TITLE: METABOLISM OF ATRACURIUM IN PATIENTS WITH RENAL FAILURE

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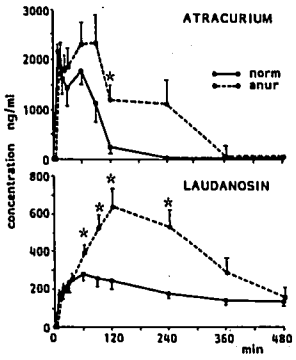
A central nervous stimulating (CNS) metabolite of Atracurium (A), Laudanosin (L) was reported to have higher plasma concentrations following a bolus dose in renal failure patients (RFP)(1). Due to the prolonged elimination half-life of L accumulation appears to be possible (2). The task of our study was to investigate the metabolism of A administered as a continuous infusion.

The protocol carried institutional approval with written informed consent from each patient. Seven ASA 2-3 patients in renal failure, aged 21-59 years, were studied, five patients with comparable age and weight and normal renal function served as controls. In balanced anaesthesia relaxation was performed with A 0.5 mg/kg. Infusion of A 0.75 mg/kg/h was started 4 min after the bolus dose and stopped 10 min before the end of operation. Neuromuscular blockade was quantified by delivering supramax. stimuli of 0.2 ms duration in a train of four (TOF) sequence to the ulnar nerve of the wrist. Venous blood samples were obtained at 0,10,20,30,60,90,120, 240,360 and 480 min. Concentrations of A and L were determined using High Pressure Liquid Chromatography with a sensitivity to L concentration of 10 ng/ml. Mean values for A and L concentrations were compared at each time interval using the Mann-Whitney U-Test. $p < 0.05$ was considered significant.

We found a significantly higher concentr. of both plasma A and L levels in RFP (Fig.). The highest concentration of L (767 ng/ml) was obtained in RFP at 120 min, as compared to a peak (367 ng/ml) at 60 min in the controls.

High blood levels of L were recently reported in patients with normal renal function after infusion of A (3). The significance of these results cannot be evaluated hitherto as there are only experimental data available concerning the CNS toxicity (4). Our results suggest that in patients with impaired kidney function continuous administration of A warrants extreme care and possible dose reduction.



References

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