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Glimepiride and Syndrome of Inappropriate Antidiuretic Hormone Secretion

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1. Introduction

Syndrome of Inappropriate Antidiuretic Hormone secretion (SIADH), is characterized by hyponatremia (serum Na < 135 mmol/L) without evidence of dehydration, increased renal excretion of sodium (urinary Na > 20 mmol/L), detectable plasma anti-diuretic hormone (ADH) in spite of hyponatremia, low plasma osmolality (< 280mOsm/kg) and high urinary osmolality (>300 mOsm/kg) in the presence of normal renal and adrenal function. Patients with diabetes are more prone to hyponatremia and it can be attributed to a numerous underlying pathogenetic mechanisms. Here we describe a possible case of SIADH induced by the third generation sulphonylurea- glimepiride.

A 67 year old female, with type 2 diabetes was being treated with metformin (500mg) and glimepiride (2mg) daily for past 1 year. She presented to the hospital with history of altered sensorium and followed by unresponsiveness. The clinical examination did not reveal any significant abnormality, and also denied the presence of dehydration, cardiac and renal insufficiency. Her random blood sugar levels at the time of presentation were 34 mg/Dl. Despite administration of 25% dextrose the patient regained consciousness, and was oriented. Her serum sodium levels on the day of admission was 129 mmol/ L. serum levels of blood urea and nitrogen was 12 mg /dL (normal range 8-22 mg/dL), serum creatinine 0.7 mg/ dL and serum cortisol were all within normal limits. Patient's thyroid profile did not reveal any abnormality. The chest X-ray showed normal cardiothoracic ratio and absence of pleural effusion. In spite of severe hyponatremia plasma ADH was detectable (0.8pg /ml). Plasma osmolality decreased to 260 mOsm /kg, urinary osmolarity of > 300 mOsm/kg and urinary sodium significantly increased to 70 mOsm/L.

The patient's hormonal examination denied the presence of hypothyroidism and adrenal insufficiency, including cortisol and ACTH deficiency. The patient was not taking diuretics. She was diagnosed as having SIADH; glimepiride was immediately discontinued (without water deprivation) and her serum Na promptly increased to 133 mmol/L after 4 days.

2. Discussion

Hagen et al. [1] reported in 1970 the first case in which sulphonylurea compounds (chlorpropamide and tolbutamide) induced SIADH. Since then, other cases of first-generation sulphonylurea [chlorpropamide (12 reports) and tolbutamide (two reports)]-induced SIADH have been reported. The development of chlorpropamide-induced SIADH was considered due to potentiation of the action of ADH on renal tubules by increasing the sensitivity of adenylate cyclase to ADH [2]. However, we could find no report of second-generation sulphonylurea-induced SIADH. Interestingly, glibenclamide (A second-generation sulphonylurea) was used to treat SIADH because this compound causes diuresis due to antagonism to the action of ADH [3]. The underlying mechanism of the glimepiride-induced SIADH observed in our present case remains unknown.

Thus, we have observed a patient with type 2 diabetes who presented with SIADH possibly due to glimepiride and who experienced prompt elevation of serum Na on discontinuation of the drug. However, we should mention the limitations of our observation. First, other drugs did not change during the previous 3 months, although we cannot completely discount the possibility that other drugs might have induced SIADH. Second, we measured hormones only once, which also cannot completely eliminate subclinical hormone deficiency.

3. Conclusion

Worldwide, glimepiride is the widely used to treat type 2 diabetes mellitus. We observed that patient presented with SIADH possibly due to glimepiride and improved on discontinuation of the drug. The clinicians need to consider hyponatremia observed in patients treated with this sulphonylurea as a possible case of glimepiride induced SIADH.

References

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