Why has PicoPrep™ replaced oral Fleet™?

Earlier this year, the bowel cleansing product, PicoPrep (sodium picosulphate/magnesium citrate) replaced oral Fleet (sodium phosphate) at Canterbury District Health Board (CDHB). This decision was made in view of safety concerns regarding the association of acute phosphate nephropathy with oral sodium phosphate (OSP). Oral Fleet is the only oral sodium phosphate bowel cleaning preparation available in New Zealand and it provides about 60gms of sodium phosphate per dose. Oral Fleet is also known as Fleet Phospho-soda buffered saline mixture. The aim of this bulletin is to highlight the reason why oral Fleet is no longer available in the CDHB.

How do bowel cleansing preparations work?
OSP preparations such as oral Fleet have a direct osmotic effect in the bowel which increases fluid retention in the intestine causing distension, which in turn promotes peristalsis and evacuation of the bowel. Preparations containing sodium picosulphate and magnesium citrate, such as PicoPrep, stimulate peristalsis which promotes water and electrolyte accumulation within the colon. Adequate fluid intake is essential to replace the diarrhoeal losses as electrolyte disturbances can occur.

What is acute phosphate nephropathy?
Acute phosphate nephropathy (also called acute nephrocalcinosis because of calcium-phosphate crystal deposition in the distal tubules and collecting ducts) presents as acute renal failure with minimal proteinuria and a bland urine sediment in patients recently exposed to OSP. Renal biopsy reveals acute and/or chronic renal tubular injury (depending on time to diagnosis).

How does oral Fleet cause nephropathy?
Bowel cleansing with OSP can cause dehydration, decreased intravascular volume, and hyperphosphataemia (due to a large oral phosphate load). Hyperphosphataemia increases phosphate concentrations in the renal tubules. Decreased intravascular volume stimulates reabsorption of water from the renal tubules further increasing the phosphate concentration in renal tubular fluid. The increased PO4− concentration in renal tubular fluid results in a secondary increase in tubular Ca++ causing precipitation of calcium-phosphate crystals in the kidney leading to acute phosphate nephropathy.

Who may be at risk?
Patients with the following conditions and/or taking the following medications may be at increased risk of acute phosphate nephropathy:
- Decreased intravascular volume (due to congestive heart failure, cirrhosis, or nephrotic syndrome)
- Acute or chronic kidney disease (particularly as eGFR approaches 30mL/min)
- Advanced age (OSP-associated hyperphosphataemia may be more severe in individuals aged >55 years)
- Medications that affect renal perfusion or renal function such as diuretics, Angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists, and possibly non-steroidal anti-inflammatory drugs.

What is the evidence?
The Nephrology Department at Christchurch Hospital is aware of several recent cases of acute phosphate nephropathy associated with OSP at Christchurch Hospital. In addition to these local cases, there are at least 23 case reports in the literature of acute phosphate nephropathy associated with OSP in patients with no history of hypercalcaemia or superimposed renal pathology. These patients tended to be elderly females taking ACE inhibitors, angiotensin II receptor antagonists, diuretics, or non-steroidal anti-inflammatory drugs.

Two distinct patterns of acute renal failure (ARF) have been reported in the context of sodium phosphate bowel cleansing. One pattern is characterised by a rapidly evolving (hour to days) form of ARF, as a component of a systemic syndrome marked by severe hyperphosphataemia and hypocalcaemia. This form of ARF is typically short-lived with rapid recovery of renal function along with correction of the electrolyte abnormalities.

The second pattern of ARF is often only identified after the fact. These patients do not have any of the features of the acute syndrome and present much later (usually weeks) with mild, nonspecific symptoms. These patients may undergo renal biopsy as part of a diagnostic workup for renal failure, and nephrocalcinosis is subsequently detected. In many patients this form of ARF improves, at least partially, but can be progressive in other instances. In either case the starting point for ARF is crystal deposition in association with an abnormally high calcium x phosphate product in the tubules.

There are currently no published reports of sodium phosphate enema (Fleet Phosphate Enema) use in isolation resulting in ARF and so these enemas are still considered for use in patients without risk factors for phosphate nephropathy.

Summary and Recommendations
Oral sodium phosphate bowel cleansing preparations such as oral Fleet are no longer used in the CDHB due to safety concerns of acute phosphate nephropathy. PicoPrep has now replaced oral Fleet. When using a bowel cleansing agent, ensure patients receive an adequate fluid intake to replace diarrhoeal losses, and prevent significant electrolyte disturbances.

References
Memo from Dr George Downward, Medical Director, Patient Safety, Canterbury DHB. Picoprep to replace Fleet, dated 7 July 2008