patients and methods

Over a period of 2.5 years (starting on 5 February 1999), we studied prospectively non-selected, consecutive, adult patients (over 14 years of age) who either on admission to our clinic or during their hospitalization were found to have hyponatraemia or hypernatraemia. The study took place in the internal medicine clinic (60 beds) at the University Hospital of Ioannina (600 beds). To be eligible, patients had to have had a serum sodium concentration ([Na\(^+\)]\(_s\)) less than 130 meq/l or more than 148 meq/l that was verified by a repeat measurement to exclude laboratory error. In hyperglycaemic patients, the corrected serum sodium concentration was evaluated. In this setting, the corrected [Na\(^+\)] was calculated by increasing [Na\(^+\)] by 1.6 meq/l for every 100 mg/dl increment in the serum glucose above normal, while the correction factor 2.4 meq/l was used for serum glucose concentration >400 mg/dl [15]. Patients with corrected >130 meq/l or <149 meq/l were excluded from the study. In all cases, a detailed history was obtained, while each patient underwent a complete physical examination with special attention to orthostatic changes in the pulse rate and blood pressure, jugular venous pressure, skin turgour, moisture and dry mucous membranes. Orthostatic hypotension and orthostatic change in pulse rate were defined as a reduction in systolic blood pressure of at least 20 mmHg and an increase in pulse rate of at least 10% after 2 min in the upright position compared with the supine position, respectively. Furthermore, special attention was paid to determine the duration as well as the presence of symptoms of the dysnatraemias. Prior to any therapeutic intervention, venous blood was obtained for the determination of serum glucose, urea, creatinine, uric acid, sodium, potassium, chloride, calcium, magnesium, phosphorus, triglycerides, osmolality (\(\text{Osm}_{\text{osm}}\)), cortisol and thyroid-stimulating hormone (TSH).

Also, a fresh urine specimen was tested for osmolality (\(\text{Osm}_{\text{osm}}\)), creatinine and sodium. A standard formula was used for the determination of the fractional excretion of sodium (\(\text{FENa}^+\)).

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than 48 h, a rapid correction of serum sodium concentration (1–2 meq/l/h) was initially performed, while a slower rate of serum sodium reduction (<0.5 meq/l/h) was attained in patients with hypernatraemia of longer or unknown duration. In all patients, though, the targeted fall in the serum sodium concentration was up to 12 meq/l per day. Finally, the goal of treatment was to reduce the serum sodium concentration to 145 meq/l. When the patients were able to take fluids orally the intravenous solutions were stopped.

Laboratory determinations were carried out by automated chemical analysis in our laboratory using an Olympus AU 600 analyser (Olympus Diagnostica, Hamburg, Germany). Specifically, urine and serum samples were analysed using ion-sensitive electrodes for sodium, potassium and calcium, and photometric assays for phosphorus and magnesium. The glutamate dehydrogenase method was used for determining urea levels and a modification of the Jaffe method for creatinine measurement. The hexokinase and uricase methods were used for determining glucose and uric acid levels, respectively. Serum triglycerides were determined by enzymatic colorimetric assay. TSH was measured by microparticle enzyme immunoassay (ABBOTT GmbH Diagnostika, Wiesbaden-Delkenheim, Germany) and serum cortisol by competitive immunoassay (competitive ELISA, Immulite, DPC, Los Angeles, CA, USA). Serum and urine osmolality was assayed using a vapour pressure osmometer.

The TBW was estimated as 60 and 50% of lean body weight in men and women, respectively. In water-depleted hypernatraemic patients, we used lower values (50% of lean body weight in men and 40% in women).

The ethics and science committee of our hospital approved the study protocol.

Statistical analysis

The results were expressed as mean ± SD. The comparison of laboratory parameters among groups was performed by one way analysis of variance (ANOVA) followed by the LSD test for paired comparison. *P*-values less than 0.05 were considered to indicate statistical significance.

**Results**

317 patients fulfilled the inclusion criterion of the serum sodium concentration. 204 patients had hypo-natraemia, while 117 exhibited hypernatraemia. In 189 patients (59.6%), the administration of intravenous solutions was required for the correction of dysnatraemias.

