ORIGINAL ARTICLE

Status of Vitamin C and Vitamin E in Acute Pancreatitis and their Prognostic Significance

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Abstract

Experimental and clinical studies have provided some support for the concept that oxidative stress is the common pathway for initiation of acute pancreatitis. Ascorbic acid (vitamin C) and alpha tocopherols (vitamin E) are the key anti- oxidants in human blood plasma. In present study our aims was to measure the levels of Vitamin-C & Vitamin-E (Alpha- Tocopherol) in patients of acute pancreatitis and to compare the levels with control group as well as to assess the prognostic significance of Vitamin-C & Vitamin-E levels in acute pancreatitis in relation to Ranson's criteria. Serum levels of vitamin C & E were measured in 50 cases having acute pancreatitis and 20 controls having pain abdomen of non pancreatic origin. Levels of vitamin C and vitamin E were compared with the controls and were correlated to the severity of disease according to Ranson's criteria. The difference in the levels of vitamin C between the study group and the control group was statistically non-significant at the time of admission and at 48 hours. However the difference was statistically significant at 7 days. The difference in the levels of vitamin E between the study group at the admission is statistically non-significant when compared to the levels in the control group at the time of admission, at 48 hours and at 7 days after the admission. No correlation was found between the levels of vitamin C and vitamin E at the time of admission, at 48 hours and at 7 days with the severity of disease according to Ranson's score. There is an initial fall in the levels of vitamin C with the rising trend towards the end of the 7 days period. The levels of the vitamin E had rising trend towards the end of the 7 days but no statistically significant initial fall in the levels as compared to the control group. Levels of vitamin C and vitamin E have no prognostic significance in the cases of acute pancreatitis.

Key Words

Acute Pancreatitis, Vitamin C, Vitamin E

Introduction

A key feature of acute pancreatitis is the elaboration of an inflammatory reaction, which results in edema of the pancreas and extensive local and systemic effects. The phenomenon of auto -digestion of a gland by its own enzymes elaborated in cascades finds no better example than acute pancreatitis. Experimental and clinical studies have provided some support for the concept that oxidative stress is the common pathway for initiation of acute pancreatitis (1). Oxidative stress occurs when there is an imbalance between pro- oxidant activity and endogenous anti-oxidant defenses.

Once produced, oxygen radicals can act as a molecular trigger of various inflammatory processes. They can directly attack biological membranes, stimulate arachidonic acid metabolism with increased production of prostaglandins, thromboxane and leukotrienes and trigger the accumulation of neutrophils and their adherence to the capillary wall. Therefore, it is very likely that ROS play a central role in the perpetuation of pancreatic inflammation and the development of extra pancreatic complications. Ascorbic acid (vitamin C) and alpha tocopherols (vitamin E) are the key anti- oxidants in human blood plasma. Studies have shown

raised levels of oxidative stress markers and lowered levels of anti oxidants like vitamin C and vitamin E in acute pancreatitis (2).

In view of all this meticulous research, this study was planned to measure the total serum vitamin C and vitamin E levels in patients of acute pancreatitis. In present study our aims was to measure the levels of Vitamin-C & Vitamin-E (Alpha- Tocopherol) in patients of acute pancreatitis at the time of admission, 48 hours & at 7 days and to compare the levels with control group as well as to assess the prognostic significance of Vitamin-C & Vitamin-E levels in acute pancreatitis in relation to Ranson's criteria.

Material and Methods

The study was undertaken on 50 patients diagnosed as suffering from acute pancreatitis, admitted in Dayanand Medical College and Hospital, Ludhiana. Only the patients with the Ranson's Criteria between 2 and 6 at the time of admission were selected.

Second group of 20 patients with pain abdomen of non -pancreatic origin served as control group. Pancreatic pathology was ruled out in the control group by measuring the levels of serum amylase and serum pancreas specific lipase. The diagnosis of acute pancreatitis in patients presenting with acute abdominal pain was from the clinical history, physical examination and laboratory aids. Blood samples were collected at the time of admission, 48 hrs and on 7th day for determination of Serum Pancreatic Specific Lipase, Serum Vitamin C Level, Serum Vitamin E (Alpha-Tocopherol) Level. Schedule of measurement is based on assumption that maximum oxidative stress will be found in the initial phase of acute pancreatitis. Severity grading of the disease was done according to Ranson's criteria. Ranson's scoring was done at time of admission and at 48 hours in all the cases. Patients having Ranson's Score >2 and <6 were included in the study.

