Hypouricemia in the Syndrome of Inappropriate Secretion of Antidiuretic Hormone

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Dear Sir,

We read with interest the article by Decaux et al. [1] on the mechanisms of hypouricemia in the syndrome of inappropriate secretion of antidiuretic hormone. They studied the mechanism of the increase of urate excretion in SIADH patients through pyrazinamide (PZA) and sulfinpyrazone (SPZ). Three grams of PZA decreased the absolute urate excretion while 300 mg of SPZ increased the urate-to-creatinine clearance ratio from 0.31 to 0.52. They conclude ‘the increase of uric acid clearance in SIADH seems to result from a decrease in the post-secretory reabsorption of uric acid’.

There had been conflicting arguments on the mechanisms of increase in urate clearance; one arguing for defective post-secretory reabsorption of urate [2, 3], another for pre-secretory defect [4]. Recently, we performed pharmacological evaluation on patients with SIADH. The data, together with the results of some previous reports, led us to pose yet another mechanism as a condition responsible for the increased urate clearance in SIADH [5]; enhanced secretion of urate by the tubule. Our results of PZA tests were consistent with those by Decaux et al. and by Meisel and Diamond [2, 3]. Increased urate clearance was suppressed remarkably after PZA. This suggested either a post-secretory reabsorptive defect or enhanced secretion. We administered 2.0 g probenecid (PBD) to SIADH patients. Their urate clearance showed marked increase. We considered the results to be compatible with increment in renal tubular urate secretion, the condition we described in the first two patients in 1982 [6].

Decaux et al. used SPZ instead of PBD. Although we believe their data using SPZ were very good, their interpretation of the data was somewhat misleading. They stated ‘SPZ inhibits essentially its post-secretory reabsorption’, citing two references [7, 8]. One article by Diamond et al. [7] deals mostly with PZA and PBD. This is a limited report on two patients as far as SPZ is concerned. It concludes that uricosuria induced by PBD and SPZ appears to represent, at least in part, inhibition of post-secretory urate reabsorption. The other article [8] by Sorensen et al. is a case report never dealing with SPZ at all. We do not know of any article which actually clarified the exact mechanism of action of SPZ on tubular urate handling. Although Diamond’s [7] observation ‘that uricosuria induced by SPZ is eliminated by PZA’ implies its significant inhibitory action on post-secretory urate reabsorption, we should be very subtle on commenting on the mechanism of abnormal tubular urate transport based on the studies by SPZ. Even if we assume, as Decaux et al. did, that SPZ specifically blocks the post-
secretory reabsorption of urate, we interpret the results by Decaux et al. to be more compatible with enhanced secretion, rather than defective post-secretory reabsorption. Increment in urate clearance due to defective post-secretory reabsorption cannot be greatly increased by a drug that interferes with the already impaired site. In Decaux’s report 300 mg SPZ increased the Cur/Ccr of SIADH patients from 14.2 ± 2.1 to 25.7 ± 2.7%. This increase caused by SPZ is large enough to be attributable to enhanced secretion by the tubule, because the post-SPZ Cur/Ccr far exceeded that of normal subjects, 18.2 ± 3.8%. They should have used PBD instead of SPZ, because PBD has been shown to produce sharp contrast in urate clearance between post-secretory reabsorptive defect and enhanced secretion. In the former type of defect, it produces little increase in urate clearance [9–11], while in the latter, it produces great increase [5, 6]. Our patients ultimately showed a notable, clear-cut increase after PBD.

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References