The major causes of hyponatraemia were as follows: syndrome of inappropriate ADH secretion (*n* = 55), extracellular volume depletion (*n* = 53), diuretic administration (*n* = 40), hepatic cirrhosis (*n* = 22), heart failure (*n* = 9) and primary polydipsia (*n* = 4). The laboratory data in patients with the three most frequent causes of hyponatraemia (SIADH, extracellular volume depletion and diuretics) are shown in Table 1. Patients with hyponatraemia due to SIADH had lower serum concentrations of uric acid, phosphorus, urea and creatinine, and urea/creatinine ratio, but higher FENa than patients with extracellular volume depletion. Compared with hyponatraemic patients due to hypovolaemia and SIADH, patients with diuretic-induced hyponatraemia had lower serum concentrations of sodium, potassium, chloride and magnesium, as well as higher serum concentrations of calcium. Also, they exhibited higher FENa (Table 1).

In patients with volume depletion (baseline serum sodium concentration 128.3 ± 3.7 meq/l), 12 h after starting the administration of intravenous solutions, the expected, based on the Adrogue–Madias formula,
serum sodium concentration was 130.2 ± 4.1 meq/l, while the achieved serum sodium concentration was 131.3 ± 5.2 meq/l (n = 45; P = NS). 24 h from the initiation of the therapeutic intervention the anticipated serum sodium concentration was 130 ± 4 meq/l, whereas the achieved serum sodium concentration was 135.6 ± 3.3 meq/l (n = 15; P = 0.002). Finally, after 36 h the expected as well as the achieved serum sodium values were 135.5 ± 3.8 and 136.8 ± 4.3 meq/l, respectively (n = 6; P = NS). In all these cases, normal saline ± potassium chloride was administered intravenously to correct the hypovolaemia and the hypokalaemia, if present. The mean volume of administered infused per each successive 12 h interval of intravenous therapy was 1.3 ± 0.4, 1.2 ± 0.3 and 1 ± 0.2 l, respectively. Finally, electrolyte-free water intake was restricted to 0.5–1 l/day.

In symptomatic hyponatraemic patients due to SIADH (baseline serum sodium concentration 122.6 ± 5.1 meq/l, n = 10), hypertonic saline (3N) with furosemide was administered, while water restriction to less than 500–750 ml/day was prescribed. The coadministration of a loop diuretic enhances solute-free water excretion, while the possible circulatory overload is prevented. In these patients, 12 h after initiating the infusion of hypertonic solution, the expected serum sodium concentration was 127.4 ± 5.7 meq/l, while the achieved serum sodium concentration was 128.9 ± 5.9 meq/l (P = NS). 24 h after starting the administration of intravenous solutions, the expected serum sodium concentration was 129.4 ± 6.3 meq/l, while the achieved serum sodium concentration was 131.4 ± 6.4 meq/l (n = 4; P = NS). The mean volume of hypertonic solution per 12 h of intravenous therapy was 310 ± 20 and 250 ± 50 ml, respectively.

In patients with diuretic-induced hyponatraemia (baseline serum sodium concentration 120.7 ± 7.6 meq/l), 12 h from the beginning of the administration of intravenous solutions, the anticipated serum sodium concentration was 123.8 ± 6 meq/l, while the achieved serum sodium concentration was 125.5 ± 5.6 meq/l (n = 31; P = NS). 24 h after starting the administration of intravenous solutions, the expected serum sodium concentration was 129.4 ± 6.3 meq/l, while the achieved serum sodium concentration was 132.5 ± 5.1 meq/l (n = 15; P = NS). Finally, after 36 h the expected as well as the achieved serum sodium values were 129.3 ± 4.9 and 132.1 ± 5.3 meq/l, respectively (n = 8; P = NS). It should be noticed that there were two subgroups of patients with diuretic-induced hyponatraemia, one with extracellular volume depletion and another with euvoalaemic state. Patients with normovolaemic hyponatraemia had lower serum concentrations of urea (28.4 ± 8.6 vs 68.2 ± 47.2 mg/dl, P = 0.005), creatinine (0.8 ± 0.1 vs 1.27 ± 0.5 mg/dl, P = 0.003), uric acid (2.7 ± 0.8 vs 7.2 ± 1.9 mg/dl, P = 0.001) and urea/creatinine ratio (34.1 ± 7.3 vs 51.6 ± 25.5, P = 0.017) than patients with hypovolaemic hyponatraemia due to diuretics. All patients were receiving thiazide or thiazide-like agents, while there were no differences between the two subgroups in age, gender distribution, or diuretic dose. In all patients, diuretic administration was withheld, whereas all patients who reported increased water intake (n = 23) were placed on water restriction (<500–750 ml/day). In patients with extracellular volume depletion (n = 25), normal saline ± potassium chloride was administered intravenously to correct the hypovolaemia and the hypokalaemia, if present. In patients with euvoalaemic symptomatic hyponatraemia (n = 6), hypertonic sodium chloride solution (3N) was administered intravenously and water was withheld to less than 500–750 ml/day. In the extracellular volume depletion subgroup, the mean volume of administered infusate (normal saline ± potassium chloride) per each successive 12 h interval of intravenous therapy was 1.2 ± 0.3, 1.05 ± 0.2 and 0.95 ± 0.1 l, respectively. In the euvoalaemic subgroup, the corresponding mean volume of administered infusate (hypertonic saline) was 315 ± 25, 260 ± 55 and 240 ± 40 ml, respectively. It should be emphasized that there were no statistically significant differences between anticipated and achieved serum sodium values in the two subgroups of patients with diuretic-induced hyponatraemia (data submitted for publication).

