Plasma vitamin A, E, C and B$_6$ levels in myocardial infarction

D. LABADARIOS,   P. A. BRINK,   H. F. H. WEICH,   L. VISSER,   M. E. J. LOUW,
G. S. SHEPHARD,   M. E. VAN STUIJVENBERG

Summary

Vitamin A, E, C and B$_6$ status was studied in 30 patients with myocardial infarction and in 19 age- and sex-matched patients after elective surgery or trauma. Plasma levels of the four vitamins studied were low, remained low or decreased transiently in both groups of patients during the acute catabolic response phase, and began to return to normal after the third day from the start of the catabolic response. These changes in plasma levels are therefore neither of any special pathophysiological importance in nor specific to myocardial infarction.

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The original work of Rinehart and Greenberg[1] indicated that vitamin B$_6$ deficiency may be a contributory factor in the development of atherosclerosis. Since then, this role for vitamin B$_6$ has been a subject of controversy.[2,3] This controversy has recently been revived by the documentation of lower than normal plasma levels of pyridoxal-5'-phosphate (PLP), the active co-enzyme form of vitamin B$_6$, early in the course of myocardial infarction (MI).[4]

It has since been shown[5] and confirmed[6] that ischaemic heart disease (IHD) bears no relationship to vitamin B$_6$ status. Furthermore, the lower than normal plasma PLP levels after MI have been confirmed, and it has been proposed[6] that the observed low levels may be due to the acute starvation attendant on the acute phase of MI. Certainly plasma PLP levels decrease by approximately 43% in normal subjects after prolonged fasting.[6]

It therefore appears that plasma PLP levels are lower than normal during the acute phase of MI. These low plasma levels may represent a transient[6] and relative state of deficiency or, alternatively and more likely, may be due to the catabolic response attendant on MI. Should this be the case, plasma PLP levels in MI patients ought to be compared with those of catabolic patients with conditions other than MI rather than with those in normal subjects.

In view of the possible role vitamin C, A and E may play in IHD via their proposed protective function against radical-mediated damage,[7,8] we have studied the status of these vitamins together with PLP in patients with MI and control patients in a catabolic state.

Patients and methods

All 30 patients investigated consecutively (mean age 56,3 ± 12 years; range 27-73 years) had acute MI on clinical, ECG and biochemical grounds. Eight had had a previous infarction, 18 had angina for a minimum of 3 years preceding the MI, and in 2 the MI was complicated by an incomplete right bundle-branch block. Blood samples were drawn on admission and at 8, 12, 24, 48, 72 and 144 hours after the onset of chest pain. Wherever possible, blood samples were also drawn at 6 weeks' and 3 months' follow-up.

The 19 age- and sex-matched patients (mean age 51,6 ± 14,8 years; range 30-75 years) who served as controls had suffered various fractures or attended Tygerberg Hospital for elective surgery. Blood sampling was done as for the MI patients, except that a pre-operative sample was taken whenever possible. The admission sample in these patients was taken immediately postoperatively or, in the case of the trauma patients, on arrival at the hospital. None of the MI patients or the controls studied was taking any vitamin supplements on admission or during the study.

Blood analysis included electrolyte, urea, creatinine, albumin, creatine kinase (CK), lactate dehydrogenase (LDH) and aspartate aminotransferase (AST) levels, as well as a full blood and differential count.

Plasma was used for the analysis of vitamins A[9], E[9], C[10], and B$_6$[11], as well as total lipids (Boehringer kit), retinol-binding protein (RBP) (Partigen plate method; Hoechst Pharmaceuticals), and C-reactive protein (CRP).[12] The blood for vitamin analysis was processed immediately in all cases, except for overnight samples which were kept at 4°C in the dark and processed within a maximum of 12 hours. Plasma was stored at –20°C and all analyses were completed within a maximum of 7 days. Stability studies under these conditions revealed no sample deterioration.

Results

Plasma CRP, an indicator of acute-phase response, gradually and significantly increased ($P < 0,001$), reaching a peak on the 2nd postoperative and 3rd post-MI day respectively in the control and MI groups before returning to normal (Fig. 1).

