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Vitamin B_{12} deficiency in the institutionalized elderly: A regional study

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ABSTRACT

The prevalence of vitamin B_{12} deficiency increases with age and is suggested to be even higher in the elderly living in institutions. This retrospective study evaluated the vitamin B_{12} and folate status of 1996 institutionalized elderly residents aged over 65 years. Among them, 34.9% had vitamin B_{12} deficiency (serum vitamin B_{12} <150 pmol/L), 11.8% had folate deficiency (serum folate <6.8 nmol/L), and 4.9% had both. The majority of vitamin B_{12} deficient residents (68%) had serum vitamin B_{12} between 100 pmol/L and 149 pmol/L. Macrocytosis was found in 24.2% of vitamin B_{12} deficient residents. A significant increase in macrocytosis was associated with a decrease in serum vitamin B_{12} below 100 pmol/L. Macrocytosis was most common in those with vitamin B_{12} ≦69 pmol/L (50.9%). Overall, vitamin B_{12} deficiency is common in the institutionalized elderly, however macrocytosis cannot predict deficiency. More liberal testing for vitamin B_{12} status in the institutionalized elderly may be warranted.

1. Introduction

Elderly people are at risk of vitamin B_{12} deficiency owing to an increased prevalence of pernicious anaemia, and high prevalence of gastric atrophy, which in turn impairs the release of vitamin B_{12} from food protein for absorption (Baik and Rusell, 1999; Carmel, 1995). Although the prevalence of vitamin B_{12} deficiency varies among studies, it appears to increase with age (Baik and Rusell, 1999). The prevalence varies between 5% and 40% in the elderly, depending on the definition of vitamin B_{12} deficiency used and the population groups studied (Lindenbaum et al., 1994; Baik and Rusell, 1999; Carmel, 2000; Chui et al., 2001; Clarke et al., 2003, 2004; Loikas et al., 2007). The institutionalized elderly represent a group of frail elderly people with multiple comorbidities increasing disabilities and dependency, which is distinct from those who are free-living. The prevalence of vitamin B_{12} deficiency among the elderly living in institutions has been suggested to be even higher reaching 30 to 40% (Matthews, 1995; Dali-Youcef and Andrè, 2009).

Vitamin B_{12} is essential for the metabolism of all cells in the body. In humans, two enzymatic reactions are dependent on vitamin B_{12}: methylmalonyl coenzyme A mutase reaction and 5-methyltetrahydrofolate-homocysteine methyltransferase reaction. They are important in the extraction of energy from protein and fat in the mitochondrial citric acid cycle, maintaining integrity of the nervous system, and for DNA synthesis. Hence, in vitamin B_{12} deficiency, multi-organ systems are affected concomitant with a wide spectrum of clinical manifestations. The clinical manifestations are usually non-specific and highly variable. Routine testing of macrocytosis and anaemia associated with vitamin B_{12} deficiency is infrequently seen in clinical practice (Thompson et al., 1987; O Broin et al., 1990; Stott et al., 1997). Possibly related to the fact that the majority of the vitamin B_{12} deficiency is of a mild degree, which is not severe enough to cause macrocytosis or anaemia, especially when the folate status is normal (Herbert, 1994). However, data is lacking confirming that macrocytosis is found more frequently in those with a more severe degree of vitamin B_{12} deficiency.

In this study, we evaluated the vitamin B_{12} and folate status in the elderly residents living in long term care institutions. We also explored the association of vitamin B_{12} concentration with macrocytosis in the vitamin B_{12} deficient residents.

2. Methods

Caritas Medical Centre is a regional public hospital under the management of Hospital Authority in Hong Kong serving a population of 380,000. The majority of residents (around 4000) living in the long term care institutions in the serving district are under the care of the outreach team of Caritas Medical Centre.

We retrospectively reviewed the electronic clinical records of the institutionalized residents under the care of the outreach team. Residents aged 65 and over with serum vitamin B_{12} concentration measured during the period 2011–2013 were included. Patients receiving vitamin

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B_{12} or folate supplements before vitamin B_{12} or folate blood tests were excluded. Patients put on tube feeding were evaluated separately. The clinical notes of all these residents were reviewed to determine the reason for serum vitamin B_{12} and folate measurement. Laboratory data on serum vitamin B_{12} and folate concentration, complete blood counts (CBC) and red cell indices (within 2 weeks before vitamin B_{12} measurement) were collected. In addition, age, medical disease including thalassaemia trait and iron deficiency, and medications at the time of vitamin B_{12} and folate measurement were also collected. This retrospective study has been approved by the Research Ethics Committee of Hospital Authority of Hong Kong before the start of study and the informed consent from the study subjects were waived.

Serum vitamin B_{12} and folate were measured by Access 2 Immunoassay System (Beckman Coulter). The reference range for the vitamin B_{12} concentration was 133–675 pmol/L and for folate was >6.8 nmol/L. Vitamin B_{12} deficiency was diagnosed if the serum vitamin B_{12} was <150 pmol/L (de Benoist, 2008; Selhub et al., 2008) and folate deficiency was diagnosed if the serum folate was <6.8 nmol/L (Hao et al., 2003). CBC was performed by LH 750 haematology analyser (Beckman Coulter). Anaemia was defined as haemoglobin level <13 g/dL for men and <11.5 g/dL for women. The normal mean corpuscular volume (MCV) range was 81 to 97 fL. Macrocytosis was defined as MCV above 99 fL and microcytosis as MCV below 80 fL. Macrocytic anaemia refers to macrocytosis with anaemia.

