Title : ENFLURANE AND GENTAMICIN IN CHRONIC RENAL FAILURE

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Because enflurane (ENF) is metabolized to inorganic fluoride (F^-), its use in patients with abnormal renal function has been questioned. In addition, gentamicin treatment has been reported to exacerbate F^- nephropathy. This study examines renal function in adult male Fischer 344 rats with chronic renal insufficiency, anesthetized with ENF or halothane (HAL) and concurrently treated with gentamicin.

Methods. Renal insufficiency was produced surgically employing a two stage procedure. Initially, the upper and lower poles of the left kidney were excised; one week later, a right nephrectomy was performed. After four weeks, the 36 surviving rats were placed in metabolic cages and randomly allocated to six groups: 1) control (saline, i.p., days 1-15); 2) gentamicin, 5 mg/kg/day, i.p., days 1-15; 3) 2% ENF for 2 hours on day 8; 4) 1% HAL for 2 hours on day 8; 5) gentamicin & ENF as above; and 6) gentamicin & HAL, as above. Serum and urinary samples were analyzed for sodium, potassium, F^-, urea nitrogen and creatinine concentrations, and osmolality. 24 hour sodium, potassium, F^-, urea nitrogen, creatinine and osmolal excretions were calculated.

Results. After operation mean serum creatinine for all groups rose from 0.56 ± 0.02 (SE) to 0.91 ± 0.02 mg/100 ml and creatinine clearance fell from 0.28 ± .008 to .23 ± .005 ml/min/100g. BUN rose from 20.4 ± 0.68 to 37.8 ± 1.05 mg/100 ml. Urine volume increased from 8.7 ± 0.23 ml/day prior to operation to 23.9 ± 0.56 ml 4 weeks later; urinary osmolality decreased proportionally. Thus, mild stable renal failure was present. Gentamicin treatment did not adversely affect renal function (Table). Serum gentamicin levels were within the clinical therapeutic range. Four hours after anesthesia, serum F^- levels in ENF treated rats, groups 3 and 5, had risen to 25.4 ± 2.8 and 21.7 ± 2.1 μM, respectively. After 24 hours, these levels had fallen to 4.6 ± 0.3 and 4.5 ± 0.2 μM. These differences were not significant. Apart from F^- levels, which did not increase in halothane treated groups, there were no significant post-anesthetic differences in laboratory data among the four groups of anesthetized rats except those which might be attributed to chance. Similarly, there were no intragroup differences in renal function before and after ENF and HAL anesthesia.

Discussion. The present study indicates that rats with mild to moderate renal insufficiency tolerate anesthesia with ENF and HAL equally well. Also, concurrent administration of therapeutic doses of gentamicin does not intensify renal insufficiency prior to anesthesia nor does it further compromise renal function following either ENF or HAL administration. How do animals (or patients) with reduced renal function handle the F^- load that results from ENF biotransformation? In normal subjects approximately 40% of a F^- load is excreted by the kidneys and the remainder incorporated into bone. Fluoride enters mineralized tissues by replacing ions and groups normally associated with hydroxyapatite crystals forming fluoroapatites. In rats and patients with abnormal renal function it is likely that the latter mechanism becomes more important, a greater proportion of F^- entering bone. This prevents exposure of the kidneys to sustained high levels of F^- following a moderate F^- load.

Table. Urine Volume and C_{Cr}, Mean ± SE*

GROUP	URINE VOLUME ml/day Preanes Day 5	URINE VOLUME ml/day Postanes Day 11	CREATININE CLEARANCE ml/100ml/100g Preanes Day 5	CREATININE CLEARANCE ml/100ml/100g Postanes Day 11
SALINE 1	21±2.9	21±2.8	.21±.014	.23±.022
GENTA 2	22±2.4	26±2.1	.19±.010	.20±.015
ENF 3	20±1.4	22±2.1	.22±.008	.23±.009
HAL 4	22±2.4	21±1.4	.20±.009	.20±.014
ENF & GENTA 5	19±1.5	22±2.2	.19±.008	.19±.012
HAL & GENTA 6	23±2.3	25±2.0	.20±.010	.19±.010

* Anesthesia administered on day 8

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