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## Vitamin B12 Status and Its Association with *Helicobacter pylori* Infection in Alcohol Dependent Patients

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**Summary** Both infection with *Helicobacter pylori* and alcohol abuse have been associated with low vitamin B12 serum levels. The interaction between both risk factors is unknown. The aim of this study was to determine whether *Helicobacter pylori* infection is associated with low vitamin B12 levels in alcohol dependent patients. Blood samples were obtained from adult alcohol dependent patients undergoing detoxification and analyzed for serum vitamin B12 levels. *Helicobacter pylori* infection was serologically measured. Patient characteristics, medication use and alcohol consumption at admission were assessed by interview. A total of 6 out of 89 patients included presented low vitamin B12 levels, all were sub clinical deficient (<250 pmol/L) and none were clinical deficient (<150 pmol/L). Infection with *Helicobacter pylori* was present in 29% of the patients. The average vitamin B12 levels in *Helicobacter pylori* seropositive and seronegative patients were 1,033 pmol/L (SD 741) and 971 pmol/L (SD 717), respectively. The relation between *Helicobacter pylori* infection and vitamin B12 deficiency was not of significance (OR=0.48; 95% CI [0.05–4.32]). In conclusion, *Helicobacter pylori* infection is not a risk factor for low vitamin B12 levels in alcohol dependent patients.

**Key Words** vitamin B12, *Helicobacter pylori*, alcohol

*Helicobacter pylori* infection and excessive alcohol consumption can be harmful for the stomach and the ileum in the development of gastritis or peptic ulcers (1, 2). Both factors seem also associated with vitamin B12 deficiency. The results from a recent study from Shuval-Sudai et al. show a higher prevalence of *Helicobacter pylori* infection among subjects with serum vitamin B12 levels that are within the lower end of the normal range (3). An explanation for this association can be found in the complex absorption of vitamin B12, in which the stomach plays an important role: pepsin and gastric acid, both secreted in the stomach, liberate vitamin B12 from its protein binding in diet. Gastric parietal cells in the stomach release intrinsic factor (IF). Only after binding to this factor, the IF-B12-complex can be absorbed by receptors in the terminal ileum. *Helicobacter pylori* interferes with this process which might explain low serum vitamin B12 levels in patients with this infection (3–6). The interference consists of irritation of the mucosal layer in the stomach, wherefore the parietal cells may not be able to release as much intrinsic factor as in patients without *Helicobacter pylori* induced gastritis.

The relation between alcohol consumption and vitamin B12 is controversial (7–10). Lower serum levels have been associated to alcohol abuse. In 1985 Kanazawa and Herbert showed that plasma vitamin

B12 levels are significantly higher in alcohol dependent patients than in non-drinkers (7). However, in another study no association between alcohol abuse and vitamin B12 was found (9, 10). The difference in outcome between the studies might be a result of interference of other risk factors, such as infection with *Helicobacter pylori*. In none of these studies the influence of *Helicobacter pylori* was taken into consideration. Therefore the aim of this study is to determine whether *Helicobacter pylori* infection is associated with vitamin B12 levels in alcohol dependent patients.

### METHODS

Consecutive patients were recruited between January and November 2002 at 4 different detoxification clinics in the Netherlands. Patients were included if they had reached the age of 18 and were alcohol dependent following DSM-IV criteria. Patients were asked to participate at the first day of admission before the detoxification process, consisted of total controlled alcohol abstinence, has started. After written informed consent, blood samples were taken at the start of detoxification and stored at –20°C. Furthermore, demographics, alcohol consumption, smoking habits and medication use at admission were reported by interview. Procedures used in human subjects were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in

1983.

Assays of plasma vitamin B12 and *Helicobacter pylori* antibodies were performed in a hospital laboratory. Samples were run at the same time to minimize assay variability. The Immulite analyzer was used for the quantitative measurement of vitamin B12 serum levels. Vitamin B12 levels <150 pmol/L were classified as clinical deficiency, between 150–250 pmol/L as sub clinical deficiency and above 250 pmol/L as normal.

Testing for antibodies against *Helicobacter pylori* infection was performed with a commercially available enzyme-linked immunosorbent assay (ELISA) (Pyloriset, Orion Diagnostics, Finland). The specific antibodies against *Helicobacter pylori* infection, measured in the serum samples, were classified according to the manufacturer's instructions. Patients were considered to be *Helicobacter pylori* seropositive when values were above 20 EIU.

Data were analyzed using SAS statistical software (version 8.0). Chi-square and *t*-test statistics were used to estimate differences in the baseline characteristics among patients with and without vitamin B12 defi-

ciency. Fisher's exact test was used where appropriate. Logistic regression analysis was performed to study the association between infection with *Helicobacter pylori* and vitamin B12 levels to estimate an Odds Ratio with 95% Confidence Intervals (CI) for these variables. Multiple regression analysis was performed to adjust for alcohol consumption and smoking habits.

## RESULTS

We included 89 alcohol dependent patients, all Caucasians: 64 males, an average age of 42 years (Table 1). The patients reported an average addiction period of more than 15 y and an average daily ethanol consumption of 140 g or more. Most patients (87%) were currently smoking and 78% underwent detoxification before. Patients often used to have co-addictions, where cannabis and cocaine use was most frequently present.

A low serum B12 level (<250 pmol/L) was found in a total of 6 out of 89 patients (7%). All deficient patients were sub clinical (150–250 pmol/L), none of them were clinical vitamin B12 deficient (<150 pmol/L). All other patient characteristics were similar between patients with and without vitamin B12 deficiency (Table 2). In 84 out of 89 patients included we were able to assess infection with *Helicobacter pylori*, 29% of the patients

Table 1. Baseline characteristics of the study population.

