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Use of vitamin B₁₂ injections among elderly patients by primary care practitioners in Ontario

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Abstract

Background: Excess use of parenteral vitamin B₁₂ has been reported from audits of clinical practices. The authors assessed the use of vitamin B₁₂ injections in patients aged 65 years and over in Ontario.

Methods: A cross-sectional analysis was conducted that included all elderly people covered by the Ontario Health Insurance Plan who received insured services from general practitioners or family physicians (GP/FPs). For each practice the proportion of elderly patients who received regular vitamin B₁₂ injections between July 1996 and June 1997 was calculated. The frequency of injections was determined for each patient receiving regular B₁₂ replacement.

Results: Of the 1 196 748 elderly patients (mean age 74.8 [standard deviation 6.8], 58.0% female) treated by 14 177 GP/FPs, 23 651 (2.0%) received regular B₁₂ injections. The rate of B₁₂ injections per patient, standardized for age and sex, varied between practices (range 0%–48.6%). Although no authoritative sources support the practice, 3303 (19.8%) of the 16 707 patients receiving long-term parenteral therapy had, on average, overly frequent injections (more than 1 injection every 4 weeks). For 76 (12.3%) of the 617 practices with 10 or more patients receiving regular vitamin B₁₂ injections, the mean injection frequency was greater than once every 4 weeks. The proportion of patients in these 617 practices who received overly frequent injections varied extensively (0%–100%).

Interpretation: Our findings indicate that some primary care physicians in Ontario administer unnecessary vitamin B₁₂ injections to elderly patients.

Although therapy for vitamin B₁₂ deficiency prevents serious morbidity, clinical audits in Britain have shown that approximately half of the patients receiving regular vitamin B₁₂ injections do not meet explicit criteria supporting its use, and up to one-fifth of patients receive unnecessarily frequent injections.^{1,2} A chart review involving more than 20 Ontario physicians revealed little evidence supporting the diagnosis of vitamin B₁₂ deficiency in almost half of the patients receiving regular injections.³ Although it is plausible that vitamin B₁₂ deficiency may be underdiagnosed and undertreated by some physicians, these and other data suggest that vitamin B₁₂ injections may be overused in some primary care practices.^{4,5}

The relatively small number of patients and physicians in these studies limits the generalizability of their findings. To our knowledge, an extensive assessment of parenteral B₁₂ administration has not been published. We therefore analysed primary care practice profiles of all physicians in Ontario and assessed the use of vitamin B₁₂ injections among elderly patients.

Vitamin B₁₂ administration is inappropriate if patients who are not deficient receive regular injections or if those who are truly deficient receive unnecessarily frequent injections. To address the first issue, the proportion of elderly patients in each physician's practice receiving vitamin B₁₂ injections can be compared with the true prevalence of vitamin B₁₂ deficiency. Four studies have shown the rate of true deficiency among elderly patients to range between 1.5% and 4.6% (Table 1). Unnecessary use of vitamin B₁₂ might exist if the proportion of elderly patients in Ontario practices receiving injections significantly exceeds these estimates. To address the second issue, the frequency of regular B₁₂ injections can be calculated to determine whether the time between injections is less than 4 weeks. Because no authoritative



reference recommends injections more frequently than once a month for long-term therapy, higher frequencies would indicate inappropriate use. These 2 measures permit vitamin B₁₂ utilization to be studied at the population level using administrative databases.

Methods

The Ontario Health Insurance Plan (OHIP) database captures all fee-for-service claims submitted to the Ministry of Health. Excluded from this database are claims from patients of physicians on salary or capitation (about 5% of primary care providers), claims from patients who do not have valid OHIP numbers and claims for services provided outside of Ontario. Prescriptions to Ontario residents aged 65 years and older are covered by the Ontario Drug Benefit program and are captured in its database. In our study we characterized physicians by linking anonymous billing data to the Ministry of Health's Registered Physician Database in which physicians were anonymous.

We examined outpatient assessments and prescription claims for all elderly people in Ontario from July 1996 to June 1997. Patients were considered to be receiving regular vitamin B₁₂ injections if they filled a prescription for injectable B₁₂ and a general practitioner/family physician (GP/FP) claimed payment for administering 2 or more injections to that patient.

To compare the prevalence of vitamin B₁₂ injections between practices, the total number of elderly patients seen in each practice was included in our calculations. Each patient was assigned to the practice of the GP/FP who claimed the most outpatient assessments for that patient during the study period. To ensure statistical stability, practice-based rate analysis was limited to practices with 50 or more elderly patients. The crude vitamin B₁₂ utilization rates for each practice were standardized for patient age and sex using indirect methods,¹³ and 95% confidence intervals (CIs) were calculated for the standardized rates.¹⁴ We calculated the proportion of practices whose lower limit of the 95% CI was more than twice the overall provincial utilization rate or the prevalence of vitamin B₁₂ deficiency established in published studies.

