

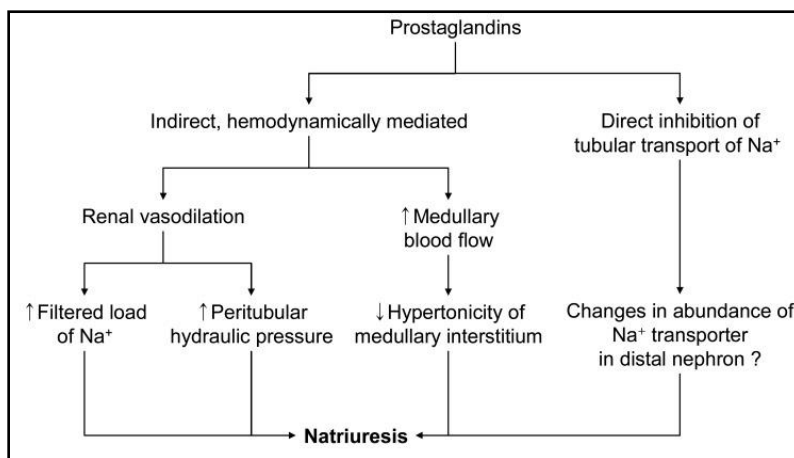


TODAY'S TOPIC: NSAIDs and SIADH: Caution?

Background:

The diagnostic criteria for the diagnosis of the Syndrome of Inappropriate secretion of AntiDiuretic Hormone (SIADH) are: hypoosmolality (plasma osmolality <280mOsm/kg, or plasma sodium concentration <134mmol/L); inappropriate urinary osmolality concentration (Uosm >100mOsm/kg) for hyponatremia; elevated urinary sodium (>40mmol/L), with normal dietary salt and water intake; patient's normovolemia; exclusion of hypothyroidism, diuretic treatment, and glucocorticoid deficiency. The most common causes of SIADH are malignancies, pulmonary disorders, central nervous system disorders, and medications.

Although rare, non-steroidal anti-inflammatory drugs (NSAIDs) can cause hyponatremia by reducing renal free water clearance – through inhibition of renal prostaglandin synthesis and potentiating the renal effects of vasopressin:



Importance:

NSAIDs can be valuable medications for palliative care providers. NSAIDs can be great for musculoskeletal pain, headaches, to bone metastases related pain. Therefore, it is important for palliative care providers to understand this connection as some other serious illnesses can decrease sodium levels. For

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example, often lung cancers (both small cell and non-small cell) can cause SIADH.

The Literature:

- [Medicina \(Kaunas\). 2012;48\(12\):619-21.](#)
Nonsteroidal anti-inflammatory drug-induced severe hyponatremia.
 - In this report, we present a case of hyponatremia in a 78-year-old man who had received meloxicam, a nonsteroidal anti-inflammatory drug.

- [Med Sci Sports Exerc. 2006 Apr;38\(4\):618-22.](#)
NSAID use increases the risk of developing hyponatremia during an Ironman triathlon.
 - 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) concentrations postrace
 - Results: 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
 - Conclusion: "NSAIDs are commonly used by athletes competing in endurance events and are a risk factor for hyponatremia and altered renal function. Notwithstanding high rates of NSAID use, the incidence of hyponatremia was low."

- [Clin Nephrol Case Stud. 2014 Jan 22;2:5-8.](#)
Syndrome of inappropriate antidiuretic hormone secretion associated with prolonged keterolac use.
 - We report a case of SIADH that was associated with keterolac in a 65-year-old male. SIADH has not previously been reported with keterolac, a strong NSAID with comparable analgesic effect as morphine and meperidine. Keterolac may have unique properties different from other NSAIDs which may predispose to the development of hyponatremia. In our case, prolonged use of keterolac may have contributed to the development of SIADH and caution is needed when keterolac is used for prolonged duration. A review of the literature regarding development of SIADH and hyponatremia in the setting of NSAIDs is also presented.

So... What does this all mean Jenn?

- It appears that NSAIDs have a lower risk of causing hyponatremia, therefore worsening SIADH
- In rare cases NSAIDs have been associated with SIADH:
 - SIADH in the setting of NSAIDs usually occurs when there are additional factors such as hypovolemia or medications causing non-suppressable ADH release
 - NSAIDs and SIADH have been reported with ibuprofen, indomethacin, piroxicam, sulindac, and diclofenac
- There is not enough literature for me to say which NSAID is the “safest” in patients with SIADH – for now, this may be sulindac. It has been hypothesized that sulindac in some patients may spare renal prostaglandin synthesis. The “worse” NSAID in this case may be indomethacin, or ketorolac, as in pharmacokinetic studies it is the most potent
- Be sure to watch out for this when considering NSAIDs in patients already with lower Na

Geriatric Considerations:

- NSAIDs can be tricky for older adults. Often NSAIDs are usually not appropriate for older adults due to concerns for acute kidney injury, gastrointestinal bleeding, or long-term cardiovascular events
- If NSAIDs are selected for an older adult, as above, consider sulindac [\[Ref\]](#)

Stay tuned for future PCP Phast Phacts on NSAIDs!

CLINICAL PEARL:

Although rare, NSAIDs have been associated with hyponatremia and rarely causes SIADH.