Treatment of hyponatraemia with vasopressin receptor 2 antagonists (V_2 RA) - Case Series;

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ABSTRACT

Vasopressin receptor 2 antagonist (V2RA) provide treatment option for patients with hyponatraeamia in the context of syndrome of inappropriate antidiuretic hormone secretion (SIADH).

We report the results of 7 patients (6 males, 1 female, average age 65.7) with hyponatraemia secondary to SIADH treated with V2RA (Tolvaptan) in years 2011-2013. 6 patients had underlying diagnosis of lung cancer, 1 patient was diagnosed with sarcoidosis. 4 patients died due to their underlying disease, 3 patients remain under the continuing follow up.

To exclude other causes of hyponatraemia we checked, thyroid function, plasma and urine osmolalities, urinary sodium, cortisol level and performed short synacthen test. The initial treatment was fluid restriction. 3 patients (42,86%) were transiently treated with Demeclocycline, subsequently switched to V2RA. V2RA doses varied with total weekly doses between 35 mg to 75mg.

The average sodium concentration before commencing V2RA treatment, was 121,74±5,09 mmol/L (range 112 to 126 mmol/L). The average correction time of hyponatraemia was 9,28 days. The sodium levels were corrected on average by 14,86±6,41 mmol/L. The average rate of correction was 4.1 mmol/day (range 0.44 to 11 mmol/day).

Patients were followed for average of 237.8 days. Total time of follow up was 1665 patient-days. Patients' renal function and electrolytes were monitored. We obtained following results, pre- and post-V2RA use: creatinine 82.67 vs. 83.67 umol/L (+1.21%), urea 5.13 vs. 7.23 mmol/L (+40.9%), potassium 4.45 vs. 4.08 mmol/L (-8.24%). Monitoring of liver function tests (LFTs) revealed following pre- and post-V2RA average levels of aspartate transaminase 44.8 vs. 43.2 iu/L (-3,7%), alanine transaminase 31.5 vs. 32.3 iu/L (+2.65%) and total bilirubin 16.3 vs. 14.0 umol/L (-14,29%) respectively.

Our case series gives evidence for effective use of V2RA in the treatment of hyponatraemia in context of SIADH without excessively rapid hyponatraemia correction or significant changes in levels of creatinine, potassium and LFTs.

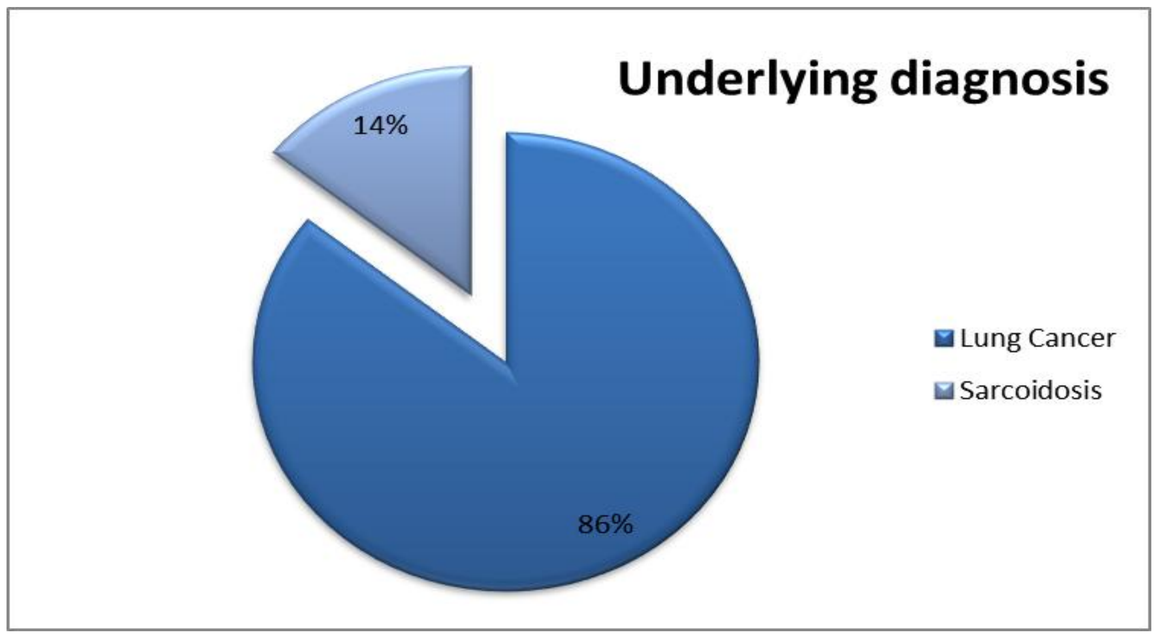
INRODUCTION

Hyponatraemia is defined as a sodium concentration below 135 mmol/L. Syndrome of inappropriate antidiuretic hormone (SIADH) secretion is one of the causes of hyponatraemia with a low serum osmolality. SIADH results from the combination of water retention and loss of sodium and potassium [1,2]. The causes of SIADH include: meningitis, head injury, subarachnoid hemorrhage, cancer, infections, medications, hypothyroidism and sarcoidosis. Treatment options for SIADH include fluid restriction, salt administration, demeclocycline, lithium and use of vasopressin receptor antagonists [1,3,4]. The importance of hyponatraemia correction rate cannot be underestimated to avoid the risk of development of osmotic demyelination syndrome.