Plasma vitamin A levels (Fig. 2) were significantly lower ($P < 0,005$) in the control group on admission and remained lower until the 6th day of observation when the difference between the two groups was no longer significant. In both the control and the MI group, however, plasma levels decreased significantly ($P < 0,005$) during the first 3 days of observation. Concomitantly, plasma RBP decreased significantly in MI patients ($P < 0,001$) from 4,96 ± 0,2 mg/l on admission to 3,34 ± 0,26 mg/l on day 3 before rising significantly ($P < 0,001$) to 5,14 ± 0,26 mg/l in the 6th week of observation. A similar decrease was seen in controls (on admission 4,04 ± 0,33 mg/l; 3rd day post-trauma/surgery 2,84 ± 0,35 mg/l; $P < 0,02$).

MRC Metabolic Research Group, Department of Internal Medicine, University of Stellenbosch and Tygerberg Hospital, Parowvallei, CP
D. LABADARIOS, M.B. CH.B., PH.D.
L. VISSER, B.SC.
M. E. J. LOUW, M.SC.
G. S. SHEPHARD, PH.D.
M. E. VAN STUIJVENBERG, B.SC. HONS
MRC Unit for Molecular and Cellular Cardiology, Department of Medical Biochemistry and Physiology, University of Stellenbosch, Parowvallei, CP
P. BRINK, M.MED. (INT.)
Department of Internal Medicine, University of Stellenbosch and Bayer Cardiovascular Clinical Research Unit and Cardiology Unit, Tygerberg Hospital, Parowvallei, CP
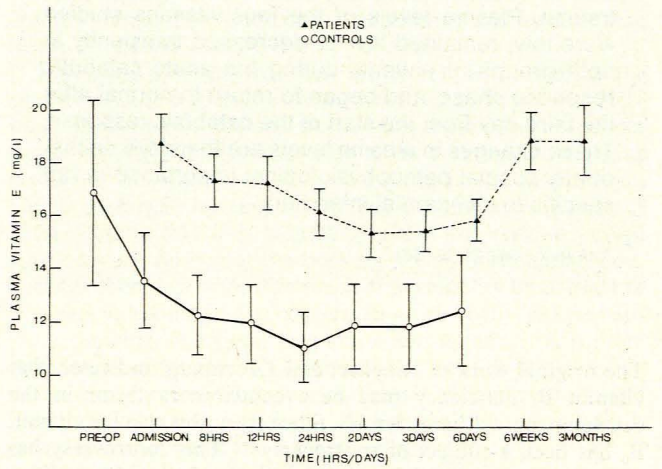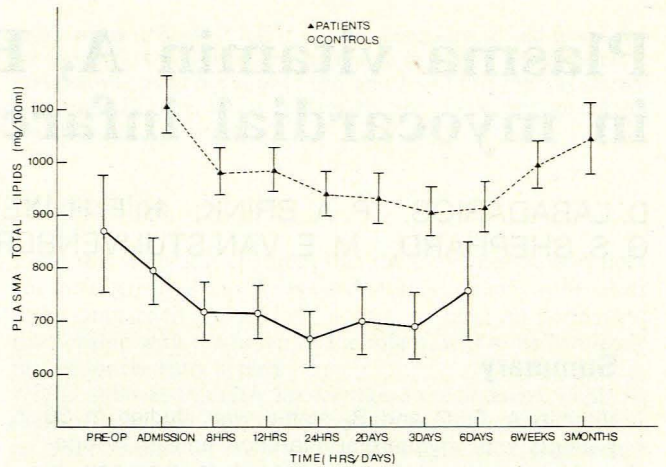H. F. H. WEICH, M.MED. (INT.), M.D., F.A.C.C.
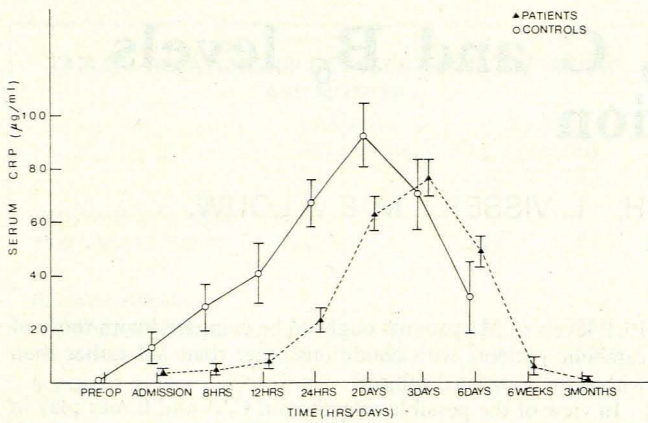
Fig. 1. The plasma CRP levels in post-MI and post-surgical/post-trauma patients who served as controls (mean ± 1 SEM).
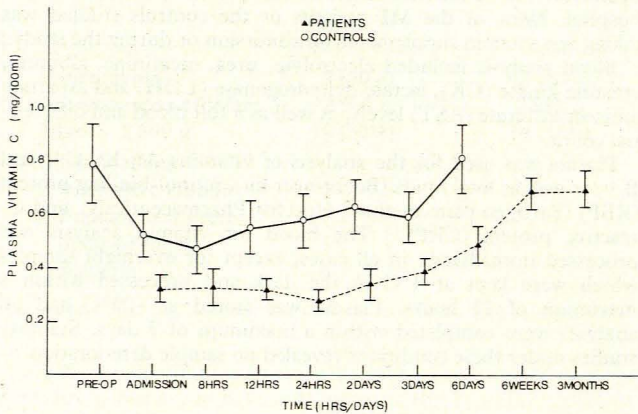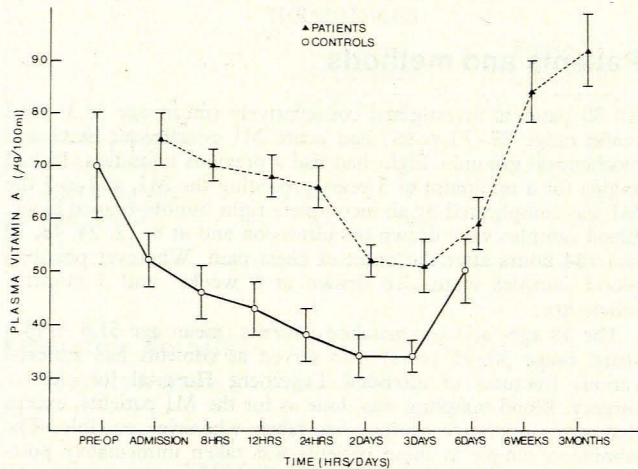
Fig. 2. Plasma vitamin A (top) and C (bottom) values in post-MI and post-surgical/post-trauma patients who served as controls (mean ± 1 SEM).

