

Ask the Expert

From the
Calgary Health Region Authority

1. Polypharmacy & the elderly
2. Vitamin B12 deficiency

1. Polypharmacy & the elderly

Question:

Is there a rationale for arbitrarily limiting the number of medications an older patient should take to avoid polypharmacy and drug-drug interactions?

David Hogan, MD, FRCPC, geriatrician, replies.

Response:

What is polypharmacy? There isn't a number of medications below which everything is fine and above which there are universal problems. "Polypharmacy" can be simply defined as the consumption of multiple medications by a given patient. In itself it is neither good nor bad. The potential problems include a higher risk for adverse drug effects (especially drug-drug interactions), excessively complicated drug regimens and excessive costs. Discretionary medications given to relieve non-specific symptoms or for the side-effects of other medications can be major contributing factors to adverse drug reactions.

What do the studies tell us? A consistent finding is that age is not a major determinant of the likelihood of adverse drug reactions. Rather, the number of drugs consumed is directly related to the risk of adverse drug-related events. The risk of drug-drug interactions in particular rises steeply with increasing numbers of co-administered drugs. When more than five drugs are being taken there is an exponential increase. All patients experience drug-drug interactions when nine or ten drugs are being co-admin-

istered. It has been estimated that there are about four potential drug-drug interactions when ten drugs are being co-administered and that this rises to ten when more than twelve drugs are being co-administered. An important study looked at the prevalence of probable adverse drug reactions in a nursing home population. 67.4% of the residents suffered at least one probable adverse drug reaction during the four years of surveillance. The affected group differed statistically from the rest of the nursing home population only in the average number of medications per day being consumed (7.8 +/- 2.6 versus 3.3 +/- 1.3). They did not seem more ill. The number of active medical problems present in the group that had suffered an adverse drug reaction was 4.0 which compares to 3.8 in those who had not.

What should you do? I think you have to constantly ask yourself whether all the medications being consumed by your patients are necessary. Use as few drugs as possible. Anticipate drug-drug interactions and adverse effects. You have to make ongoing efforts to do a medical "debridement" on your patients. While there is no "magic number", I would suggest that when five or more medications are being regularly consumed per day, alarm bells should go off.

2. Vitamin B12 deficiency

Question:

What is the bottom line in vitamin B12 deficiency in the elderly?

Darren Burbuck, MD, FRCPC, geriatrician, replies.

Response:

How is it tested? Vitamin B12 deficiency is actually a complex issue. It is estimated to have a prevalence of 10-15% in people over 60. Vitamin B12 is part of a group known as cobalamins. Cobalamin is an important co-factor for 2 enzymatic reactions: the conversion of homocysteine to methionine, and the conversion of L-methylmalonyl CoA to succinyl CoA. A low serum vitamin B12 level is the most commonly used laboratory test to make the diagnosis. The test is usually performed through a radioassay using purified intrinsic factor.

However, there is controversy over the laboratory diagnosis of vitamin B12 deficiency. It has been shown that serum vitamin B12 levels are normal in a minority of patients with vitamin B12 deficiency. In addition, there have been concerns that vitamin B12 levels may be falsely low in a proportion of cases, particularly when older microbiological assays were used.

Due to these concerns, work has been done using other measures. When vitamin B12 deficiency occurs, it results in elevated levels of homocysteine and methylmalonic acid. It has been shown that elevations of these serum metabolites above the reference range precede a fall in the serum vitamin B12, and also show a more consistent correlation with objective vitamin deficiency than do blood vitamin levels. However, the tests are more difficult and expensive to perform, and their precise role as diagnostic tests has not been established yet.

Another measure used is the deoxyuridine suppression test. This test is based on the ability of deoxyuridine to suppress the incorporation of thymidine into thymidylic acid and DNA, which is dependent on metabolically active folate and cobalamin. This process is, therefore, impaired with

vitamin B12 or folate deficiency. The test is performed using incubated marrow cells. Underlying deficiency is determined by adding folate or cobalamin compounds in vitro, to determine if they will correct an abnormal result. The test is very sensitive, but obviously invasive and expensive due to the need for a bone marrow sample.

What are the acceptable ranges? The serum vitamin B12 assay is used by Calgary Lab Services. Although I do not know the manufacturer's exact methods for establishing the reference range, vitamin B12 levels

were likely correlated with levels of homocysteine and methylmalonic acid, and possibly with results of the deoxyuridine suppression test. A range between 140-800 pmol/L has been deemed "normal," between 115-139 pmol/L is considered "borderline low," and less than 115 pmol/L indicates "deficiency."

External testing is performed by Calgary Lab Services, whereby a blind specimen is sent to the lab, in

order to help verify the reference range.

Although the serum B12 level is not perfect, it is the best test available at this point for determining deficiency in a large volume of patients. CME

References

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