

BLOOD LEVEL OF VITAMIN A, ASCORBIC ACID AND FOLATE IN HAEMOPHILIC PATIENTS

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INTRODUCTION

Haemophilia - a chronic illness - may be associated with variable degrees of tissue destruction, that may require additional nutritional factors for tissue repair; as the nutritional status is known to be related to different kinds of environmental stress (Herbert, 1980). The nutritional demands imposed by such physical stresses in man have been linked to alterations of various vitamins and minerals (Omer and Mowat, 1989). Unfortunately, the reflection of haemophilia upon different kinds of vitamins is still not well established (Gough et al., 1990).

Accordingly; the aim of the present work is to assess the blood level of vitamin A, ascorbic acid and folic acid in haemophilic patients.

MATERIAL AND METHODS

A. Material :

This study was carried out on 23 patients with haemophilia A. Their age ranged between 3 and 24 years (M: 8.24), besides 16 normal healthy subjects as a reference group with an age ranging from 5 to 29 years (M: 11.4). All subjects were males. Hereditary and acquired bleeding disorders were ruled out in the control subjects. Patients with impaired hepatic and/or renal functions that may affect the vitamin levels were excluded.

All subjects were informed with the dietary instructions using the 24 hours recall method before the sampling day (Adams, 1975) and (Perloff & Butran, 1977). The dietary intake of each individual was compared to the Recommended Dietary Allowances (RDA)

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put by the nutrition board in 1980 and expressed as a percent of RDA.

All cases were subjected to a full medical history including dietary data, complete clinical examination besides the necessary laboratory investigations that comprized: urine and stool analysis, haemogram, liver and renal profiles, cardiac enzymes, serum uric acid, electrolytes and assay of plasma coagulation factors namely VIII, IX and XI (Dacie & Lewis, 1991).

Accordingly, the patients were categorized into : mild cases in whom factor VIII activity ranged between 6-30% (9 cases); moderate cases in whom factor VIII activity was 2-5% (7 cases); and severe cases with factor activity less than 2% (7 cases). As regards the presence of complications (haemophilic arthropathy), 9 cases had arthropathy while 14 cases were free.

B. Methods :

1. Serum vitamin A level : performing the trifluoroacetic acid method (Tietz, 1976).

2. Plasma ascorbic acid : using the 2,4-dinitrophenylhydrazine method (Tietz, 1970).

3. Serum folic acid was done by the method described by Herbert (1964), while the red cell folate was determined by the method of Hoffbrand et al. (1966).

STATISTICAL ANALYSIS

Statistical analysis of the resulting data were done using the Statistical Package For Social Sciences (SPSS) (Nie et al., 1975) and (Klecka et al., 1975). The mean, standard error of the mean, t-test and one way analysis of variance with pairwise multiple comparison of means were computed using SPSS. One way analysis of variance with pairwise multiple comparison of mean was used for analysis of vitamin A, ascorbic acid and folic acid, where comparisons within groups were made. Correlation coefficient by multiple regression was calculated using the standard formulas (Bartz, 1976).

RESULTS

The differences in the mean serum vitamin A level between the control and all the haemophilic groups was not significant. Moreover, there was no relation between vitamin A level among the total group of haemophilia and the dietary vitamin A intake ($r=0.066$).

A highly significant reduction in the mean plasma ascorbic acid could be observed in each of the haemophilic groups as compared to the control. This reduction is not affected neither by the degree of severity nor the presence of complications. In table (2) a correlation between plasma ascorbic acid level and vitamin C intake is shown. Although plasma ascorbic acid level was increased proportionately with the dietary intake, its level in haemophiliacs consuming more than 66% RDA had been still significantly lower than the control ($P>0.05$). Furthermore, a positive correlation had been found between the frequency of bleeding attacks and the plasma vitamin level ($r=0.189$).

The difference in the mean serum folic acid and red cell folate activity between the control and the haemophilic groups is not significant. Moreover, on measuring the dietary intake of total folacin by the dietary recall, there was no correlation between the dietary intake of total folacin and the serum folate ($r=0.218$) or red cell folate levels ($r=-0.047$).

