SYSTEMATIC LITERATURE REVIEW: PENGARUH PENGGUNAAN *PROTON PUMP INHIBITOR* JANGKA PANJANG TERHADAP KADAR VITAMIN B12

TUGAS AKHIR

Untuk Memenuhi Persyaratan

Memperoleh Gelar Sarjana Kedokteran

Oleh

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RINGKASAN

Firmansyah, Dicky. Fakultas Kedokteran, Universitas Islam Malang. *Systematic Literature Review:* Pengaruh Pembimbing Penggunaan Proton Pump Inhibitor Jangka Panjang Terhadap Kadar Vitamin B12. Pembimbing 1: H.R.M. Hardadi Airlangga. Pembimbing 2: Helmin Elyani

Pendahuluan: *Proton Pump Inhibitor* (PPI) merupakan obat yang secara luas digunakan untuk penyakit yang berkaitan dengan lambung. Penggunaan PPI jangka panjang biasanya dilakukan pada penyakit-penyakit kronis seperti gastritis kronis. Namun, penelitian terbaru mengungkapkan bahwa penggunaan PPI jangka panjang dapat menyebabkan gastritis atrofik dengan penurunan kadar vitamin B12 serum yang signifikan. Terdapat juga data yang bertentangan dimana tidak terjadi defisiensi vitamin B12. Tujuan dari review ini adalah mengetahui efek dari penggunaan obat PPI jangka panjang terhadap kadar vitamin B12.
Metode: Penelitian ini merupakan *Systematic Literature Reviews* (SLR). Penelitian menggunakan pencarian data menggunakan 3 database yaitu PUBMED, GOOGLE SCHOOLAR, WEB OF SCIENCE dengan memasukan *keyword: PPI use, longterm, vitamin B12, cobalamin.*
Hasil: Dari 11 artikel, terdapat 9 jurnal yang menyebutkan PPI dapat menurunkan kadar vitamin B12 dan 2 jurnal tidak terdapat pengaruh antara PPI dengan kadar vitamin B12. Sebelas jurnal tersebut, 5 diantaranya tidak valid.
Kesimpulan: Penggunaan Proton Pump Inhibitor (PPI) jangka panjang berpengaruh dalam menurunkan kadar Vitamin B12.

Kata Kunci*:* *Proton Pump Inhibitor* (PPI), vitamin B12, jangka Panjang, kobalamin

SUMMARY

Firmansyah, Dicky. Systematic Literature Review: Effects of Long-Term Proton Pump Inhibitor Use on Vitamin B12 Levels. Supervisor 1: H.R.M. Hardadi Airlangga. Supervisor 2: Helmin Elyani

Introduction: Proton Pump Inhibitor (PPI) is a drug that is widely used for diseases related to the stomach. Long-term use of PPIs is usually used for chronic diseases such as chronic gastritis. However, recent research has revealed that long-term use of PPIs can lead to atrophic gastritis with a significant reduction in serum vitamin B12 levels. There are also conflicting data where vitamin B12 deficiency does not occur. The aim of this review was to determine the effect of long-term use of PPI drugs on vitamin B12 levels.
Method: This study is a Systematic Literature Reviews (SLR). The research used data search using 3 databases, namely PUBMED, GOOGLE SCHOOLAR, WEB OF SCIENCE by entering keywords: PPI use, longterm, vitamin B12, cobalamin.
Result: Of the 11 articles, there were 9 journals that said PPIs could reduce vitamin B12 levels and 2 journal had no effect between PPIs and vitamin B12 levels. Of the eleven journals, 5 of them are invalid.
Conclusion: Long-term use of Proton Pump Inhibitor (PPI) has an effect on reducing Vitamin B12 levels.