Group characteristics

7 patients (6 males, 1 female)

Average at presentation	Age [years]	65.7
	Sodium (Na) [mmol/L]	117.14
	Potassium (K) [mmol/L]	4.45
	Creatinine (Cre) [µmol/l]	82.67
	Urea (Ur) [mmol/L]	5.13
Percentage of tests performed in the our group of patients [%]	Cortisol level	85.71
	Short synacthen test (SST)	66.7
	Thyroid Function Tests (TFTs)	100
	Serum osmolality	100
	Urine osmolality	71.43
	Urine sodium	71.43

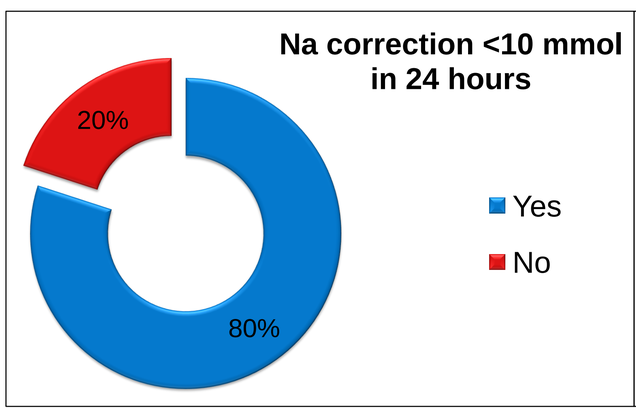


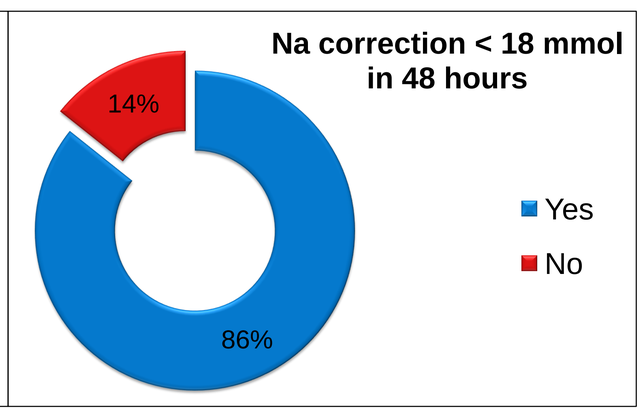
Treatment of hyponatraemia in our group of SIADH patients (years 2011-2013):

- exclusion of other causes of hyponatraemia with tests of thyroid function, plasma and urine osmolalities, urinary sodium, plasma cortisol levels and short synacthen test
- initial treatment was fluid restriction.
- 3 patients (42.86%) were transiently treated with demeclocycline
- subsequently switched to vasopressin receptor (V_2) antagonist (V_2RA) - Tolvaptan
- In 4 patients (57.14 %) Tolvaptan was commenced after fluid restriction.
- total weekly doses of Tolvaptan varied between 35 mg to 75mg
- 100% of patients have responded to treatment with full correction of hyponatraemia to normal sodium values.

RESULTS

Average	Na levels before V_2 RA (Tolvaptan) treatment [mmol/L]	121.71 +/- 5.09
	Time for full correction of hyponatraemia [days]	9.29 +/- 14.9
	Correction of Na levels [mmol/L]	14.85 +/- 6.42
	Correction rate [mmol/L/day]	4.11 +/- 3.38
	Na correction in <24 hours of V_2 RA treatment [mmol]	6.2
	Na correction in <48 hours of V_2 RA treatment [mmol]	9.14
	Follow up time [days]	237.8





	Alkaline phosphatase (ALP) [iu/L]	Alanine transaminase (ALT) [iu/L]	Aspartate transaminase (AST) [iu/L]	Bilirubin (BIL) [umol/L]	K [mmol/L]	Cre [umol/L]	Ur [mmol/L]
Pre- V_2 RA Treatment average	124.7	31.5	44.8	16.3	4.4	82.7	5.1
Post V_2 RA Treatment average	141.7	32.3	43.2	14.0	4.1	83.7	7.2
Change (%)	13.64%	2.65%	-3.72%	-14.29%	-8.24%	1.21%	40.91%

DISCUSSION

The results provided in our case series report suggest that treatment with V_2RA (Tolvaptan) is an effective measure of hyponatraemia correction in patients diagnosed with SIADH.

We demonstrated that the rate of hyponatraemia correction in the majority of our patients did not exceed the recommended 10 mmol in the first 24 hours of treatment and 18 mmol in the first 48 hours of treatment [5]. In one case , where these criteria were not met, the correction rates were exceeded only by 1 mmol in 1st 24 hours and 2 mmols in 1st 48 hours.

We followed up the patients for a total of 1665 patient-days. The average follow up time per patient was 237.8 days.

Some literature reports suggest adverse effects of treatment with tolvaptan on liver function tests (LFTs) [6,7]. We have not observed any significant changes in the results of creatinine, potassium, liver function tests. We observed 40.9% increase in the levels of urea over the course of the follow up.

Our case series supports use of V_2RA in the treatment of hyponatraemia in the context of SIADH without excessively rapid correction of sodium levels.

References

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