Fig. 3. Plasma vitamin E (bottom) and total lipids (top) in post-MI and post-surgical/post-trauma patients who served as controls (mean ± 1 SEM).

Vitamin C levels (Fig. 2) were consistently and significantly lower ($P < 0.025$) in the MI group than in controls. In the latter group a significant decrease ($P < 0.05$) was present between the pre- and postoperative values. Although some patients in both groups had plasma vitamin C levels below the lower limit of normal for this laboratory (0,25 mg/100 ml), all patients had values within the normal range by the 6th day of observation. The levels of vitamin C were significantly higher at 6 weeks and 3 months post-MI than any of the values during the first 6 days after MI.

Plasma vitamin E and total lipid levels were significantly higher ($P < 0.001$) in the MI group than in the control group throughout the period of observation (Fig. 3). It can be seen that both groups of patients showed a transient and significant decrease ($P < 0.01$) in plasma levels during the first 3 days post-MI/post-trauma and that levels began to rise again to those on admission from the 6th day onwards.

Plasma albumin levels, although significantly lower ($P < 0.01$) in the control group, showed a progressive decrease in both groups of patients and were significantly lower ($P < 0.001$) on the 6th day (Fig. 4). Plasma PLP levels (Fig. 4) were similar in both groups of patients and began rising to above admission levels from the 3rd day onwards, being significantly higher ($P < 0.025$) than admission values in the MI group at 6 weeks and 3 months after MI.

Discussion

This study has shown that low plasma PLP levels after MI are not in any way of special pathophysiological importance since levels of other vitamins such as vitamin C, and of other nutrients such as magnesium[13] also appear to be low in these patients. Furthermore, this study has shown that the levels of the four vitamins studied are low, remain low or decrease transiently during the acute catabolic response to injury, irrespective of aetiology, and begin to return to normal after the 3rd day from the start of the response to injury.