Keyword: Proton Pump Inhibitor (PPI), vitamin B12, Longterm, cobalamin

BAB I
PENDAHULUAN

1.1 Latar Belakang

Penggunaan PPI sebagai obat yang banyak diresepkan pada gangguan asam lambung ternyata masih menimbulkan masalah kesehatan. Di Indonesia 40-70 % pasien yang dirawat inap di rumah sakit mendapatkan terapi obat PPI dan dua per tiga diantaranya memiliki indikasi yang kurang tepat (Mirdhatillah, 2015). Efek samping dari penggunaan PPI jangka panjang seperti hal nya defisiensi, infeksi, dan resiko lain ikut meningkat. Salah satu defisiensi yang dapat disebabkan yaitu vitamin B12 (Haastrup *et al., 2018).* Studi yang dilakukan Katz dkk. Menyatakan penggunaan tanpa indikasi yang jelas secara jangka panjang dapat meningkatkan resiko gangguan status fungsional dan juga komorbiditas. Pada pengguna jangka panjang memiliki kadar vitamin B12 yang lebih rendah yaitu 11% dan kadar Methylmalonic acid yang lebih tinggi yaitu 75% (Katz, 2010).

Proton Pump Inhibitor (PPI) bekerja di lambung dengan cara memblokir enzim K+H+ATPase yang berfungsi sebagai pompa pengeluaran ion H+ dari sel parietal lambung kedalam lumen lambung yang mana akan bereaksi dengan ion Cl- untuk membuat asam klorida (HCl), HCl mendorong konversi dari pepsinogen menjadi pepsin. Kekurangan HCl akibat penggunaan PPI dapat menurunkan kinerja dari sel parietal yang mana akan mengeluarkan factor intrinsik, ketika factor intrinsik menurun maka vitamin B12 yang dapat diikat ikut menurun dan absorbsi vitamin B12 di distal illeum juga ikut menurun, sehingga vitamin B12 yang akan diserap oleh tubuh juga ikut berkurang (Miller J. W., 2018).

Pada suatu studi disaat penyerapan vitamin B12 dihambat, ditemukan *output* HCl dan penyerapan vitamin B12 yang terikat pada protein terpengaruh kadarnya. Oleh karena itu terdapat kemungkinan bahwa PPI berpengaruh juga terhadap penyerapan vitamin B12 dan dapat mempengaruhi vitamin B12 yang bersirkulasi (Damião *et al*., 2016).

Pengaruh obat golongan PPI terhadap absorbsi vitamin B12 dipengaruhi oleh beberapa faktor antara lain dosis penggunaan, usia berkisar antara 25-60 tahun, lama pemakaian obat diatas 12 bulan, jenis kelamin, dan fasilitas perawatan yang didapatkan oleh pasien. Factor tersebut dapat mempengaruhi resiko defisiensi vitamin B12 secara signifikan (Heidelbaugh J. J., 2013).

Berdasarkan data diatas peneliti ingin menjelaskan riset-riset tentang obat PPI terhadap vitamin B12 pada dekade terakhir, sebagai bahan *systematic literature review*.

1.2 Rumusan Masalah

Apakah penggunaan PPI jangka panjang dapat mempengaruhi kadar Vitamin B12?

1.3 Tujuan Penelitian

Mengetahui pengaruh penggunaan PPI jangka panjang terhadap kadar Vitamin B12.

1.4 Manfaat Penelitian

Manfaat Teoritis

Sebagai landasan teoritis penunjang riset tentang *Proton Pump Inhibitor* terhadap kadar Vitamin B12 dengan menyajikan rangkuman hasil telaah dari jurnal-jurnal internasional terakreditasi.

Manfaat Praktis

Sebagai upaya pengembangan pemahaman tentang *Proton Pump Inhibitor* terhadap kadar Vitamin B12.

BAB VII
PENUTUP

7.1 Kesimpulan

Berdasarkan hasil penelitian dan pembahasan *Systematic Literature Review* yang telah dilakukan dapat menyimpulkan bahwa konsumsi obat *Proton Pump Inhibitor* (PPI) dalam jangka waktu yang panjang dapat berpengaruh pada penurunan kadar Vitamin B12 dalam darah

7.2 Saran

Berdasarkan dari hasil pembahasan penelitian *Systematic Literature Review* ini, peneliti menyarankan untuk:

1. Memperbanyak dan memperbaharui literature, baik berupa studi *clinical trials* maupun studi epidemiologi, mengenai data prevalensi penggunaan *Proton Pump Inhibitor* dan efek sampingnya di Indonesia.

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