The proportion of patients in each practice for whom the average time between injections was less than 4 weeks was also deter-

mined. Only patients who received a vitamin B₁₂ prescription before the study were included in this calculation because daily or weekly injections are often administered for newly diagnosed vitamin B₁₂ deficiency. To ensure statistical stability, we included only practices with 10 or more patients receiving regular vitamin B₁₂ injections.

Using a χ^2 test for trend, we determined the association of the injection rates for each practice, adjusted for patient age and sex, with 3 factors: the total number of elderly patients in the practice, the number of years since the physician graduated from medical school and the proportion of elderly patients receiving overly frequent vitamin B₁₂ injections.

Results

There were 1 196 748 patients in Ontario aged 65 years and over who had one or more outpatient assessments during the study year. The mean age was 74.8 (standard deviation [SD] 6.8) years, and 694 114 (58.0%) of the patients were women. In all, 23 651 (2.0%) of the patients received regular vitamin B₁₂ injections; 16 707 (70.6%) had at least one prescription for vitamin B₁₂ before the study, which we considered to indicate long-term therapy. Women were significantly more likely than men to receive parenteral vitamin B₁₂ therapy (2.3% v. 1.6%; $p < 0.001$), and patients receiving vitamin B₁₂ were significantly older than those not receiving it (77.4 [SD 6.9] years v. 74.8 [SD 6.8] years; $p < 0.001$).

Of the 14 177 GP/FPs (76.9% male; median number of years since graduation 19 [25th–75th percentile 11–30]) assessed in the study, 6891 (48.6%) managed 50 or more elderly patients in their practices. The proportion of patients in these practices who received regular vitamin B₁₂ injections, adjusted for patient age and sex, ranged from 0% to 48.6%. The lower limit of the 95% CI of the utilization rates for 339 (4.9%) of these practices was more than double the provincial average of 2.0%. The lower limit of the 95% CI for 144 (1.7%) practices was greater than 7.1%, which is the highest estimate from the studies measuring

Table 1: Studies that measured the prevalence of true vitamin B₁₂ deficiency among elderly patients

Study	Sample	Criteria for vitamin B ₁₂ deficiency	Prevalence, % (and 95% CI)*
Carmel ⁹	729 patients > 60 yr nonrandomly sampled from community	Serum vitamin B ₁₂ level < 190 pg/mL and < 8.0% of dose excreted in Schilling test	1.5 (0.7–2.5)
Lindenbaum et al ¹⁰	548 ambulatory survivors from Framingham cohort > 65 yr	Serum vitamin B ₁₂ level < 200 pg/mL and MMA level > 376 nmol/L	2.2 (1.1–3.6)
Joosten et al ¹¹	348 ambulatory and hospitalized patients > 60 yr nonrandomly sampled from teaching centre	Serum vitamin B ₁₂ level < 139 pg/mL and 1 of: MMA level > 247 nmol/L, HC level > 13.3 μ mol/L, CT level > 245 nmol/L or MCA > 192 nmol/L	4.6 (2.6–7.1)
Elsborg et al ¹²	273 elderly patients in hospital with no history of vitamin B ₁₂ deficiency, gastrectomy or current antibiotic therapy nonrandomly sampled from teaching centre	Serum vitamin B ₁₂ level < 200 pg/mL, megaloblastic bone marrow, achlorhydria (FIGLU test), abnormal Schilling test result and normal GI tract (barium meal)	1.8 (0.6–3.8)

Note: MMA = methylmalonic acid, HC = homocysteine, CT = cystathionine, MCA = 2-methylcitric acid, FIGLU = formiminoglutamic acid secretion test and GI = gastrointestinal.

*Calculated from data presented in study.



the prevalence of true vitamin B₁₂ deficiency among elderly patients (Table 1).

The overall mean number of days between injections for patients receiving regular vitamin B₁₂ therapy was 41.8 (SD 27.6). Of the 16 707 patients receiving long-term therapy, the average time between injections for 3303 (19.8%) was less than 4 weeks. In the 617 practices with 10 or more patients receiving long-term vitamin B₁₂ injections, 76 (12.3%) had a mean injection frequency of less than 4 weeks. The proportion of patients whose injections were overly frequent within the 617 practices varied extensively (0%–100%).

Physicians with the greatest proportion of patients receiving unnecessarily frequent vitamin B₁₂ injections also had the highest rates of vitamin B₁₂ injections (Table 2). Female physicians were slightly more likely than male physicians to administer regular injections (2.3% v. 1.9%, *p* < 0.001). The physicians' experience had an inconsistent effect on injection rates (Table 2).

Interpretation

To our knowledge this is the first assessment of utilization rates of parenteral vitamin B₁₂ in an entire patient population. We found large variations between practices in the proportion of elderly patients who received regular vitamin B₁₂ injections; the rates for some practices were much higher than the provincial mean and exceeded the estimates from previous studies for the true prevalence of vitamin B₁₂ deficiency.⁹⁻¹² Almost one-fifth of the patients in our study who were receiving long-term vitamin B₁₂ therapy received injections more frequently than is deemed necessary. GP/FPs with high utilization rates gave injections more frequently than did their colleagues.

