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# EVALUATION OF VITAMIN K DEFICIENCY AND IT'S EFFECT IN COMPLICATED SEVERE ACUTE MALNUTRITION

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**ABSTRACT** **Objective:** The World Health Organization (WHO) updates SAM management protocol regularly but still it is not clear whether Vitamin K should be given to SAM children or not. But in our institute we observed that many children of complicated SAM had various bleeding manifestations on admission that's why we planned to study the evaluation of vitamin K deficiency and effect of vitamin K in complicated SAM.

**Methods:** It was a hospital based prospective interventional study conducted in 150 complicated SAM children, 100 in group A and 50 in group B. Group A children received Vitamin K 5 mg via intravenous route on admission while group B did not received Vitamin K. The PT-INR, aPTT along with routine investigations were done on admission in both the groups. Repeat PT-INR and aPTT were done after 24 hours of Vitamin K administration in group A and before discharge (on day 10 of admission) in group B children who had abnormal INR on admission. All the collected data were managed and analyzed with standard software Biostatics (SPSS Version 20)

**Results:** Forty two (28%) out of 150 children, 27 in group A and 15 in group B had abnormal INR on admission. In group A, 12 (44.4%) children had bleeding manifestations and most of children (66.6%) had GI bleeding and Malena. In group A, After 24 hour of vitamin K administration all 27 children had significant improvement in INR and 20 out of 27 with abnormal aPTT had significant improvement in aPTT. But in the group B where no vitamin K was administered more than 50% had persistence of abnormal PT, INR and aPTT on day 10 of admission.

**Conclusion:** More than one fourth complicated SAM children had vitamin K deficiency and significant improvement was seen in children who received vitamin K on admission compared to children who did not receive vitamin K and kept on diet alone.

**KEYWORDS :** Activated partial thromboplastin time (aPTT), International normalized ratio (INR), Prothrombin time (PT), Severe acute malnutrition, Vitamin K.

## INTRODUCTION:

Malnutrition makes a major contribution to the global disease burden, accounting for more than one-third of child deaths worldwide.

In severe acute malnutrition (SAM) many factors like malabsorption, inadequate intake or impaired metabolism of fat-soluble vitamins, impaired protein synthesis and alteration of the absorptive surface of the intestine may lead to vitamin K deficiency.[1] Vitamin K deficiency causes prolongation of both prothrombin and partial thromboplastin times. Prothrombin time is highly sensitive to vitamin K deficiency and parenteral administration of Vitamin K, which restores the prothrombin time to normal. The World Health Organization (WHO) updates SAM management protocol regularly but still it is not clear whether Vitamin K should be given to SAM children or not. But in our institute we observed that many children of complicated SAM had bleeding manifestation like ecchymosis, petechiae, purpura, gastrointestinal bleeding, malena and rarely intracranial haemorrhage that's why we planned to study the evaluation of vitamin K deficiency and effect of vitamin K in complicated SAM.

## MATERIALS AND METHODS:

It was a hospital based prospective interventional study conducted in 150 complicated SAM children with aged 6 months to 59 months, 100 in group A and 50 in group B of comparable characteristics like age, sex etc.They were admitted at Malnutrition Treatment Center (MTC), of Tertiary hospital attached to a medical college in last one year. Ethical clearance from the ethical committee of the institute was taken. Only complicated SAM were getting admission in our MTC. Uncomplicated SAM were treated on outpatient basis.

Criteria to define SAM with complications were taken as bipedal edema /or MUAC<115mm and /or WFH<-3SD and one of the following: anorexia, not alert, medical complications e.g. - lower respiratory tract infection, high grade fever, anaemia, hypoglycaemia, severe dehydration.[2] Those children were excluded who had any disease causing change in coagulation profile like liver disease, kidney disease/hemodialysis, Cholestatic disease, Cystic fibrosis, multiple abdominal surgeries, long-term parenteral nutrition, viral hepatitis, massive blood transfusion and on drug therapy like Antibiotics , cholestyramines, warfarin, salicylates, anticonvulsants, and certain sulfa drugs or received vitamin K one week prior to admission.

