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Association Between Proton Pump Inhibitor Use & Dementia: A Two-Fold Approach

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It is estimated that over 15 million patients were prescribed proton pump inhibitors and dementia by examining Hamzat et al. Based upon the results of the studies examined in this literature review, there is a significant difference in the proportion of patients using proton pump inhibitors versus no proton pump inhibitor use.

What proposed pathophysiology links dementia to proton pump inhibitor use?

Based upon the results of the studies examined in this literature review, there is a significant difference in the proportion of patients using proton pump inhibitors versus no proton pump inhibitor use. It can be interpreted that the longer a person was a proton pump inhibitor user, the risk of developing dementia also increases. Hamzat et al. (2005) found the use of proton pump inhibitor medication increased the risk of any dementia compared to no proton pump inhibitor use. This study was an observational study. Consequently, fundamental biological mechanisms were not explored. However, this study remains significant due to the association found between proton pump inhibitor use and the increasing risk of dementia. Both studies provide a statistical association between proton pump inhibitors and dementia. Therefore, elderly patients who are already at risk for developing dementia due to their age will have an additional risk in developing dementia if they use proton pump inhibitors chronically.

The study by Wijmenga et al. (2016) established an increased risk of dementia among proton pump inhibitor users, however, it was performed via literature search. A total of four studies were analyzed and the analysis comprised of randomized control trials that were either case-control studies or the use of meta-analysis. All the research was to evaluate proton pump inhibitor related to non-users. Their study did not establish a link between proton pump inhibitors and dementia that was non-based and based upon previously published studies.

Alkofid et al. (2015) described that such a relationship between proton pump inhibitors and dementia could have been created by using the CANTAB software. This software allowed for actual results to be assigned to the participants of the proton pump inhibitor group and provided insight to the mechanisms of their operations. The results of the study found a statistically and clinically significant improvement in visual memory, attention, executive function, working and planning function. Yet, this study is a short-term study. If Alkofid et al. (2015) could produce these profound results in a short-term study, it would be valuable to aware in a long-term study. A long-term study, utilizing the CANTAB software, has the potential to provide more awareness into this association.

Pathophysiology behind the association between proton pump inhibitors and dementia:

Baezola et al. (2013) studied cellular and animal models. This study suggests a relationship between proton pump inhibitors and an increase in the extracellular deposition of amyloid beta peptides in the brain which do deposits can result in excitatory and inflammatory lesions. These lesions can lead to synaptic dystrophy. This study makes a reasonable assumption, but more evidence is needed to investigate the relationship. Studies investigating this particular theory are few. It would be interesting to investigate this relationship further and more notably investigate if it can be linked to the development of dementia.

The study completed by Lam et al. (2015) verified the association vitamin B12 deficiency and chronic use of proton pump inhibitors by using a review of information which found that the likelihood of vitamin B12 deficiency was higher among users of proton pump inhibitors with a current association of vitamin B12 deficiency. Jung et al. (2015) performed a systematic review of existing studies, which found an association between proton pump inhibitor use and vitamin B12 deficiency. These studies provided an association between proton pump inhibitors and dementia by examining previously assembled data.

Dharmarajan et al. (2008) monitored proton pump inhibitor users and histamine-2 receptor antagonist users and their serum vitamin B12 levels were monitored. This study was interesting because it found a relationship between serum levels and the absence of chronic use of proton pump inhibitors. The increased duration of proton pump inhibitor use was significant for egsmation of serum vitamin deficiency. This evidence can be understood that the chronic use of proton pump inhibitors contributes to the lowering serum B12 levels. It is important to monitor chronic users of proton pump inhibitors for vitamin B12 deficiency or stop the use of proton pump inhibitors. The problem with diminishing serum vitamin B12 levels only becomes apparent after long time. Also, it can be assumed that serum vitamin B12 level levels decrease for those who use histamine-2 receptor antagonists.

Originally, it was thought that the association between proton pump inhibitor use and dementia was due to the vitamin B12 deficiency. However, Kuspoito et al. (2009) and Raviglione et al. (2005) found that there are other risk factors that contribute to this association. The results of these two studies provided awareness into other cellular mechanisms behind dementia and proposed an extension of the association of proton pump inhibitors and dementia. Exploring the biological mechanisms further into the association would not only provide a greater understanding, but also more treatments for preventable outcomes.