In two patients with symptomatic hyponatraemia due to primary polydipsia (admission serum sodium concentration: 116 ± 4.2 meq/l), 12 h after initiating the infusion of hypertonic solution the expected serum sodium concentration was 122.5 ± 0.7 meq/l, while the achieved serum sodium concentration was 127.8 ± 1.4 meq/l (P = 0.02). The mean volume of administered hypertonic solution was 350 ± 20 ml. Over the treatment, these patients were also placed on water restriction (less than 500–750 ml/day).

117 patients exhibited hypernatraemia. 52 were hypernatraemic on hospital admission and 65 developed hypernatraemia during hospitalization. In the vast majority of hypernatraemic patients, more than one condition contributed to the development of hypernatraemia; the most common factors were: febrile illnesses (72%; mainly pulmonary infections), uncontrolled diabetes mellitus (30%), mannitol (21%) or diuretics (10%; mainly furosemide) administration, gastrointestinal losses (10%) and environment’s high temperature (30%). Additionally, in almost all cases (91%) the water intake was markedly diminished because of the patients’ altered mental status. In patients with hypernatraemia (baseline serum sodium concentration 157.8 ± 8.8 meq/l), 12 h from the beginning of the administration of intravenous solutions, the anticipated as well as the achieved serum sodium concentrations were 153.6 ± 7.5 and 156.5 ± 8.9 meq/l, respectively (n = 92; P = 0.021). There was, however, a subgroup of eight patients (8.7%) in whom a considerable disparity between the anticipated and achieved serum sodium concentration was observed over the first 12 h of treatment (152.2 ± 5.8 vs 161 ± 4.8 meq/l, P = 0.003). These patients had higher serum concentrations of urea (290 ± 109.6 vs 113.4 ± 48.3 mg/dl, P = 0.000) and creatinine (3.3 ± 1 vs 1.7 ± 0.8 mg/dl, P = 0.000), whereas they exhibited lower serum sodium concentrations of urea (28.4 ± 8.6 vs 68.2 ± 47.2 mg/dl, P = 0.005), creatinine (0.8 ± 0.1 vs 1.27 ± 0.5 mg/dl, P = 0.003), uric acid (2.7 ± 0.8 vs 7.2 ± 1.9 mg/dl, P = 0.001) and urea/creatinine ratio (34.1 ± 7.3 vs 51.6 ± 25.5, P = 0.017) than patients with hypovolaemic hyponatraemia due to diuretics. All patients were receiving thiazide or thiazide-like agents, while there were no differences between the two subgroups in age, gender distribution, or diuretic dose. In all patients, diuretic administration was withheld, whereas all patients who reported increased water intake (n = 23) were placed on water restriction (<500–750 ml/day). In patients with extracellular volume depletion (n = 25), normal saline ± potassium chloride was administered intravenously to correct the hypovolaemia and the hypokalaemia, if present. In patients with euvoalaemic symptomatic hyponatraemia (n = 6), hypertonic sodium chloride solution (3N) was administered intravenously and water was withheld to less than 500–750 ml/day. In the extracellular volume depletion subgroup, the mean volume of administered infusate (normal saline ± potassium chloride) per each successive 12 h interval of intravenous therapy was 1.2 ± 0.3, 1.05 ± 0.2 and 0.95 ± 0.1 l, respectively. In the euvoalaemic subgroup, the corresponding mean volume of administered infusate (hypertonic saline) was 315 ± 25, 260 ± 55 and 240 ± 40 ml, respectively. It should be emphasized that there were no statistically significant differences between anticipated and achieved serum sodium values in the two subgroups of patients with diuretic-induced hyponatraemia (data submitted for publication).

