Geriatrik Bilimler Dergisi / Journal of Geriatric Science 2019; 2 (1): 27-29

Expert Opinion on Association of Metformin Use and Vitamin B12 Deficiency in Older Adults

Uzman Görüşü: Yaşlılarda Metformin Kullanımı ve B12 Vitamin Eksikliği

Fatma Sena Dost Günay[1], Ahmet Turan Isik[1]

[1]Department of Geriatric Medicine, Dokuz Eylul University, Faculty of Medicine, Izmir, Turkey

Wong Chit Wa ve ark. bakım evinde kalan yaşlılarda metformin kullanımının B12 vitamini eksikliği ile ilişkili olup olmadığını araştırdıkları çalışmada metformin kullanımının B12 vitamini eksikliği riskinin ve ciddiyetinin artmasına yol açtığını bulunmuştur. Bu çalışmada serum B12 konsantrasyonunun <150 pmol / L olan olgular vitamin B12 eksikliği olarak değerlendirilmiş olup kişilerin klinikleri hakkında bilgi verilmemiştir. Serum B12 konsantrasyonunun 150 pmol/L'nin altında seçilmesi, B12 eksikliğini teşhis etmek için yeterli değildir. B12 vitamini eksikliğini teşhis etmek için klinik başvuru, fonksiyonel testler, intrakorpusküler vitamin B12 düzeyi ve B12 vitaminini etkileyen komorbiditeler değerlendirilmelidir.

Wong Chit Wa et al., in which they aimed to investigate whether metformin use is associated with vitamin B12 deficiency in the institutionalized elderly, and found that metformin use lead to an increased risk and severity of vitamin B12 deficiency. In this study vitamin B12 deficiency was diagnosed if the serum vitamin B12 concentration was <150 pmol/L and the clinical presentation of cases defined as vitamin B12 deficient was not mentioned. Selecting serum vitamin B12 concentration below 150 pmol/L is not enough to diagnose B12 deficiency. Clinical presentation, functional tests, intracorpuscular vitamin B12 levels and the comorbidities which have effect on vitamin B12 should be evaluated to diagnose vitamin B12 deficiency.

Sorumlu Yazar/ Corresponding Author: Prof.Dr. Ahmet Turan Işık
E-posta/E-mail: atisik@yahoo.com
Adres/ Adress: Yaşlanan Beyin ve Demans Unitesi, Geriatri Bilim Dalı Dokuz Eylul Universitesi Tıp Fakultesi, Balcova, Izmir, Turkey, 35340
Telefon/ Phone: +90 232 4124341
Geliş Tarihi/ Received: 03.04.2019 **Kabul Tarihi/ Accepted:** 26.04.2019

We read with interest the study by Wong Chit Wa et al., in which they aimed to investigate whether metformin use is associated with vitamin B12 deficiency in the institutionalized elderly, and found that metformin use lead to an increased risk and severity of vitamin B12 deficiency (1). We think that some methodological issues should be considered while determining this relationship.

The diagnosis of vitamin B12 deficiency has been based on low serum vitamin B12 levels, less than 150 pmol/L (200 ng/L), along with its own clinics. In addition, patients with vitamin B12 levels more than 295 pmol/L (400 ng/L) is defined as normal, while those with between 200 and 400 ng/L are considered borderline and should be evaluated further by functional tests such as methylmalonic acid (MMA) and homocysteine, to clarify or exclude the diagnosis of Vitamin B12 deficiency (2).

Clinical presentation is the most important factor for assessing vitamin B12 status. In geriatric population neurologic abnormalities may occur before the hematologic changes. In this study vitamin B12 deficiency was diagnosed if the serum vitamin B12 concentration was <150 pmol/L and the clinical presentation of cases defined as vitamin B12 deficient was not mentioned. If there is no clinical suspicion, the low value can be considered as vitamin B12 deficiency (2,3). Selecting serum vitamin B12 concentration below 150 pmol/L is not enough to diagnose B12 deficiency. Without testing serum MMA concentrations, the threshold level of the serum vitamin B12 is not suitable for diagnosis of the vitamin B12 deficiency.

Metformin is the first-line drug for the treatment of type II diabetes mellitus. The use of metformin is contraindicated in patients with an estimated glomerular filtration rate (eGFR) <30 mL/min, and the initiation of metformin is not recommended in patients with an eGFR between 30 and 45 mL/min (4). In the present study the authors conclude that the metformin dose was lower due to renal failure and gastrointestinal intolerance but eGFR is unspecified. It would be good to disclosure the eGFR measurement of the cases. Furthermore, Van Loon reported that vitamin B12 and MMA levels without adjustment in eGFR may lead to 40% more vitamin B12 deficiency diagnosis (5).

Metformin use is known to decrease the level of vitamin B12 and it was shown that metformin treatment was associated with low serum vitamin B12 and improved intracellular vitamin B12 metabolism despite low serum vitamin B12 (6). As in this study it is obvious that metformin decreases serum vitamin B12 levels and some of the patients may not have their own clinic of vitamin B12 deficiency (not mentioned in the study), diagnosed as vitamin B12 deficiency incorrectly. There is no significant difference in MCV when metformin and non-metformin groups are compared. This may be an indication of the necessity of the measurement of intracellular vitamin B12. In this case the percentage of vitamin B12 deficiency will be different from the calculated.

In conclusion, Wong Chit Wai et al. contributes valuable data to medical literature, but the studies investigate that the relationship between metformin use and vitamin B12 deficiency should evaluate aforementioned factors to provide a clearer picture to the readers.

REFERENCES

1. Wong, C.W., Leung, C.S., Leung, C.P., et al. Association of metformin use with vitamin B12 deficiency in the institutionalized elderly. Archives of Gerontology an Geriatrics, 2008; 79: 57-62
2. Devalia, V., Hamilton, M.S., Molloy, A.M. British Committee for Standards in Haematology. c. Br J Haematol, 2014; 166(4): 496-513.
3. Matchar, D.B., McCrory, D.C., Millington, D.S., et al. Performance of the serum cobalamin assay for diagnosis of cobalamin deficiency. Am J Med Sci, 1994, 308(5): 276-83.
4. Lu, W.R., Defilippi, J., Braun, A. Unleash metformin: reconsideration of the contraindication in patients with renal impairment. Ann Pharmacother, 2013, 47(11): 1488-1497.
5. Van Loon, S.L., Wilbik, A.M., Kaymak, U., et al. Improved testing for vitamin B12 deficiency: correcting

MMA for eGFR reduces the number of patients classified as vitamin B12 deficient. Ann Clin Biochem, 2018, 55(6): 685-692.

6. Obeid, R., Jung, J., Falk, J., et al. Serum vitamin B12 not reflecting vitamin B12 status in patients with type 2 diabetes. Biochimi, 2013, 95(5): 1056-61.