DISCUSSION

Some nutritional demands imposed by physical stress have been linked to alterations of various vitamins and minerals in man (Irwin & Hutchins, 1976). Furthermore, many stressful conditions - even psychological ones - can frequently lead to spontaneous bleeding into joints and tissues in the haemophilic patients (Agle & Mattson, 1976 and Omer & Mowat, 1989).

The present work revealed non significant changes in the serum vitamin A level in the haemophilic patients which is also neither affected by the severity of the disease nor the presence of complications. These findings could be attributed to the fact that

subjects with serum vitamin A level less than 20 ug/dl are liable to suffer from the consequences of hypovitaminosis A, (The Ten State Nutrition Survey, 1972). Moreover; Owen et al. (1971) reported that the serum vitamin A level can be maintained nearly constant until the liver stores become nearly exhausted. Therefore, determination of serum vitamin A level provides a limited information about the actual body stores of this vitamin especially in the liver.

On the other hand, a significant reduction in plasma ascorbic acid was observed in haemophilic cases as compared to the control subjects. The degree of reduction was more manifested in the groups with moderate and severe haemophilia. Meanwhile, the presence of complications did not yield a significant difference on comparing such patients with those free of complications. These findings have been found to be in agreement with those reported by Toy et al. (1983). The reduced plasma ascorbic acid in haemophilic patients could be referred to either the increased demands or

the high rates of utilization in such cases. Ascorbic acid is one of the essential factors necessary for collagen synthesis and for the intact peripheral vascular system (Baker, 1967). Moreover, Karmar et al. (1979) concluded that vitamin C acts as a cofactor for proline hydroxylation and collagen production, and they pointed that a mega dose of ascorbic acid is indicated for higher production of hydroxyproline during the active stage of healing. Haemophilic patients are frequently exposed to a continuous process of physical as well as psychological stresses like anxiety and emotional tension which in turn result in spontaneous haemorrhage in the muscles and/or joints as proved by Agle & Mattson (1976) and Davis & Hughes (1985), and hence, more nutritional demands are required in those patients. On the other hand; excess amounts of ascorbic acid are also consumed in the process of repairing the destroyed tissues (Mullen and Wilson, 1976). Therefore, we recommend a supply of extranormal doses of ascorbic acid for haemophilic patients aiming at compensation of its

deficiency and to support the healing process in such patients.

be below 140 ng/ml and 3 ng/ml respectively.

In the present study, 36% of haemophilic patients showed a red cell folate level below 140 ng/ml, and 9% had a serum folate below 2 ng/ml. The difference in both parameters was found to be non significant when compared to the control figures. Moreover, neither the severity nor the presence of complications - degenerative joint disease had affected the folate level in such disease. Unfortunately, literatures concerning serum or red cell folate levels in haemophilic patients are not available. However, serum folate was studied by Alter et al. (1971) and Dellar et al. (1986) in patients with rheumatoid arthritis. They reported that 49% of their cases had a serum folate level 3-5 ng/ml, while 22% had values below 3 ng/ml. Hall et al. (1975) stated that the red cell folate is considered to be a more accurate and a less variable index than serum folate in studying folate deficiency. Meanwhile, Hoffbrand et al. (1966) and Owen et al. (1971), defined the serum and red cell folate deficiency level to

SUMMARY AND CONCLUSIONS:

The target of this work was to search for any relation between the nutritional status and haemophilia and whether the disease alters the level of certain vitamins. Therefore, serum vitamin A, plasma ascorbic acid, serum and red cell folate had been determined in 23 haemophilic patients together with 16 normal control persons. From the forementioned discussion, we concluded that there was a significant reduction in plasma ascorbic acid in haemophilics despite their dietary vitamin C intake was in excess of 66% of RAD. Meanwhile, the demands for ascorbic acid needed for tissue repair in haemophilic patients could be reduced with prompt medical care of bleeding episodes and optimal nutritional care. A non significant differences had been observed in the serum vitamin A, red cell and serum folate in haemophilic patients as compared to the control subjects.

