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Prophylactic aluminium hydroxide and hyperaluminaemia in intensive care

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Abstract. Prophylactic antacid therapy is widely used in intensive care units. We show that significant hyperaluminaemia may occur during the course of prophylaxis with aluminium hydroxide in patients with compromised renal function. Since a significant proportion of patients in intensive care have, or are at risk of developing, renal failure we suggest that the routine use of aluminium hydroxide should be avoided.

Key words: Aluminium hydroxide – Hyperaluminaemia – Gastrointestinal Haemorrhage – Prophylaxis – Renal failure

The need for prophylaxis against gastrointestinal haemorrhage in intensive care units (ICUs) is widely acknowledged. A recent survey of teaching and specialist ICUs in the United Kingdom has shown that 73% use prophylactic regimens. Of these 63% use antacids, either alone or in combination with H_2 receptor antagonists. (TM Bird, unpublished observations). Aluminium hydroxide is the antacid used in a number of these units. Recent reports of hypermagnesaemia during antacid therapy, together with the evidence that aluminium hydroxide used as a phosphate binder is a significant cause of hyperaluminaemia and aluminium toxicity in renal failure, prompted us to see whether hyperaluminaemia occurred during aluminium hydroxide therapy in this ICU. We report a case in which hyperaluminaemia did occur, and discuss the significance of this.

Case report

An 57-year-old man, known to suffer from chronic obstructive airways disease, was admitted to this hospital following an episode of self-poisoning with theophylline. His renal function on admission was mildly abnormal (urea 7.9 $mmol \cdot l^{-1}$, creatinine 128 $\mu mol \cdot l^{-1}$) but there was no evidence of chronic renal disease (Hb 12.6 $g \cdot dl^{-1}$, inorganic phosphate 1.2 $mmol \cdot l^{-1}$). He had a grand mal convulsion and was subsequently treated with charcoal haemoperfusion. His pre-treatment theophylline level was 164.8 $\mu g \cdot l^{-1}$. Over the next 7 days he gradually improved and was transferred to a psychiatric assessment ward for treatment of his underlying depression. However, whilst on that ward, he developed a chest infection, stopped drinking and developed acute renal failure (urea 39 $mmol \cdot l^{-1}$, creatinine 1403 $\mu mol \cdot l^{-1}$). He was transferred to the ICU because of increasing hypoxia and was commenced an intermittent positive pressure ventilation (IPPV). His renal failure was treated with fluids, urine output being maintained with diuretics. He was commenced on a regimen of aluminium hydroxide 20 ml 4 hourly as prophylaxis against gastrointestinal bleeding.

He stabilised on IPPV and his renal failure slowly resolved with the high fluid throughput (urea 17 $mmol \cdot l^{-1}$, creatinine 192 $\mu mol \cdot l^{-1}$). Problems arose when weaning from the ventilator was attempted and an elective tracheostomy was performed. Despite repeated attempts to wean him from his ventilatory support, no progress was achieved and he died, still attached to the ventilator, some 30 days after admission to the ICU. No cause for his renal failure was established. Specifically, Legionella titres were not raised. At the Coroner's postmortem the kidneys were noted to be swollen, but no histological sections were taken.

Serum aluminium was assayed 3 days before he died and found to be 91 $\mu mol \cdot l^{-1}$ (Perkin Ellmer graphite furnace: normal range 5–15 $\mu mol \cdot l^{-1}$). Aluminium hydroxide prescribed as above was the on-

ly source of aluminium, apart from 10 units of 4.5% human albumin solution infused during the course of his stay in the ICU.

Discussion

Stress ulceration in critically ill patients is associated with sepsis, trauma, respiratory failure, renal disease, major surgical procedures, burns, head injury and other conditions. The incidence of detectable bleeding has been reported at 100% but bleeding of a life threatening nature may occur in only 5% of those at risk. Antacid prophylaxis has been shown to reduce the risk of haemorrhage [3], and to be more effective than the H_2 receptor antagonist cimetidine used alone [5]. There has been no well designed study to compare the efficacy of antacid, used alone, with a combination of antacid and H_2 receptor antagonist. Such studies as there are suggest that there is little benefit to be gained by the addition of a H_2 receptor antagonist, unless acid-base disturbance complicates antacid therapy.

Against this background many ICUs use antacids for prophylaxis. A high prevalence of side effects is recognised, but most are of a minor nature and do not require a change in therapy.

The relationship between serum aluminium level and aluminium toxicity is controversial. Serum levels are more likely to reflect recent aluminium exposure, rather than total aluminium load [2]. However the 1982 International Workshop on the Role of Biological Monitoring in the Prevention of Aluminium Toxicity in Man [4], concluded that concentrations above 60 $\mu g \cdot l^{-1}$ indicated increased aluminium absorbtion and that efforts should be made to identify the sources and reduce them. Furthermore, concentrations above 100 $\mu g \cdot l^{-1}$ were considered to be of potential clinical concern. The level found in our patient is worrying for our local renal unit aims to reduce aluminium levels in the chronic dialysis population to less than 10 $\mu g \cdot l^{-1}$, and institutes specific treatment for hyperaluminaemia when levels excede 30 $\mu g \cdot l^{-1}$.

In the light of our experience with this case we have abandoned the use of aluminium hydroxide. An attempt to abandon antacids altogether and rely on the H_2 receptor antagonists alone was followed by gastrointestinal haemorrhage in two patients within 2 weeks. One of these haemorrhages was fatal. There had been no significant gastrointestinal haemorrhages in this ICU during the preceeding 18 months, despite a high number of patients at risk. Our present policy is to use the aluminium/magnesium mixture Magaldrate[1], as this reduces the incidence of bowel disturbance, while providing adequate antacid therapy. We maintain gastric pH at more than 5. Serum magnesium is monitored routinely, and serum aluminium is measured in patients with compromised renal function. There have been no further significant episodes of gastrointestinal haemorrhage since the reintroduction of antacid therapy.

Research into other prophylactic regimens has continued and recently sucralfate has been compared favourable with antacids [1]. If the efficacy of sucralfate is confirmed, then the ease of administration and lack of systemic effects will make it more desirable than antacids in routine use.

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[1] Magaldrate Antacid Suspension USP: Galen Ltd, Northern Ireland