e - ISSN - 2349 - 8005

INTERNATIONAL JOURNAL OF ADVANCES IN CASE REPORTS

Journal homepage: www.mcmed.us/journal/ijacr

SIADH FOLLOWING TWO DOSES OF ORAL CIPROFLOXACIN

A Hutchinson* and B Mc Grath

Institution University Hospital South Manchester, Manchester, United Kingdom.

Corresponding Author:- **A Hutchinson**
E-mail: adelhutchinson@hotmail.com

Article Info

Received 15/11/2015
Revised 27/11/2015
Accepted 02/12/2015

Key words:
Trans-rectal prostate biopsy, Urologist

ABSTRACT

A 72 year old, previously well gentleman attended for a day case trans-rectal prostate biopsy under the care of a consultant urologist. The procedure was carried out uneventfully and did not involve bladder irrigation. As per local protocol, he received a prophylactic dose of oral ciprofloxacin followed by a further dose at home that evening. The following morning he became generally unwell and felt nauseous. He presented to the emergency department and subsequently developed four grand mal seizures. He was treated with benzodiazepines but unfortunately appeared to have aspirated gastric contents. His conscious level remained low and so he was intubated and ventilated to facilitate ongoing assessment and management and he was transferred to the intensive care unit. He had no prior history of seizures.

CASE REPORT

Clinical examination was unremarkable and he was clinically euvolaemic. Initial blood results revealed a serum sodium of 118 mmol/l, potassium 3.2 mmol/l, urea 4 mmol/l and creatinine 63 mmol/l. This prompted further tests including a urinary sodium (111 mOsm /l), urine osmolality (441 mOsm/l) and serum osmolality (262 mOsm /l), leading to a working diagnosis of a Syndrome of Inappropriate Anti-Diuretic Hormone secretion (SIADH) of unclear aetiology. On examination his reflexes were brisk and he demonstrated marked clonus but no focal neurological deficit.

The only other past medical history was hypertension and hypercholesterolaemia but there had been no recent medication changes.

This gentleman had received no other medications known to cause SIADH and his own long-term medications could not account for sudden severe hyponatraemia (sodium 4 weeks previously had been measured at 138 mmol/l). CT brain and CXR were performed and were reported as unremarkable. Serum WCC and CRP along with cultures of blood, sputum and urine cultures ultimately ruled out other common causes of SIADH such as infection or malignancy. Management on the ICU included stopping ciprofloxacin, fluid restriction and monitoring of serum sodium levels to ensure a slow rise in his serum sodium (see table 1). He made a good recovery and was extubated the following day with only some temporary mild confusion.

DISCUSSION

The most widely accepted definition of hyponatraemia is a serum sodium of less than 135 mmol/L and is the commonest electrolyte abnormality [1]. Life threatening sequelae can occur if the serum sodium concentration falls below 125 mmol/L. The in-patient hospital incidence of hyponatraemia is high (15-40% as defined as a serum sodium level of < 135 mEq/L), while only 1-4% of patients who are hospitalised have a serum sodium level of less than 130 mEq/L.) [2, 3]. Usually the aetiology involves diuretic administration or iatrogenic administration of hypotonic fluids. Having considered clinical or laboratory evidence of cardiac, renal or liver failure, endocrine causes of hyponatraemia should be investigated. SIADH is one of the more common causes, although adrenal failure and thyroid disorders should also be considered. Causes of SIADH can be divided into three broad categories, as shown in Table 2.

It seemed reasonable to conclude that ciprofloxacin administration was the aetiology behind the

hyponatraemia in this case. This assumption was made by exclusion of more common aetiologies and observing correction of hyponatraemia by free water restriction and cessation of ciprofloxacin therapy. Ciprofloxacin is a flouroquinolone with a broad spectrum of activity against both gram positive and gram negative bacteria, and is commonly used to treat respiratory, gastro-intestinal and urinary pathogens. There are many classes of drug which have been thought to cause SIADH, including antibiotics [4-6]. The quinolones, including ciprofloxacin, are known to have CNS side effects, but the incidence and awareness of ciprofloxacin-associated SIADH seems extremely low [7]. CNS quinolone reactions vary in severity and include dizziness, psychosis, and convulsions. Seizures are usually dose-related and sometimes associated with a second predisposing factor, such as mild hyponatremia or hypomagnesemia [8]. The mechanism of seizures associated with quinolone intake is thought to be related to a lowering of the epileptogenic threshold via a reduction in GABA-ergic neuronal inhibition [9]. SIADH has been described as a result of fluroquinolone administration [10] with one case report of SIADH in relation to ciprofloxacin [8]. Furthermore in a review of fluoroquinolone-associated seizures, the serum sodium was found to be less than 125mmol/L in 4 out of 14 reported cases, indicating a possible link [11].

Table 1. Observation

Date		Value
27 July	15:00	118
27 July	19.50	121
27 July	22.30	122
28 July	02.00	124
28 July	05.00	128
28 July	08.30	126
28 July	09.50	130
28 July	12.40	134
28 July	20.10	134
29 July	09.20	134
30 July	13.00	134
31 July	15.10	134
1 August	11.40	136

Table 2. Causes of SIADH

1.	Increase in ADH production a. drug administration (anti psychotics, chemotherapeutic agents, monoamine oxidase inhibitors) b. malignancy c. intracranial lesions, infection or haemorrhage bleeds d. respiratory causes such as pneumonia or TB
2.	Exogenous administration of ADH a. E.g. vasopressin, oxytocin
3.	Potentiation of ADH effect through drug administration a. E.g. carbamazepine, cyclophosphamide

CONCLUSION

With increasing concerns about the side-effects of cephalosporins (with scrutiny of associated clostridium difficile rates in particularly) and more rigorous antibiotic stewardship, new prescribing patterns and guidance for peri-procedural antibiotic prophylaxis are emerging [12]. Current HPA guidelines on antibiotic prescribing 'start SMART then FOCUS' may lead to an increase in the use of antibiotics such as quinolones [13]. Clinicians should therefore remain vigilant that even short courses of 'prophylactic' ciprofloxacin may lead to SIADH and life-threatening hyponatraemia.

ACKNOWLEDGEMENT: None

CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest.

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