Variations between practices in vitamin B₁₂ administra-

tion might be related to factors other than inappropriate therapy. First, some of the practices may have had higher proportions of elderly patients with vitamin B₁₂ deficiency. There were many practices in which no patients received injections; therefore, some practices may have gathered most of the patients with vitamin B₁₂ deficiency in a particular region. Also, the GP/FPs in practices with low or negligible utilization rates may have referred their patients with vitamin B₁₂ deficiency to specialists, and this would artificially reduce the measured utilization rate in the average primary care practice. We believe that these explanations are implausible, however. It is unlikely that any GP/FP would have gathered a disproportionate number of elderly people with vitamin B₁₂ deficiency. Moreover, although some primary care practitioners may rely on specialists to confirm the initial diagnosis of vitamin B₁₂ deficiency, regular parenteral therapy is standard in primary care.

Second, low utilization rates may be a consequence of physicians not billing for vitamin B₁₂ injections. Alternatively, some practices may have a disproportionate number of housebound patients receiving injections from home care nurses or patients who use oral vitamin B₁₂ supplementation.¹⁵ This highlights a major problem with our study in that overutilization, but not underutilization, is identified.

Third, because we adjusted the utilization rates for the age and sex of patients managed in the practice, variations in these parameters between practices would not account for variations in utilization rates. We were unable to adjust for other factors associated with vitamin B₁₂ deficiency such as gastrectomy¹⁶ or dysfunction in any of the steps of vitamin B₁₂ absorption,¹⁷ but we could not postulate why these factors would vary between practices in Ontario.

Finally, interpractice variation in utilization rates may have resulted from differences in physicians' diagnostic thresholds. Some physicians may aggressively search for vitamin B₁₂ deficiency, whereas others may order tests only when specific symptoms are present. Some physicians may treat all patients with levels that are outside of the normal range, whereas others may treat only if other evidence consistent with deficiency exists. This would explain why the utilization rates in some practices greatly exceeded the prevalence of true deficiency identified in clinical studies, all of which confirm the veracity of low serum vitamin B₁₂ levels with other laboratory findings (Table 1). Perhaps automatic laboratory confirmation of low serum levels using methylmalonic acid or homocysteine levels would decrease interpractice variation in vitamin B₁₂ administration, improve physician response to low serum vitamin B₁₂ levels and decrease the proportion of patients with vitamin B₁₂ deficiency who do not receive therapy.¹⁸

Given the low prevalence of true vitamin B₁₂ deficiency, we suspect that aggressive diagnostic strategies may lead to a large number of false-positive results and overtreatment.¹⁹ Some practitioners may defend the questionable use of vitamin B₁₂ injections on the grounds that such therapy is a placebo that maintains contact between physicians and elderly patients. Although parenteral vitamin B₁₂ therapy is

Table 2: Association between physicians' practice characteristics and utilization rates of vitamin B₁₂ injections

Characteristic; rate	Quartile			
	1st	2nd	3rd	4th
Practice size*				
No. of elderly patients	< 10	10–49	50–124	125
Adjusted utilization rate	0.31	0.91	1.84	2.13
Physician experience†				
No. of years in practice	< 10	10–19	20–29	30
Adjusted utilization rate	1.89	1.96	2.23	1.75
Vitamin B₁₂ injection frequency*				
% of patients receiving injections more frequently than once a month	< 1	1–14	15–30	> 30
Adjusted utilization rate	5.92	6.26	6.50	7.15

Note: Rates are expressed per 100 elderly patients and are adjusted for patient age and sex. For practice size and physician experience, practices with 50 or more elderly patients were considered (*n* = 6891). For injection frequency, practices with 50 or more elderly patients, of whom 10 or more received regular vitamin B₁₂ injections, were considered (*n* = 617).

**p* < 0.001 by ² test for trend.
†*p* < 0.05 by ² test for trend.



safe, its use in patients without a true deficiency is expensive, causes discomfort and could impede the identification of disorders that are the true cause of a patient's symptoms.

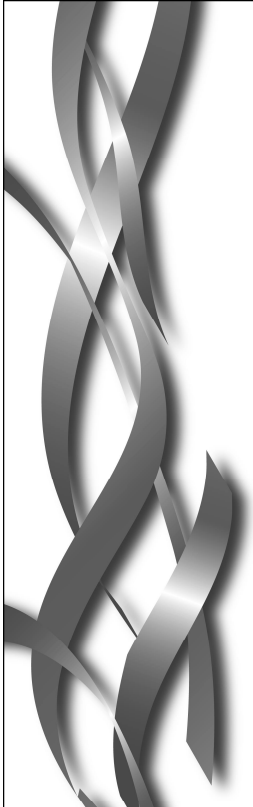
In conclusion, our practice-based analysis is consistent with chart audits that show some unnecessary use of vitamin B₁₂ injections. Cochrane and Moore⁵ came to a similar conclusion in a study in 1971. They cautioned, "If we do this with B₁₂, how efficiently are we using more difficult and more dangerous drugs such as steroids and antibiotics?"

Competing interests: None declared.

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