Random selection of patients was done as group A and group B.Group A children received vitamin K 5 mg via intravenous route on admission while group B did not. If child had evidence of bleeding on admission was included in group A. Both the group children were treated according to WHO protocol for SAM management including diet. Prothrombin time (PT), International normalized ratio (INR), activated partial thromboplastin time (aPTT) along with routine investigations like complete blood count, urea, creatinine, electrolytes, urine complete and chest x-ray were done on admission in both the groups. The PT-INR and aPTT were repeated after 24 hours of Vitamin K administration in group A or before discharge (on day 10 of admission) in group B children who had abnormal INR on admission. Prolongation of the prothrombin time (PT) was defined as a five second increase outside the upper limit of the normal range[3] (abnormal PT $\geq$18 seconds, control was 12 seconds and abnormal INR $\geq$1.5). Vitamin K deficiency was considered based on abnormal PT-INR. All the collected data was managed and analyzed with standard software Biostatics (SPSS Version 20). Statistical analysis of data was done with Chi-square analysis (for quantitative analysis), Student t-test with assistance of qualified statistician. The analysis of the data was made on the basis of important statistical parameters like the mean, standard deviation, standard error, t-test and proportion test where applicable. All values was compared at 5% or 0.05 and 1% or 0.01 levels of significance for the corresponding degrees of freedom to arrive at the conclusion regarding the objectives of the study.

## RESULTS:

Total 150 children, of which 100 in group A and 50 in group B were enrolled for evaluation of vitamin K deficiency and effect of vitamin K in SAM. In this study 52% were male and 48% were female and majority (72.7%) of children were in 6 to 24 months age group.

Table 1 shows mean age of group A was 16.18±9.6 months while in group B was 18.72±13.4 months, mean weight was 5.72±1.32, 6.33±1.9 ,mean height 69.76±7.17, 72.46±10.0 and MUAC was 10.45±1.39, 10.5±1.15 in group A and group B respectively.

**Table 1: Basic Anthropometric Variables in SAM Patients**

| Values | Group A (100) | | Group B (50) | | P value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Age (months) | 16.18 | ±9.6 | 18.72 | ±13.4 | 0.185 |
| Weight (kg) | 5.72 | ±1.32 | 6.33 | ±1.9 | 0.045 |
| Height (cm) | 69.76 | ±7.17 | 72.46 | ±10.0 | 0.093 |
| MUAC (cm) | 10.45 | ±1.39 | 10.5 | ±1.15 | 0.7703 |

Table 2 Shows abnormal INR distribution in both the group on admission. Forty two (28%) out of 150 children, 27 in group A and 15 in group B had abnormal INR on admission and overall 27 (18%) had INR from 1.5 to 2.0, 9 (6%) had INR from 2.0 to 2.5 and 6 (4%) had INR more than 2.5. All 6 children with INR more than 2.5 present in group A.

**Table 2: Abnormal INR in both group on admission**

| INR | GROUP A | GROUP B | TOTAL |
|---|---|---|---|
| Less than 1.5 | 73 | 35 | 108 (72%) |
| 1.5 to 2.0 | 15 | 12 | 27 (18%) |
| 2.0 to 2.5 | 6 | 3 | 9 (6%) |
| More than 2.5 | 6 | 0 | 6 (4%) |
| TOTAL | 100 | 50 | 150 (100%) |

Table 3 shows the effect of vitamin K and diet alone on INR. In group A 27 children had abnormal INR on admission and received vitamin K along with diet. In group B 15 children had abnormal INR and they were kept alone on diet with supplements except vitamin K. In group A, after 24 hours of vitamin K administration 22 (81.5%) had INR less than 1.5 and 5 (18.5%) had INR more than 1.5 (they shows improvement in INR from more than 2.0 to less than 2.0). In group B, before discharge or on day 10 of admission, 7 (46.7%) had INR less than 1.5 and 8 (53.3%) still had INR more than 1.5 (4 out of 8 had increased INR but within 1.5 to 2.0).

**Table 3: Change of INR in group A and B after intervention**

| INR after intervention | Group A | | Group B | |
|---|---|---|---|---|
| | Vitamin K | % | Alone diet | % |
| Less than 1.5 | 22 | 81.5% | 7 | 46.7% |
| More than 1.5 | 5 | 18.5% | 8 | 53..3% |
| Total | 27 | | 15 | |

P=0.019

Table 4 shows that in group A out of 27 with abnormal INR, 20 children had aPTT more than 40 seconds on admission and after 24 hour of vitamin K administration 18 out of 20 had aPTT less than 40 seconds, 2 still had aPTT more than 40 seconds (these all 2 children had improvement in aPTT from more than 60 to less than 60). In group B out of 15 with abnormal INR, 8 children had aPTT more than 40 seconds on admission and before discharge 5 children had normal aPTT and 3 still had aPTT more than 40 seconds.

