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RISK FACTOR FOR HYPONATREMIA: SYSTEMATIC REVIEW IN LITERATURE

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Abstract:
This review is aiming to discuss the Risk factor for hyponatremia. The present review was conducted by searching in Medline, Embase, Web of Science, Science Direct, BMJ journal and Google Scholar for, researches, review articles and reports, published over the past years. Books published on Risk factor for hyponatremia. If several studies had similar findings, we randomly selected one or two to avoid repetitive results. On the basis of findings and results this review found Diabetes mellitus was identified as an independent risk factor for hyponatremia and hypomagnesemia, whereas hypertension was associated with hypokalemia. Diuretics were independently associated with several electrolyte disorders: thiazide diuretics (hyponatremia). The frequency of hyponatremia (Na+ ≪134 mEq/L) was 29.9% among OXC-treated patients and 13.5% among CBZ-treated patients ($p < 0.0001$). Hyponatremia (Na+ ≪128 mEq/L) was severe: 12.4% of OXC-treated patients and 2.8% of CBZ-treated patients ($p < 0.001$). Advanced age was a risk factor for hyponatremia.

Keywords: *Risk factor, hyponatremia.*

Abbreviation:
Non-steroidal anti-inflammatory drug (NSAID). oxcarbazepine-treated (OXC) carbamazepine-treated (CBZ)

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INTRODUCTION:

Hyponatremia is a low sodium level in the blood[1] It is generally defined as a sodium concentration of less than 135 mmol/L (135 mEq/L), with severe hyponatremia being below 120 mEq/L.[2] Symptoms can be absent, mild or severe.[2]Mild symptoms include a decreased ability to think, headaches, nausea, and poor balance. Severe symptoms include confusion, seizures, and coma. [1]

The causes of hyponatremia are typically classified by a person's body fluid status into low volume, normal volume, or high volume. Low volume hyponatremia can occur from diarrhea, vomiting, diuretics, and sweating. [3] Normal volume hyponatremia is divided into cases with dilute urine and concentrated urine. Cases in which the urine is dilute include adrenal insufficiency, hypothyroidism, and drinking too much water or too much beer. [3]

Treatment is based on the underlying cause. [4] Correcting hyponatremia too quickly can lead to complications. [4] Rapid partial correction with 3% normal saline is only recommended in those with significant symptoms and occasionally those in whom the condition was of rapid onset. [5] Low volume hyponatremia is typically treated with intravenous normal saline. [3] SIADH is typically treated with fluid restriction while high volume hyponatremia is typically treated with both fluid restriction and a diet low in salt. Correction should generally be gradual in those in whom the low levels have been present for more than two days. [3]

Hyponatremia occurs in about 20% of those admitted to hospital and 10% of people during or after an endurance sporting event.[4] Among those in hospital, hyponatremia is associated with an increased risk of death. [4]

METHODS:

The present review was conducted Jan 2019 in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) declaration standards for systematic reviews. We reviewed all the topics on Risk factor for Hyponatremia. To achieve this goal, we searched Medline, EMBASE, Web of Science, Science Direct, and Google Scholar for, researches, review articles and reports, published over the past 15 years. Books published on Risk factor for hyponatremia. Our search was completed without language restrictions. Then we extracted data on study year, study design, and key outcome of Risk factor for Hyponatremia. The selected studies were summarized, and unreproducible studies were excluded. Selected data are shown in the Table 1.

Inclusion criteria

We included studies of consecutive patients' representative of the Hyponatremia population. We included randomized controlled trials in this study. The participants were adults who had undergone Hyponatremia.

Exclusion criteria

Randomized controlled trials on many evaluations of new technologies comprise selected populations, and furthermore, it is outside the scope of this review to assess whether these reflect best clinical practice.

Data extraction and analysis

Information relating to each of the systematic review elements was extracted from the studies and collated in qualitative tables. Direct analysis of the studies of risk factor for Hyponatremia is done with extreme caution, as different sampling techniques can provide bias as an overview of the assemblage.

RESULTS:

As independent risk factors (gender and age) for hypo- and hypernatremia and describes the prevalence of hypo- and hypernatremia in different population groups. Details of all serum Na results with accompanying patient demographics for 2 years were downloaded from the laboratory database into Microsoft Access for multiple logistic regression analysis using SPSS. Female gender and age <30 years were the reference groups. Data from 303,577 samples on 120,137 patients were available for analysis. Prevalence at initial presentation to a health care provider of Na<136, <116, >145, and >165 mmol/l were for acute hospital care patients: 28.2%, 0.49%, 1.43%, and 0.06%, ambulatory hospital care: 21%, 0.17%, 0.53%, and 0.01%, community care: 7.2%, 0.03%, 0.72%, and <0.01%. Age odds ratios rose with increasing age to 1.89 and 8.70 (Na<136 and <116 mmol/l) and 7.09 and 24.39 (Na>145 and >165 mmol/l, respectively) for age >81 years. Male gender was a mild risk factor for Na<136 mmol/l and was otherwise unimportant. [5]