It has been argued[1-7] that vitamin B_6 deficiency, especially marginal chronic deficiency, may play a role in the pathogenesis of IHD. Evidence put forward for such a role includes, among others, the catalytic function of the vitamin in the methionine-
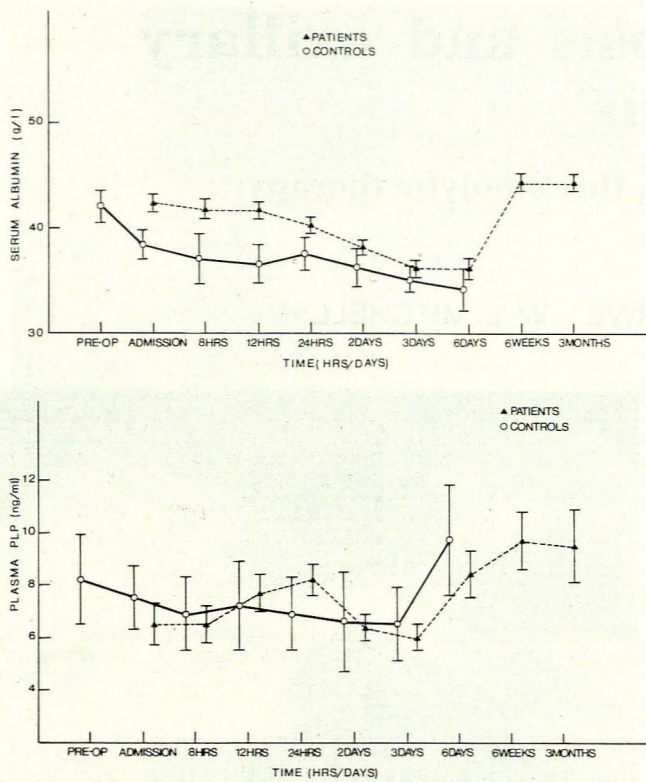
Fig. 4. Serum albumin (top) and plasma PLP (bottom) in post-MI and post-surgical/post-trauma patients who served as controls (mean ± 1 SEM).

homocysteine metabolism,[14] the tendency to increased thrombus formation,[15] the catalytic role in the cross-linking of collagen,[16] and its possible role in cholesterol metabolism.[17] While this may be so, and with the possible exception of the involvement of vitamin B₆ in thrombus formation, none of the other evidence applies exclusively to vitamin B₆. Abnormal homocysteine accumulation in body fluids can occur not only by genetic block or block from relative B₆ deficiency in the conversion of homocysteine to cystathionine (cystathionine synthetase deficiency),[18] but also by inhibition of the conversion pathway of homocysteine to methionine, which requires methylated derivatives of both vitamin B₁₂ and folic acid,[18,19] the latter being one of the commonest deficiencies known.[20] Vitamin B₆ is important in the maintenance of the activity of lysyl oxidase,[16] an enzyme involved in the normal cross-linking of collagen, but so is copper,[21] and not only cross-link defects are seen in copper-deficient animals[22,23] but also elevated plasma cholesterol levels in both animals[24,25] and man,[26] not to mention the interaction of zinc and copper and their possible role in IHD.[27]

Finally, vitamin B₆ may have a role to play in cholesterol metabolism,[17] but so has vitamin C in perhaps an equal or more important way. Vitamin C deficiency is known to interfere directly with the metabolism of the vascular wall by impairing collagen and glycosaminoglycan metabolism[28] to induce hypercholesterolaemia by reducing the activity of the cholesterol 7α-hydroxylation system,[29] and to induce hypertriglyceridaemia.[30]

Any controversy may have significant negative implications. The controversy regarding the role of vitamin B₆ deficiency in the pathogenesis of IHD has certainly caused confusion. It does, however, highlight the importance of nutrition as a whole and the delicate, and often ignored, interaction of

nutrients. It is for this reason that no one single nutrient should be afforded special status in any one given pathogenetic process, unless such special status can be proved.

In conclusion, this study shows that the low or transiently decreased plasma vitamin levels in MI patients are not indicative of any special pathogenetic relationship between vitamin status and MI but rather reflect a response to the catabolic process induced by injury.

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