Levels of vitamin C and vitamin E were compared with the controls and were correlated to the severity of disease according to Ranson's criteria.

Serum vitamin C level and Alpha –Tocopherol level were estimated in the department of Biochemistry, Dayanand Medical College and Hospital.Ascorbic acid was measured in plasma by titration method using 2, 6 dichlorophenolindophenol. Alpha tocopherol was measured by colorimetric method using Emmeric Engel reaction of Varley.

Results

In this study, 50 patients diagnosed as having acute pancreatitis on the basis of history, standard investigations and imaging techniques and having Ranson's score between 2 and 6 were studied. The trend in the levels of vitamin C and vitamin E in the study group was analyzed for the first seven days after the admission and were compared to the control group consisting of 20 patients having pain abdomen of non pancreatic origin. The levels of vitamin C and vitamin E were measured at admission, at 48hours and 7 days after the admission.

We found that 69% of patients were male with mean age of 44.4 years and 31% were female with mean age of 37.7 years. The alcohol intake was found to be the major etiologic factor contributing to 46% of the cases with gall stones25% and idiopathic 29%. Alcoholic pancreatitis was more common in males where as gall stone-induced pancreatitis was more common in females.

Mean value for serum lipase was high i.e. 1500 U/L in the study group. We studied the levels of Pancreas Specific Lipase in acute pancreatitis and the mean value in the study group was significantly high i.e. 733 IU/L than in healthy population (7-60 U/L).

Patients were divided into three groups I, II and III with Ranson's score 2-3, 4 and 5-6. There were 19 patients in group I, 13 patients in group II and 20 patients in group III. The mean level of vitamin C in the study group was 0.74 mg/ml at admission, 0.88 mg/ml at 48 hours after the admission and 1.06 mg/ml at 7 days after the admission (Table 1). The mean level of vitamin C in the control group was 0.77 mg/ml at admission. The difference in the levels was significant when samples at 7 days were compared to the control group and when samples in the study group at 48 hours were compared with the samples at 7 days (Table 2).

The mean levels of vitamin E in the study group was 10.02 mg/ml at admission, 9.93 mg/ml at 48 hours and 10.76 mg/ml at 7 days after the admission (Table 3). The levels of vitamin E largely remained unaffected for the first 7 days when compared to the control group (Table 4). But the rising trend was observed in the levels of vitamin E when samples at 48 hours and 7 days after the admission from the study group were compared.

Most of the patients irrespective of their Ranson's score were discharged from the hospital in a stable condition. There were only two mortalities (3.85%) that died from the systemic complications of acute pancreatitis.

Table 1. Mean value and standard deviation of vitamin C level

Group	Number	C1(Admn.) µg/ml	C2(48 Hrs) µg/ml	C3(7 Days) µg/ml
I	19	0.78 ± 0.279	0.90 ± 0.276	1.01 ±0.314
II	13	0.76 ±0.246	0.88 ±0.313	1.24 ± 0.226
III	20	0.71 ± 0.201	0.86 ± 0.125	0.99 ± 0.217
STUDY	52	0.74 ± 0.241	0.88 ± 0.237	1.06 ± 0.274
CONTROL	20	0.77 ± 0.261	-----------	---------

Table 2. Comparison of C1, C2 and C3 with control group and C2 with C3.

Comparison	T – Value	Significance
CONT Vs C1	0.46	P >0.01
CONT Vs C2	1.69	P >0.01
CONT Vs C3	4.02	P <0.01
C2 Vs C3	Z - 3.55*	P <0.01

* t – test could not be applied as the sample size was large in this comparison

Table 3. Mean value and standard deviation of vitamin E level

Table 4. Comparison of E1, E2 and E3 with control group and E2 with E3.