In observational cohort study aimed to determine whether NSAID use is a risk factor for exertional hyponatremia and altered renal function during endurance exercise. METHODS: A total of 330 athletes in the 2004 New Zealand Ironman triathlon (3.8-km swim, 180-km cycle, and 42.2-km run) were weighed before and after the race. A blood sample was drawn for measurement of plasma sodium (Na), potassium (K), urea (urea), and creatinine (creatinine)

Risk	Authors	Design	Population	Main Results
gender	Robert C. Hawkins. (2003)[5]	2 years were downloaded from the laboratory database	Female gender and age <30 years were the reference	Prevalence at initial presentation to a health care provider of Na<136, <116, >145, and >165 mmol/l were for acute hospital care

concentrations postrace. The incidence of NSAID use was 30%, whereas the overall incidence of hyponatremia was 1.8%. NSAID use was related to the incidence of hyponatremia (P = 0.0002). The NSAID group had lower plasma Na (P = 0.02) and higher plasma K (P = 0.002), urea (P = 0.05), and creatinine (P = 0.01). Lower Na was also significantly related to female gender, lower prerace body weight, younger age and a smaller weight loss during the race. Race times were not associated with plasma Na, however, faster triathletes lost more weight. Estimated fluid intake was not different in the NSAID group, but heavier triathletes reported greater fluid intakes. [6]

Recent studies suggest that mild hyponatremia is associated with fractures, but prospective studies are lacking. We studied whether hyponatremia is associated with fractures, falls, and/or bone mineral density (BMD). A total of 5208 elderly subjects with serum sodium assessed at baseline were included from the prospective population-based Rotterdam Study. The following data were analyzed: BMD, vertebral fractures (mean follow-up 6.4 years), nonvertebral fractures (7.4 years), recent falls, comorbidity, medication, and mortality. Hyponatremia was detected in 399 subjects (7.7%, 133.4 ± 2.0 mmol/L). Subjects with hyponatremia were older (73.5 ± 10.3 years versus 70.0 ± 9.0 years, $p < .001$), had more recent falls (23.8% versus16.4%, $p < .01$), higher type 2 diabetes mellitus prevalence (22.2% versus 10.3%, $p < .001$), and more often used diuretics (31.1% versus 15.0%, $p < .001$). Hyponatremia was not associated with lower BMD but was associated with increased risk of incident nonvertebral fractures [hazard ratio (HR) =1.39, 95% confidence interval (CI) 1.11–1.73, $p = .004$] after adjustment for age, sex, and body mass index. [7]

A total of 5179 subjects aged 55 years or more were included from the population-based Rotterdam Study. We focused on hyponatremia, hypernatremia, hypokalemia, hyperkalemia, and hypomagnesemia. Multivariable logistic regression was used to study potential associations with renal function, comorbidity, and medication. The adjusted mortality also was determined for each electrolyte disorder.

A total of 776 subjects (15.0%) had at least 1 electrolyte disorder, with hyponatremia (7.7%) and hypernatremia (3.4%) being most common. Diabetes mellitus was identified as an independent risk factor for hyponatremia and hypomagnesemia, whereas hypertension was associated with hypokalemia. Diuretics were independently associated with several electrolyte disorders: thiazide diuretics (hyponatremia, hypokalemia, hypomagnesemia), loop diuretics (hypernatremia, hypokalemia), and potassium-sparing diuretics (hyponatremia). The use of benzodiazepines also was associated with hyponatremia. Hyponatremic subjects who used both thiazides and benzodiazepines had a 3 mmol/L lower serum sodium concentration than subjects using 1 or none of these drugs ($P < .001$). Hyponatremia and hypomagnesemia were independently associated with an increased mortality risk. [8]

The study examined sodium concentrations from 97 oxcarbazepine-treated (OXC) and 451 carbamazepine-treated (CBZ) patients with epilepsy using cross-section and follow-up studies. The frequency of hyponatremia ($Na^+ \ll 134$ mEq/L) was 29.9% among OXC-treated patients and 13.5% among CBZ-treated patients ($p < 0.0001$). Hyponatremia ($Na^+ \ll 128$ mEq/L) was severe: 12.4% of OXC-treated patients and 2.8% of CBZ-treated patients ($p < 0.001$). Advanced age was a risk factor for hyponatremia. Hyponatremia, once present, persisted in both groups. [9]

Table (1) Results from Sequencing Studies.