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concentration (155.1 ± 7.3 vs 157.8 ± 8.9 meq/l, \( P = 0.135 \)) as compared to the rest of hypernatraemic patients. In fact, in these cases an increase in the serum sodium concentration was initially found contrary to the expected decrement. On the other hand, a simultaneous reduction in the serum concentration of urea (243.5 ± 96 vs 290.4 ± 109.6 mg/dl, \( P = 0.4 \)) and creatinine (2.5 ± 0.9 vs 3.3 ± 1 mg/dl, \( P = 0.18 \)) was observed. It should be mentioned that these patients' haemodynamic status was sufficiently compromised, consequently normal saline was initially administered intravenously to correct the hypovolaemia. Not including this subgroup of patients, there were no statistically significant differences between the anticipated and the achieved serum sodium concentration in the remaining hypernatraemic patients (153.1 ± 7.2 vs 154.3 ± 7.8). Furthermore, 24 h from the initiation of the therapeutic intervention in the whole group of patients (\( n = 67 \)) the anticipated serum sodium concentration was 151.5 ± 6.4, whereas the achieved serum sodium concentration was 153.3 ± 8.3 meq/l (\( P = 0.15 \)). Finally, after 36 h the expected as well as the achieved serum sodium concentration was 149 ± 6.2 and 150 ± 6.8 meq/l, respectively (\( n = 34; P = 0.28 \)). It is of interest that a considerable percentage of the hypernatraemic patients had clinical findings (such as postural changes in blood pressure and pulse rate, decreased skin turgor or axillary moisture and dry mucous membranes) and laboratory evidence (serum urea to creatinine ratio greater than 40, urine sodium less than 20 meq/l and FEna− <1%) of extracellular volume depletion. Based on both the patients' clinical state and laboratory findings, 71 subjects (62.8%) exhibited hypovolaemic hypernatraemia. Except for the previously mentioned eight patients with severe hypovolaemia (who were treated initially with isotonic saline) all the remaining hypovolaemic patients received half-isotonic (\( n = 22 \)) or quarter-isotonic saline (\( n = 41 \)). The mean volume of administered infusate per each successive 12 h interval of intravenous therapy was 2.2 ± 0.4, 1.8 ± 0.3 and 1.5 ± 0.21, respectively. In contrast, hypernatraemia due to pure water loss was found in 36 patients (31.8%). Of those, 24 patients received free water intravenously, while the remaining orally. The mean volume of administered infusate (as dextrose 5% in water) per each consecutive 12 h interval of intravenous treatment was 1.8 ± 0.4, 1.5 ± 0.3 and 1.3 ± 0.21, respectively.

The expected as well as the achieved serum sodium concentrations are summarized in Table 2.

### Discussion

The present study, for the first time in the literature, provides an external validation of the formula proposed by Adrogue and Madias in prescribing fluid therapy for patients with dysnatraemias [13–15].

This study showed that the Adrogue–Madias formula predicted with relative accuracy the changes of the serum sodium concentration in patients with diuretic-induced hyponatraemia, SIADH patients, volume depleted patients (before euvolaemia’s restoration) as well as in the majority of hypernatraemic patients. Indeed, in these cases, there were no statistically significant differences between anticipated and achieved values of serum sodium concentration, thus supporting the clinical utility of the formula. This favourable assessment is noticeable taking into consideration that the formula’s output depends on a reliable estimate of TBW (equation 1); yet the clinical estimate of TBW is a rough approximation at best. It is noteworthy, however, that the mean serum sodium values anticipated by the formula were consistently somewhat lower (by 1–3 meq/l) than those achieved. This disparity should be attributed to the fact that the Adrogue–Madias formula considers the patient as a closed system, not taking into account any ongoing urinary, dermal and respiratory fluid losses. As the sum of the sodium and potassium concentrations in these fluid losses is lower than that of serum, these losses would contribute to the increase in serum sodium values. Finally, despite the lack of statistical significance between anticipated and achieved serum sodium values, there were some cases in which a considerable aberration (>4 meq/l) between the anticipated and achieved serum sodium concentration was observed. Therefore, serial measurements of the serum sodium values are required to ascertain that the desired rate of correction is being achieved.