Baseline characteristics		
Male/female (no.)		69/20
Mean age (y)		42
Vitamin B12 deficient (%)		7
<i>H. pylori</i> seropositive (%)		29
Beverage use (%)	Beer	98
	Wine	13
	Liquor	8
Mean alcohol intake (g/d)		139
Mean addiction duration (y)		17
Previous detoxification (%)		78
Current smoking (%)		87
Co-addiction (%)	Cannabis	25
	Cocaine	23
	Opiates	12



Fig. 1. Alcohol consumption and vitamin B12 serum levels for *Helicobacter pylori* seropositive and seronegative patients. ●, *H. pylori* negative; ○, *H. pylori* positive.

Table 2. Frequency of possible risk factors for B12 deficiency.

Vitamin B12		Deficiency		No deficiency		Differences OR (95% CI)
		N=6	(%)	N=83	(%)	
Gender	M	5	(83)	64	(77)	1.53 (0.17–13.92)
	F	1	(17)	19	(23)	
Age (y)	≤40	2	(33)	33	(40)	1.32 (0.23–7.62)
	>40	4	(67)	50	(60)	
<i>H. pylori</i>	Pos	1	(17)	24	(29)	0.48 (0.05–4.32)
	Neg	5	(83)	59	(71)	
Smoking	Yes	3	(50)	45	(54)	0.84 (0.16–4.43)
	No	3	(50)	38	(46)	
Alcohol intake (g/d)	≤120	4	(67)	43	(52)	0.55 (0.10–3.18)
	>120	2	(33)	40	(48)	

were *Helicobacter pylori* seropositive (Table 1). One out of six alcohol dependent patients with low vitamin B12 levels (<250 pmol/L) (17%) was *Helicobacter pylori* seropositive in comparison to 5 being seronegative (83%). In the non vitamin B12 deficient group (>250 pmol/L) this proportion was 29% and 71%, respectively. The relation between *Helicobacter pylori* infection and vitamin B12 deficiency was not of significance (OR=0.48; 95% CI [0.05–4.32]). The average serum vitamin B12 levels of *Helicobacter pylori* infected and not infected patients was 1,033 (SD 741) and 971 pmol/L (SD 717), respectively. The average alcohol consumption of vitamin B12 deficient patients (<250 pmol/L) did not differ with non-deficient patients (>250 pmol/L), alcohol consumption were 127 and 134 g/d ( $p>0.5$ ), respectively (Fig. 1). In this figure the alcohol dependent patients were subdivided into *Helicobacter pylori* infected and non-infected, but it showed no difference between both groups.

### DISCUSSION

There is controversy whether alcohol dependent patients have decreased or increased serum vitamin B12 levels. In our study population vitamin B12 deficiency was not very common. All found serum vitamin B12 deficiencies were between 150 and 250 pmol/L, which indicates a sub clinical deficiency. Clinical relevant deficiencies were not found in our population. Although *Helicobacter pylori* infection was not associated with a sub clinical deficiency, the vitamin B12 levels were higher in *Helicobacter pylori* seropositive patients. This association is however not clinical relevant due to the high vitamin B12 levels found.

In contrast to the results of this study, other studies showed low vitamin B12 levels in alcohol dependent patients. The difference in these findings could be explained by the way in which vitamin B12 were assessed. In a systematic review exploring vitamin B12 status and chronic alcoholism, Cravo et al. report vitamin B12 assessments in serum and plasma, with respectively lower and higher levels (10). There were not given insights in the way of analysis, but an explanation for this difference could be that frozen plasma samples become a turbid suspension after defrosting. This causes a false increased vitamin B12 level up to 50% when assessed in an immunochemical way. Another reason for the differences might be the type of beverage consumed by the studied alcohol abusing population. In our Dutch population the reported alcohol consumption consisted mostly of beer, which contains more vitamin B12 than other beverages. Moreover, the prevalence of the use of vitamin preparations use in the Dutch population is increasing (11). However, none of the alcoholics in our study used a vitamin supplement which might have increased vitamin B12 levels.

Vitamin B12 metabolism is complicate, several organs are involved. Vitamin B12 deficiency, assessed as low circulating concentrations, is thought to be less common in chronic alcoholics, probably because of large stores of vitamin B12 in the liver. In general, it is

known that vitamin B12 concentration decreases in hepatic tissues of patients with liver disorders. This hepatic vitamin B12 concentration is affected not only by alcohol consumption, but also by other dietary conditions, such as unbalanced diet and lack of ingesting vitamin B12 rich foods. Therefore the serum vitamin B12 concentration changes according to the condition of the liver disorder due to alcohol abuse. Nonetheless, tissue deficiencies of this vitamin may occur despite subnormal, normal, or even high circulating concentrations. Kanazawa and Herbert showed that plasma vitamin B12 levels are significantly higher in alcohol dependent patients than in non-drinkers (7). However, analysis of liver biopsies demonstrated that vitamin B12 concentrations in liver tissue were significantly lower in alcohol dependent patients than in non-drinkers, thus implying that chronic alcohol intake may impair the uptake or retention of this vitamin by the liver and perhaps by other peripheral tissues as well.

In the study of Gloria et al. vitamin B12 in serum was higher in the alcoholic group than in the non-alcoholic group (9). This observation might be a reflection of poor retention of this vitamin by the peripheral tissue as previously implicated by Kanazawa and Herbert.

In conclusion, vitamin B12 deficiency was not very common in alcohol dependent patients. As a result we did not find an association between *Helicobacter pylori* infection and serum vitamin B12 deficiency in alcohol dependent patients. Infection with *Helicobacter pylori* is not a risk factor for low serum vitamin B12 levels in alcohol dependent patients.

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