2.1. Statistical methods

In the analysis of the influence of different serum vitamin B_{12} concentrations with macrocytosis and anaemia, residents with folate deficiency or iron deficiency, or haematological disease, or thalassaemia trait were excluded, as these can affect red cell indices and there is 8% thalassaemia carrier rate in our locality.

Student's *t* test and ANOVA were used for comparisons between groups for continuous data. Chi-square test was used to compare the percentage of patients with macrocytosis and anaemia in different vitamin B_{12} concentration subgroups. Association of vitamin B_{12} concentration with age was assessed using linear regression.

3. Results

During the period 2011–2013, 2176 institutionalized elderly residents aged 65 years or older had serum vitamin B_{12} concentration measured. 80 residents already receiving vitamin B_{12} supplements before vitamin B_{12} blood test performed were excluded. 100 residents on tube-feeding were evaluated independently. Of the remaining 1996 residents, 858 (43%) were men and 1138 (57%) were women (Table 1). All had serum vitamin B_{12} concentration measured but only 1885 residents had serum folate measured. The majority (>70%) did not have clear indication for vitamin B_{12} and folate measurement. Most had vitamin B_{12} and folate measurement together with complete blood count, renal and liver function test and glucose, as a routine check-up.

3.1. Vitamin B_{12} and folate concentration and the prevalence of deficiency in the institutionalized elderly

The mean serum vitamin B_{12} and folate concentration of the study population was 227 pmol/L and 16.2 nmol/L, respectively (Table 1). Among them, 34.9% (696) had vitamin B_{12} deficiency (serum vitamin B_{12} <150 pmol/L) and 11.8% had folate deficiency (serum folate <6.8 nmol/L). There was no significant difference in the prevalence of vitamin B_{12} deficiency between men and women but more men than women had folate deficiency (16.2% vs 8.5%, $P < 0.001$). The mean serum concentration of vitamin B_{12} in those with vitamin B_{12} deficiency was 110 pmol/L and 5.4 nmol/L for folate deficient residents. Only 4.9% had both vitamin B_{12} and folate deficiencies.

Among vitamin B_{12} deficient residents, 11 residents (1.6%) had post-gastrectomy, 100 residents (14.4%) had metformin intake and 36 residents (5.2%) had proton pump inhibitor intake. Anti-intrinsic factor antibody and anti-parietal cell antibody were done in 301 of 696 residents with vitamin B_{12} deficiency. Only 20 residents had positive results for anti-intrinsic factor antibody and were presumed to have pernicious anaemia.

There were no significant differences in serum vitamin B_{12} and folate concentration, and the prevalence of deficiencies by age even further

Table 1
Vitamin B_{12}/folate status and selected characteristics of the institutionalized elderly[a].

	Total n = 1996	Men n = 858 (43%)	Women n = 1138 (57%)	*P* value[b]
Age (years)	83.3 ± 7.6	80.4 ± 7.2	85.5 ± 7.2	<0.001
Age 65–74 years (n)	267 (13.4%)	185 (21.6%)	82 (7.2%)	<0.001
Age ≥ 75 years (n)	1729 (86.6%)	673 (78.4%)	1056 (92.8%)	<0.001
Serum vitamin B_{12} (pmol/L)	227 ± 155	222 ± 150	230 ± 158	0.21
• Vitamin B_{12} deficiency[c]	110 ± 29	112 ± 25	109 ± 32	0.17
Vitamin B_{12} deficiency (n)	696 (34.9%)	301 (35.1%)	395 (34.7%)	0.86
Serum folate (nmol/L)	16.2 ± 13.1	14.8 ± 15.2	17.2 ± 11.2	<0.001
• Folate deficiency [d]	5.4 ± 1.1	5.4 ± 1.1	5.3 ± 1.2	0.62
Folate deficiency[†] (n)	222 (11.8%)	130 (16.2%)	92 (8.5%)	<0.001
Both vitamin B_{12} and folate deficiencies[†] (n)	93 (4.9%)	54 (6.8%)	39 (3.6%)	0.002
Haemoglobin (g/dL)	11.8 ± 2	12.2 ± 2	11.5 ± 1.7	<0.001
Anaemia[e] (n)	1126 (53.7%)	561 (63.3%)	565 (46.7%)	<0.001
MCV (fL)	92.6 ± 10.4	93.3 ± 9.4	92.6 ± 11.1	0.014
Macrocytosis (MCV >99 fL) (n)	397 (20%)	191 (22.3%)	206 (18.1%)	0.021
Thalassaemia trait (n)	135 (6.4%)	50 (5.6%)	85 (7%)	0.201
Post-gastrectomy (n)	19 (1%)	9 (1%)	10 (1%)	0.516
Vegetarian (n)	1	0	1	–
Metformin (n)	188 (9.4%)	73 (8.5%)	115 (10.1%)	0.227
Proton pump inhibitor (n)	173 (8.7%)	72 (8.4%)	101 (8.9%)	0.477

*Abbreviations: MCV, Mean corpuscular volume; n, number.

[a] Mean and standard deviation, number and percentage of the pathological results. Vitamin B_{12} deficiency is defined by serum vitamin B_{12} <150 pmol/L and folate deficiency is defined by serum folate <6.8 nmol/L.

[b] Difference between men and women (Student's *t* test for continuous data; chi-square test for categorical data).

[c] Serum vitamin B_{12} concentration in residents with vitamin B_{12} deficiency.

[d] Serum folate concentration in residents with folate deficiency.

[e] Anaemia: haemoglobin < 13 g/dL for men and <11.5 g/dL for women.

[†] Only 1885 residents had serum folate measured.