Nevertheless, the expected, based on the Adrogue–Madias formula, serum sodium values were statistically significant lower than those achieved in cases of hyponatraemia due to extracellular volume depletion (at 24 h after starting the infusion of intravenous solution) and primary polydipsia. In fact, the Adrogue–Madias equation underestimates the increment of the serum sodium concentration in patients

<table>
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<th>Table 2. Anticipated and achieved serum sodium concentration at 12, 24 and 36 h after starting the infusion of intravenous solution for treatment in patients with dysnatraemias</th>
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<tr>
<td>Anticipated serum Na⁺ concentration (meq/l)</td>
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<tr>
<td>Volume depletion</td>
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<td>12 h (( n = 45 ))</td>
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<td>24 h (( n = 15 ))</td>
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<td>12 h (( n = 29 ))</td>
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<td>24 h (( n = 15 ))</td>
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<td>36 h (( n = 8 ))</td>
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<td>Primary polydipsia</td>
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<td>12 (( n = 2 ))</td>
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<td>Hypernatremia</td>
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<td>12 h (( n = 92 ))</td>
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<td>24 h (( n = 67 ))</td>
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<td>36 h (( n = 34 ))</td>
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with polydipsia or volume depletion after water restriction or euvolaemia’s restoration, respectively. In each of these conditions, ADH release is appropriately suppressed, thereby allowing the excess water to be rapidly excreted in a dilute urine and correction of the hyponatraemia at an overly rapid pace.

Moreover, the formula was unable to predict correctly the serum sodium concentration changes in a subgroup of patients with hypernatraemia and severe extracellular volume depletion as well as marked reduction of renal function. In these cases, in spite of administering relatively hypotonic solutions as compared to patients’ serum, an increase in the serum sodium concentration was initially observed, while the renal function was improved. This increment of the serum sodium values can be attributed to the fact that the administered solutions were relatively hypertonic compared with the ongoing hypotonic fluid losses, which are not taken into consideration by the Adrogue–Madias equation.

The sodium deficit equation as well as the water deficit equation are frequently utilized for guiding treatment of hyponatraemia and hypernatraemia, respectively [17,18]. However, there are several limitations regarding the use of these formulas [19]. For example, the water deficit equation is only applicable in patients with hypernatraemia caused by pure water loss without concomitant Na⁺ loss. Our study, on the contrary, clearly showed that the majority of hypernatraemic patients (62.8%) exhibited hypovolaemic hypernatraemia. Consequently, the Adrogue–Madias formula both being applicable to the treatment of hyponatraemia and hypernatraemia of any origin and guiding the physician as regards the composition or the infusion rate of anyone of the infusates excels in managing patients with dysnatraemias as compared to the sodium deficit equation as well as the water deficit equation. Furthermore, its simplicity is the main advantage in comparison with two novel formulas proposed by Nguyen and Kurtz as well as Barsoum and Levine, respectively [19,20]. It should be emphasized, however, that our study was not designed to compare the Adrogue–Madias equation with the other equations.

In conclusion, our study clearly showed that the Adrogue–Madias formula predicted with relative accuracy the changes in serum sodium concentration in the majority of patients. Thus, it should be considered as a very useful tool for the management of dysnatraemias. However, caution is warranted in prescribing therapy, since the formula-based quantitative projections tend to underestimate the mark. Moreover, extra attention should be paid and serial measurements of the serum sodium concentration are required when this equation is used, especially in patients with hyponatraemia due to extracellular volume depletion after euvolaemia’s restoration and primary polydipsia as well as in patients with hypernatraemia and severe hypovolaemia in order to avoid rapid correction of hyponatraemia and deterioration of hypernatraemia, respectively.

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References


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