Effect of Ranitidine and Omeprazole on Phosphorus Serum Level in Patients Performing Renal Dialysis

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List of abbreviations

ADQI	Acute Dialysis Quality Initiative
AIN	Acute interstitial nephritis
AKI	Acute kidney injury
ALP	Alkaline Phosphatase
APAs	Acid pump antagonists
ARF	Acute renal failure
ATN	Acute tubular necrosis
ATPase	Adenosine triphosphatase
Ca x P	Calcium –Phosphorus product
$CaCl_2$	Calcium chloride
$CaCO_3$	Calcium Carbonate
cAMP	Cyclic Adenosine monophosphate
CasR	Calcium sensing receptor
CKD	Chronic kidney disease
CNT	Connecting tubules
CRI	Chronic renal insufficiency
CUA	Calcific uremic arteriolopathy
CVD	Cardiovascular disease
CVVH	Continuous venovenous hemofiltration
DCT	Distal convoluted tubules
ECF	Extracellular fluid
EDTA	Ethylenediaminetetraacetic acid
(E.I.P.I.CO.)	Egyptian International Pharmaceutical Industries Co
ESRD	End-stage renal disease
ESRF	End stage renal failure
GFR	Glomular filtration rate
GI	Gastrointestinal
HD	Hemodialysis
iPTH	Intact Parathyroid hormone
IU/L	International unit per liter

K/DOQI	Kidney Disease Outcome Quality Initiative
MBD	Metabolic bone disease
NKF	National Kidney Foundation
Npt2b	sodium phosphate co-transporter
OCPC	Ortho-cresophthalein complexone
PD	Peritoneal dialysis
PMT	Photomultiplier Tube
PO_4	Phosphorus
PPI	Proton Pump Inhibitors
PT	Proximal tubules
PTH	Parathyroid Hormone
PTx	Parathyroidectomy
RIFLE	Risk, Injury, Failure, Loss and End stage renal disease
RRT	Renal replacement therapy

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Abstract

Background: Hyperphosphatemia has been reported to induce extraskeletal calcification of soft tissue particularly in the heart as well as bone disease; a link has been reported between gastric hyperacidity and hyperphosphatemia in dialysis patients.

Objectives: To evaluate the effect of ranitidine or omeprazole in combination with $CaCO_3$ (as a phosphate binder) versus phosphate binders alone $CaCO_3$ on the serum phosphorus level (PO_4) in patients performing renal dialysis.

Setting: National Institute of Urology and Nephrology and Ain Shams University Specialized Hospital, Cairo, Egypt, from October 2009 to October 2010.

Methods: Patients were categorized into three groups, group I (38 patients) represents the control group, they received $CaCO_3$ (3gm daily), group II (39 patients) received the same dose of $CaCO_3$ with ranitidine (150 mg twice daily) andgroup III (31 patients) received the same dose of $CaCO_3$ with omeprazole (20 mg once daily). Blood samples were collected monthly for six months during hemodialysis sessions.

Results: The obtained data revealed that, patients in group II showed marked increase in serum (PO_4) level at 2^{nd} month extended for the whole study period 6 months. Stable serum level of calcium (Ca) and decreasedalkaline phosphatase (ALP), elevated serum parathyroid hormone (PTH) level was observed, while in group III, the results showed no significant change in serum level of Ca, PO_4, increased PTH, and significant decrease in serum ALP.

Conclusion:

Co-administration of ranitidine with $CaCO_3$ may aggravate hyperphosphatemia. Co-administration of omeprazole with $CaCO_3$ reduced ALP and did not modulate PO_4, Ca and increased serum PTH.

Keywords: Ranitidine, Omeprazole, $CaCO_3$, Hyperphosphatemia, Hypocalcaemia.

Maintenance of the normal homeostasis of calcium–phosphate in patients undergoing renal dialysis is a sophisticated problem particularly those receiving acid suppressive therapy ***(Ganesh et al., 2001).***

Abnormalities in calcium–phosphate balance develop early in the course of chronic kidney disease (CKD).A tight association has been observed between elevated serum phosphate, intact parathyroid hormone, Ca × P product, and mortality. These associations cannot be explained simply by osteodystrophy and its complications. It seems likely that, the relationship between calcium–phosphate balance and outcome of patients on dialysis can be explained to a large extent by the effect of the observed abnormalities on the cardiovascular system ***(Block et al., 2004).***

The clinical consequences of altered phosphorus and calcium metabolism and hyperphosphatemia include an increased risk of mortality, cardiovascular diseases (CVD), bone disease, and extraskeletal calcification of soft tissues, including blood vessels, lungs, kidneys, and joints ***(Block and Port., 2000; Ganesh et al., 2001).***

Although dietary phosphorus restriction and dialysis play important roles in regard to the management of hyperphosphatemia, the role of phosphate-binding therapies in this regard is still needed to be delineated ***(Drueke, 2001).***

Phosphorus sequestering agents contain either calcium or aluminum. The use of the latter is limited by toxicity. Calcium containing agents may have potential for increasing calcium load and soft tissue calcification. The challenge in the renal failure patient is to reduce effectively and safely serum phosphorus and Ca x P product without increasing serum calcium levels and the likelihood of vascular calcification. It is in this context that metal-free, calcium-free phosphate binders may have an important role ***(Block and Port., 2000; Jono et al., 2000).***

In chronic renal failure and particularly end stage renal failure (ESRF), it is accompanied by digestive bleeding from gastroduodenal ulcers erosive gastritis, or esophagitis are frequent. The use of gastric acid inhibitors is the base for the preventive or curative treatment of these complications. A link has been reported between gastric hyperacidity and hyperphosphatemia in dialysis patients ***(Nilas et al. 2008).***

The present study was designed to investigate the effect of ranitidine or omeprazole in combination with phosphate binder $CaCO_3$ versus phosphate binders alone $CaCO_3$ on the serum level of phosphorus in patients performing renal dialysis. As a trial to improve therapeutic outcome of $CaCO_3$ by co-administration with acid suppressive therapy.

The present study aimed to:

Study the effect of ranitidineor omeprazole in combination with aphosphate binder $CaCO_3$versus phosphate binder alone$CaCO_3$ on the serum level of phosphorus in patients performing renal dialysis.