**Table 4: Comparison of aPTT in both group children with Abnormal INR**

| aPTT (in seconds) | GROUP A | | GROUP B | |
|---|---|---|---|---|
| | On admission | After Vitamin K | On admission | Before discharge |
| Less than 40 | 7 (26%) | 25 (93%) | 7 (46.7%) | 12 (80%) |
| 40 to 60 | 16 (59%) | 2 (7%) | 8 (53.3%) | 3 (20%) |
| More than 60 | 4 (15%) | 0 | 0 | 0 |
| TOTAL | 27 | 27 | 15 | 15 |
| P value | | 0.001 | | 0.06 |

Table 5 shows that mean INR on admission in group A children was 2.31±1.33 and in group B children 1.75±0.18.Mean INR after 24 hours of vitamin K in group A was 1.31±0.19 and before discharge in group B was 1.48 ±0.21. Mean aPTT on admission in group A children was 47.70±10.91 and in group B children 41.02±4.18. Mean aPTT after 24 hours of vitamin K in group A was 34.07±4.11 and before discharge in group B was 36.11 ±4.11.

**Table 5: Mean INR and aPTT comparison between group A and B children with abnormal INR on admission**

| | Group A (27) | | Group B (15) | | P value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| INR on admission | 2.31 | 1.33 | 1.75 | 0.18 | 0.119 |
| INR After intervention | 1.31 | 0.19 | 1.48 | 0.21 | 0.011 |
| Change (effect of intervention) | -1.00 | 1.35 | -0.27 | 0.23 | 0.045 |
| aPTT on admission | 47.70 | 10.91 | 41.02 | 4.18 | 0.029 |
| aPTT After intervention | 34.07 | 4.11 | 36.11 | 4.11 | 0.132 |
| Change (effect of intervention) | -13.63 | 10.43 | -4.91 | 5.82 | 0.005 |

In group A, 12 (44.4%) children had bleeding manifestation with abnormal INR and aPTT on admission. Majority of children (66.6%) had GI bleeding and Malena, 4 (33.3%) had Ecchymosis, 2 (16.7%) had Petechiae, 2 (16.7%) had Purpura and 1 (8.3%) Mucosal bleeding.

## DISCUSSION:

Based on abnormal PT-INR and aPTT results in both the groups, 28% means every fourth child is having vitamin K deficiency in complicated SAM. In group A, Vitamin K 5 mg administration was done in all 27 children with abnormal INR. After 24 hour of vitamin K administration all 27 children had significant improvement in INR (22 had less than 1.5 and 5 had decreased INR) and 20 out of 27 with abnormal aPTT had significant improvement in aPTT. But in the group B where no vitamin K was administered more than 50% had persistence of abnormal PT, INR and aPTT even after 10 days treatment according WHO treatment protocol. The change of mean PT, INR and aPTT was statistically significant in intervention group A.

Out of 27 in group A, 12 children (44.4%) had bleeding manifestation rest were not having clinical bleeding even with abnormal PT, INR and aPTT. This finding suggests that if they were not identified and not treated early any time they would have developed clinical bleeding.

Various studies had been carried out in malnutrition based on IAP classification and other comorbidities like diarrhea, prolong antibiotic therapy but to our best of knowledge no such studies in SAM available. Bay A, et al[4] in 90 children with diarrhoea. A total of 3 mg of vitamin K was administered to patients with prolonged PT and/or aPTT. Coagulation parameters were restudied 8 to 12 hour after vitamin K was administered. Significant improvement in PT and aPTT and an increase in coagulation factors were observed after vitamin K had been administered.

Bhat R.V, et al[5] in 66 children with malnutrition on prolonged antibiotic therapy. A total of 22 (33.33%) children out of 66 developed hypoprothrombinemia. All children with prolonged PT had prolonged aPTT also. Children who had developed an abnormal coagulation profile received therapeutic vitamin K and had a repeat PT determination within 12 hours and hypoprothrombinemia was corrected in all children. All children with severe coagulation abnormalities also had higher grades of malnutrition. Therefore malnutrition may be a contributing factor in the development of hypoprothrombinemia.

Children with severe malnutrition had a higher incidence of hypoprothrombinemia, a finding similar to Bhat R.V, et al.[5], Ehsanipour, et al.[6], Kark, et al.[7] and Pineo, et al.[8] Possible explanation could be that malnutrition limits the availability of oral phylloquinone causing hypoprothrombinemia. In children with abnormal INR and aPTT, improvement was noted in coagulopathy after vitamin K administration.

## CONCLUSIONS:

In complicated SAM more than one fourth (28%) children had vitamin K deficiency and significant improvement was seen in children who received vitamin K on admission compared to children who did not receive vitamin K and kept on diet alone. Majority of SAM children with abnormal PT, INR had Gastro-intestinal bleeding manifestation.

So we recommend from this present study that the PT and INR to be done in all children of complicated SAM. All complicated SAM children should receive Vitamin K at the time of admission. Further studies are needed to decide recommended dose of Vitamin K whether it should be 2.5 mg or 5 mg. and how many days. Because in our study giving single dose of vitamin K does not get normalisation of PT-INR in all SAM children.

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