		into Microsoft Access for multiple logistic regression analysis using SPSS.	groups. 303,577 samples on 120,137 patients were available for analysis	patients: 28.2%, 0.49%, 1.43%, and 0.06%, ambulatory hospital care: 21%, 0.17%, 0.53%, and 0.01%, community care: 7.2%, 0.03%, 0.72%, and <0.01%. Age odds ratios rose with increasing age to 1.89 and 8.70 (Na<136 and <116 mmol/l) and 7.09 and 24.39 (Na>145 and >165 mmol/l, respectively) for age >81 years. Male gender was a mild risk factor for Na<136 mmol/l and was otherwise unimportant..
NSAID use	Wharam etal (2006)[6]	observational cohort study	total of 330 athletes in the 2004 New Zealand	The incidence of NSAID use was 30%, whereas the overall incidence of hyponatremia was 1.8%. NSAID use was related to the incidence of hyponatremia (P = 0.0002). The NSAID group had lower plasma Na (P = 0.02) and higher plasma K (P = 0.002), urea (P = 0.05), and creatinine (P = 0.01). Lower Na was also significantly related to female gender, lower prerace body weight, younger age and a smaller weight loss during the race. Race times were not associated with plasma Na, however, faster triathletes lost more weight. Estimated fluid intake was not different in the NSAID group, but heavier triathletes reported greater fluid intakes.
fractures, falls, and/or bone mineral density	Hoorn et al (2011)[7]	prospective study	Atotal of 5208 elderly subjects	Hyponatremia was detected in 399 subjects (7.7%, 133.4 ± 2.0 mmol/L). Subjects with hyponatremia were older (73.5 ± 10.3 years versus 70.0 ± 9.0 years, p < .001), had more recent falls (23.8% versus16.4%, p < .01), higher type 2 diabetes mellitus prevalence (22.2% versus 10.3%, p < .001), and more often used diuretics (31.1% versus 15.0%, p < .001). Hyponatremia was not associated with lower BMD but was associated with increased risk of incident nonvertebral fractures [hazard ratio (HR) =1.39, 95% confidence interval (CI) 1.11–1.73, p = .004] after adjustment for age, sex, and body mass index.
Age	Liamis et al (2013)[8]	population-based Rotterdam Study.	total of 5179 subjects aged 55 years or more	A total of 776 subjects (15.0%) had at least 1 electrolyte disorder, with hyponatremia (7.7%) and hypernatremia (3.4%) being most common. Diabetes mellitus was identified as an independent risk factor for hyponatremia and hypomagnesemia, whereas hypertension was associated with hypokalemia. Diuretics were independently associated with several electrolyte disorders: thiazide diuretics (hyponatremia, hypokalemia, hypomagnesemia), loop diuretics (hypernatremia, hypokalemia), and potassium-sparing diuretics (hyponatremia). The use of benzodiazepines also was associated with hyponatremia.

				Hyponatremic subjects who used both thiazides and benzodiazepines had a 3 mmol/L lower serum sodium concentration than subjects using 1 or none of these drugs (P < .001). Hyponatremia and hypomagnesemia were independently associated with an increased mortality risk.
xcarbazepine and carbamazepine	Xiaoming et al (2005)[9]	cross-section and follow-up studies	97 oxcarbazepine-treated (OXC) and 451 carbamazepine-treated (CBZ) patients with epilepsy	The frequency of hyponatremia (Na+ ≪134 mEq/L) was 29.9% among OXC-treated patients and 13.5% among CBZ-treated patients (p < 0.0001). Hyponatremia (Na+ ≪128 mEq/L) was severe: 12.4% of OXC-treated patients and 2.8% of CBZ-treated patients (p < 0.001). Advanced age was a risk factor for hyponatremia. Hyponatremia, once present, persisted in both groups.

DISCUSSION:

These data show that many people with a Hyponatremia is a common but generally mild condition while hypernatremia is uncommon. Increasing age is a strong independent risk factor for both hypo- and hypernatremia.

Exertional hyponatremia ((Na) < 135 mmol x L (-1)) is a potentially serious condition associated with endurance sports. It has been postulated that no steroidal anti-inflammatory drug (NSAID) use may be a risk factor. NSAIDs are commonly used by athletes competing in endurance events and are a risk factor for hyponatremia and altered renal function. Not with standing high rates of NSAID use, the incidence of hyponatremia was low. We attribute this to changes in fluid replacement guidelines and drink station availability that reduce the risk of overdrinking, the principal cause of this condition.

The focus of this study[7] was on the complications (ie, fractures, mortality) rather than on the causes of hyponatremia. Nevertheless, the possible etiology of hyponatremia merits consideration because it remains unclear whether hyponatremia by itself predisposes to fractures or whether hyponatremia is a surrogate marker for another risk factor for fractures. The higher frequency of use of diuretics in subjects with hyponatremia suggests

that diuretics were a common cause of hyponatremia. Indeed, thiazides and, to a lesser extent, potassium-sparing diuretics are a common cause of hyponatremia. The use of psycholeptics at baseline, another common cause of hyponatremia, was low and not higher in subjects with hyponatremia. Diabetes mellitus is another well-known cause of hyponatremia either because of hyperglycemia or because of altered vasopressin metabolism.

Electrolyte disorders are common among older community subjects and mainly associated with diabetes mellitus and diuretics. Subjects who used both thiazides and benzodiazepines had a more severe degree of hyponatremia. Because even mild electrolyte disorders were associated with mortality, monitoring of electrolytes and discontinuation of offending drugs may improve outcomes.

CONCLUSIONS:

In conclusion, we observed that elderly subjects with mild hyponatremia at baseline had an increased risk of incident nonvertebral fractures and of prevalent but not incident vertebral fractures. The increased fracture risk was not explained by increased comorbidity, the use of diuretics, or a history of recent falling. Mild hyponatremia is a new and important risk factor for fractures in the elderly. Gender is not an important risk factor for disturbances of serum Na concentration.

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