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한국인 항이뇨호르몬부적절분비증후군 환자에서 Tolvaptan이 혈청 나트륨에 미치는 영향

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Serum Sodium Profile with and without Tolvaptan in Korean Patients with SIADH

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This clinical study, a multicenter, nonrandomized and open label trial in 8 tertiary medical centers in Korea, was carried out to evaluate changes in serum sodium concentrations ([Na]) during 11 days on tolvaptan (TLV) daily and at the 7th day after discontinuation of the drug in euvolemic patients with chronic hyponatremia (<135 mEq/L) due to SIADH. A total of 39 patients (23 men and 16 women, with the mean age of 71±11.3 yrs) without acute neurologic symptoms were studied from Jun 1, 2013 to Dec 31, 2014. All patients received 15 mg of TLV as the initial daily dose and then further increased to 60 mg per day as needed in the hospital. Serum [Na] (mEq/L) increased prominently from baseline during first 8 hrs (127±4.3 vs 133±4.6, p<0.0001), but gradually to day 2 (133±4.6 vs 135±3.0, p<0.01), and then maintained a plateau until discontinuation of TLV at day 11 (day 2 to 4, 135±3.0 vs 136±3.6, p=NS; day 4 to 11, 136±3.6 vs 137±4.5, p=NS). The changes in serum sodium (ΔSna) from the baseline during first 24 hrs were 2.8±3.3 in 4 hrs, 5.9±4.1 in 8 hrs, and 6.8±4.2 in 24 hrs, respectively. Although the rate of increase in serum [Na] was greater than the rate generally considered safe, 0.5 mEq/L/hour, no patient developed any neurological signs. When hyponatremia is stratified into 3 groups, mild (I, 130-134, n=12), moderate (II, 125-129, n=18), and severe (III, <124, n=9) groups. ΔSna during first 24 hrs was significantly higher in group III (11.1±4.8, p<0.01 vs I, p<0.05 vs II) than in group II (6.4±2.5) and group I (4.3±3.3). Furthermore, those with ΔSna/hr greater than 0.5 mEq/L during first 24 hrs (n=5) had significantly lower baseline serum sodium (119±2.2 vs 128±3.3, p<0.001), and were younger (63±3.1 vs 72±11.6 yrs, p<0.05). Although serum [Na] one week after discontinuation of TLV (day 18, n=29) was not significantly different from the baseline (128±4.0 vs 129±8.6, p=NS), one patient developed markedly symptomatic hyponatremia (106 mEq/L). Two patients stopped medication because of nausea on day 2, 6 patients withdrew from the study on day 4, and 1 patient died on day 18 because of the exacerbated COPD. In conclusion, oral tolvaptan therapy is effective for treatment of chronic hyponatremia, and well tolerated in Korean patients. However, the rapid correction (<0.5 mEq/L/hr) may occur in the 24 hours of treatment with the drug, and close monitoring in the hospital is particularly required in younger geriatric patients with severe hyponatremia.

Key Words: 나트륨, 항이뇨호르몬부적절분비증후군, 저나트륨혈증
Sodium, SIADH, Hyponatremia