CORRESPONDENCE

PIVKA-II concentrations in patients with cystic fibrosis

Montalember et al report that PIVKA-II was detected in 33% of patients with cystic fibrosis, while vitamin K, plasma concentrations were normal.1 It is astonishing that determinations of 5-10 mg vitamin K, PIVKA-II was detectable in these patients. The authors conclude that PIVKA-II is not associated with vitamin K deficiency, but with the use of antibiotics.

There is some doubt as to whether the assay for PIVKA-II used by the authors is reliable. Widdershoven et al compared different methods for measuring PIVKA-II and reported that techniques involving adsorption of normal factor II may result in false positive values, because the carboxylated prothrombin may not be removed completely.2 Determination of PIVKA-II by monoclonal antibody was found to be the most specific and sensitive method.2 We did not detect PIVKA-II in any of eight patients with cystic fibrosis who were supplemented with vitamin K (4-30 mcg/day).1 In only one of five unsupplemented patients with cystic fibrosis was PIVKA-II found (0-16 AU/ml). This patient took antibiotics, had a low vitamin K, concentration of 0-06 µg/l and a Thrombost of 56%.3 The authors do not mention the amount of vitamin K. Except for vitamin K, vitamin K must be accounted for when assessing vitamin K status. Antibiotics may disturb vitamin K production by intestinal flora and hence reduce the amount of total vitamin K available for the carboxylation of PIVKA-II to functional factor II. A correlation between subnormal coagulation tests and antibiotics in cystic fibrosis was reported by Komp and Selden.4 As there was no information on concentrations of vitamin K, it is impossible to establish normal values for vitamin K, PIVKA-II, however, is a direct reflection of the availability of total vitamin K in the liver and hence is associated with vitamin K deficiency. In our study PIVKA-II was found in only one unsupplemented patient with cystic fibrosis, and hence we conclude that vitamin K deficiency occurs infrequently in cystic fibrosis.

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Dr Lefrère et al comment:

Our PIVKA-II assay, based on the activity of staphylocoagulase, is widely used in many laboratories. The results obtained with this procedure with those of laboratories measuring PIVKA-II using monoclonal antibody, in particular in patients with hepatocellular carcinoma.4 Furthermore, we measured PIVKA-II concentrations in a large population of healthy individuals (blood donors) and obtained no false positive result in these individuals.

Dr Cornelissen et al do not raise the possibility of increased PIVKA-II in context other than vitamin K deficiency, such as hepatocellular carcinoma3 or hepatocholangioma9,10 effect of oral anticoagulants and cephalosporins.11 Indeed, vitamin K deficiency is not the only mechanism to generate PIVKA-II. In hepatocellular carcinoma increased PIVKA-II concentration is probably due to an acquired enzymatic anomaly which disturbs the γ-carboxylation of all vitamin K dependent factors.2 We could not explain this increase in our patients with cystic fibrosis and without vitamin K deficiency. This increase might have been linked to the interference of certain drugs on the enzymatic system of γ-carboxylation of vitamin K dependent factors.

Dr Cornelsen does not say if the eight patients they studied with a normal PIVKA-II concentration received certain drugs (such as antibiotics). However, we agree with his conclusion: vitamin K deficiency is rare in patients with cystic fibrosis supplemented with vitamin K.


In a partly similar study Bareford and Hayling1 sent each consultant a monthly statement of use of the laboratory by his firm, compared with that of other clinicians. This practice, with three other interventions, they concluded, resulted in a considerable reduction in inappropriate (my emphasis) requests for laboratory investigations. In my opinion, both groups are falling into the trap of making unjustified value judgements based on evidence for only one half of the equation: less tests = better/no worse treatment. Modifications in clinicians' laboratory testing behaviour patterns can only be regarded as desirable or "judicious" if demonstrated to improve patient care, or at least to result in no worse care. Similarly, requests can only be claimed to be "inappropriate" if it is shown that the "normal" results from laboratories were not giving their patients worse care than before as a result of curtailing their laboratory requests. In fact, Gama et al's statement that as a result of their initiative "fewer outpatient tests were investigated, and when investigated had fewer tests performed on them" would suggest, prima facie, that these patients were receiving worse medical treatment than before.

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Dr Gama et al comment:

There is ample evidence that many laboratory investigations may be unnecessary for adequate patient care and that the recent increased laboratory use has not been associated with an improvement in patient outcome. In our study, unlike Blecher, we made no unfounded assumption about the quality of patient care. Although we were unable to assess clinical outcome: we agree with Blecher that this, in practice, would be almost impossible to trace. We believe it unlikely that the reduction in laboratory use through more thoughtful and discretionary ("judicious") testing adversely affected patient management. The fact that fewer outpatient tests were investigated suggests that clinicians were reducing venepunctures (considered unnecessary by the attendant physician) and this, contrary to Blecher's assertion, represents an improvement in the quality of patient care.

Motivation for improving laboratory use should not be limited to better quality of patient care but should also include more efficient and desirable use of laboratory resources. We believe that this involves tackling not only laboratory overseer but also underuse and misuse. Gama, Pickford, Jones, McCaulay, Peters. Proceedings of the ACB national meeting, 1990:63.
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*J Clin Pathol* 1992 45: 742
doi: 10.1136/jcp.45.8.742-a

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