What is NEXT with PPI and adverse events, Dementia?

Interesting isn't it. If your facility sees its share of admissions from an acute care setting you will see most likely patients are on a Proton Pump Inhibitor (PPI). Certainly we understand that the PPI order in most cases is a prophylaxis for a stress ulcer. The question is, do we still need the PPI? Is the continued administration of a PPI wise for the geriatric patient? Does that patient truly have gastroesophageal reflux disease (GERD) or is there a routine NSAID or steroid on board? After some 25 plus years we are now seeing issues with the prolonged administration of this medication class. According to some research, up to 70% of all PPI prescriptions could be inappropriate. Is it possible we have conditioned the system to associate GERD with all PPIs on the admission sheet?

Let's take a look at the history of PPIs.

Omeprazole was discovered in 1979. In 1980, an Investigational New Drug (IND) application was filed and in 1982 omeprazole was taken into Phase III trials. By 1990 Prilosec, omeprazole (The Purple Pill) was released in the United States.

It quickly became one of the most prescribed medications in the United States and around the world. PPIs are indicated for GERD, esophagitis, acid hyper-secretory states, peptic ulcers and eradication of *Helicobacter pylori*. PPIs are also used for treating dyspepsia and prophylaxis of peptic ulcers in the intensive care setting, and among high-risk patients prescribed aspirin, NSAIDs, anti-platelets and anticoagulants.

As time always does, issues began to show themselves the more the PPIs were prescribed. Looking at Table ONE with F-Tag 329 of the State Operations Manual, it identifies that extended use of PPIs in the elderly is associated with increased risk of clostridium difficile colitis.

Even though the evidence could be better we are seeing discussions with the elderly that PPIs should be use with caution in patients at risk for bone fracture. The mechanism behind impaired bone strength is based on profound acid suppression and its triple effect of impairing vitamin B_{12} and

calcium absorption. By reducing the B12 absorption this in turn decreases osteoblastic activity resulting in reduced metabolic bone density and strength. In addition we are hearing issues with deficiencies with iron and magnesium too.

From *JAMA Neurol*. Published online on February 15, 2016, a new study from Germany has confirmed an association between PPIs and increased risk for dementia in older patients. Having diabetes and being prescribed five or more drugs other than the PPI were also associated with significantly elevated dementia risk.

Evidence suggests some PPIs may cross the blood–brain barrier and interact with brain enzymes and, in mice, may increase beta amyloid levels in the brain.

Although the current study did not include vitamin B_{12} levels, other research has linked PPI use to vitamin B_{12} deficiency, which has been shown to be associated with cognitive decline.

This is only the beginning of the discussion associating dementia and PPIs. Much more needs to be done. Time will clarify this discussion with PPIs and point us in the right direction.