Table (1) : Shows the results of vitamin assays in the studied groups.

| | Control (n : 16) | Total (n : 23) | Haemophilia | | | | |
|----------------------|---------------------|-------------------|-----------------|-----------------|-------------------|-----------------|---------------------|
| | | | Severity | | | Complications | |
| | | | Mild (n : 9) | Mod. (n : 7) | Severe (n : 7) | with (n : 9) | without (n : 14) |
| Vit. A (ug/dl) | | | | | | | |
| M | 76.12 | 80.02 | 89.04 | 78.18 | 72.82 | 72.82 | 80.74 |
| SEM \pm | 18.87 | 11.42 | 15.32 | 20.26 | 18.06 | 20.24 | 16.82 |
| Asc. acid (mg/dl) | | | | | | | |
| M | 1.32 | 0.74 | 0.88 | 0.72 | 0.76 | 0.74 | 0.72 |
| SEM \pm | 0.06 | 0.09 | 0.13 | 0.18 | 0.10 | 0.14 | 0.12 |
| Serum folate (ng/ml) | | | | | | | |
| M | 8.78 | 8.34 | 9.48 | 9.40 | 6.14 | 7.76 | 8.22 |
| SEM \pm | 0.84 | 0.98 | 1.60 | 1.54 | 1.38 | 1.62 | 1.30 |
| RBC folate (ng/ml) | | | | | | | |
| M | 192 | 217 | 222 | 225 | 254 | 236 | 296 |
| SEM \pm | 16 | 29 | 31 | 28 | 34 | 42 | 39 |

The mean (M) and the standard error of the mean (SEM) of serum vitamin A, ascorbic acid, serum and RBC folate in the control and haemophilic groups (n: number of cases).

Table (2) : Changes in the vitamin levels in the blood and the vitamin intake in haemophilic cases.

| Vitamin intake | <50% RDA (n:5) | <66% RDS (n:5) | >66% RDA (n:6) | >100% RDA (n:5) |
|--------------------------|-------------------|-------------------|-------------------|--------------------|
| Serum Vit. A (ug/dl) | | | | |
| M | 76.92 | 75.14 | 76.28 | 81.64 |
| SEM \pm | 15.72 | 20.02 | 14.26 | 16.80 |
| Plasma Asc. acid (mg/dl) | | | | |
| M | 0.55 | 0.62 | 0.84 | 0.88 |
| SEM \pm | 0.11 | 0.15 | 0.14 | 0.12 |
| Serum folate (ng/ml) | | | | |
| M | 8.16 | 7.28 | 8.44 | 8.46 |
| SEM \pm | 0.78 | 1.04 | 0.92 | 1.62 |
| RBC folate (ng/ml) | | | | |
| M | 219 | 232 | 228 | 240 |
| SEM \pm | 24 | 29 | 22 | 34 |

RDA = Recommended Dietary Allowance.

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مستوى فيتامين أ وحمض الاسكوربيك والفوليك في مرضى الهيموفيليا

ملخص البحث:

تهدف هذه الدراسة إلى البحث عن علاقة بين الحالة الغذائية ومرض الهيموفيليا وعمّا إذا كان هذا المرض يؤثر على مستوى فيتامينات معينة، وعلى ذلك فقد تم تعيين مستوى فيتامين أ وحمض الاسكوربيك وحمض الفوليك في الدم في ٢٣ مريضاً بالهيموفيليا إلى جانب ١٦ من الأصحاء كمجموعة ضابطة وقد استنتج وجود انخفاض ملحوظ في حمض الاسكوربيك على الرغم من زيادته في الغذاء وفي نفس الوقت يمكن تخفيض الاحتياجات لحمض الاسكوربيك لعملية الالتئام في الهيموفيليا وذلك بالعناية بالنوبات النزفية. ولم تلاحظ تغييرات ذات دلالة في فيتامين أ أو حمض الفوليك في مرضى الهيموفيليا بالمقارنة للمجموعة الضابطة.

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