Comparison	T – Value	Significance
CONT Vs E1	0.50	P >0.01
CONT Vs E2	0.66	P >0.01
CONT Vs E3	1.79	P <0.01
E2 Vs E3	Z - 2.67*	P <0.01

* t – test could not be applied as the sample size was large in this comparison

Hence the above comparison shows that the difference in the levels of vitamin C between the study group and the control group is statistically non-significant at the time of admission and at 48 hours. However the difference is statistically significant at 7 days. The difference in the levels of vitamin C between the study group at 48 hours after the admission is statistically significant when compared to the levels in the study group at 7 days after the admission. The difference in the levels of vitamin E between the study group at the admission is statistically non-significant when compared to the levels in the control group at the time of admission, at 48 hours and at 7 days after the admission.

	Coefficient of correlation
Ranson's score/ C1	-0.14308
Ranson's score/ C2	-0.05934
Ranson's score/ C3	-0.00823
Ranson's score/ E1	-0.14189
Ranson's score/ E2	0.183337
Ranson's score/ E3	0.138281

Since the value of correlation coefficient was non-significant at the time of admission, 48 hours and seven days for both vitamin C and vitamin E. No correlation was found between the levels of vitamin C and vitamin E with the severity of disease according to Ranson's score at the time of admission, at 48 hours and at 7 days.

Discussion

Research work on antioxidants was initiated in experimental models of acute pancreatitis. Studies by several authors in experimental pancreatitis have shown the oxidative stress in early phase of acute pancreatitis. Some authors have shown intravascular margination of granulocytes in the pancreatic gland at an early stage of cerulean induced pancreatitis and suggested that oxygen derived free radicals may play a role in the experimentally induced acute pancreatitis (3, 4). Oxygen free radicals are formed during normal cellular metabolism. Under normal physiological conditions, most of the molecular oxygen is reduced tetravalently by efficient intracellular reduction system, such as cytochrome oxidase in mitochondria. However some of the cellular oxygen consumption proceeds by a univalent pathway resulting in the formation of the several oxygen radicals (5, 6). Mechanism of injury includes peroxidation of membrane lipids, oxidation of sulfhydryl groups of membrane proteins and destruction of nucleic acids in DNA (7, 8). Defenses against this damage include free radical scavenging enzymes vitamin C, vitamin E and beta carotene. After the success of antioxidants in experimental pancreatitis, the focus shifted to the measurement of antioxidants in acute and chronic pancreatitis in human beings. Antioxidant deficiency was found in the patients with hereditary pancreatitis (9).

Ascorbate is increasingly being recognized as the most important antioxidant in human blood plasma as it has peculiar activity against hypochlorus acid which is released extracellularly when phagocytosis is excessive

(10). Ascorbic acid is the fast acting antioxidant in plasma and constitutes first line of defense against neutrophils derived oxidants. Ascorbic acid is also a key antioxidant within the cells where it helps to recycle vitamin E and thus indirectly to refurnish reduced glutathione after its oxidation (11).

Vitamin E is an important plant derived antioxidant. In contrast to vitamin C, vitamin E is a lipid phase antioxidant and is known to be consumed only after plasma vitamin C is depleted. Antosiewicz J showed that cerulean induced pancreatitis diminished vitamin E concentrations in plasma and increased in pancreas (12). Vitamin has been reported to be an ineffective scavenger for the oxidants released by the neutrophils (10). This makes plausible our finding that there was no significant difference in the levels of vitamin E in the study and the control group when compared at the time of admission, at 48 hours and at 7 days.

In the present study we observed the trend in the levels of vitamin C and vitamin E in patients with acute pancreatitis for the first seven days after the admission. When compared with the control group, the fall in the levels of vitamin C was not statistically significant when compared at the time of admission and at 48 hours. But the fall in the levels of vitamin C was statistically significant when compared with the control group at 7 days ($p < 0.01$) and also there was a statistically significant fall in the levels of vitamin C when the samples of study group at 48 hours after the admission were compared to samples of study group 7 days after the admission ($p < 0.01$). The results show that there is the evidence of oxidative stress early in the course of the disease but it was not statistically significant. However there significant evidence for the oxidative stress at the 7 days.

The fall in the levels of vitamin E when compared with the control group at the time of admission, at 48 hours and at 7 days after the admission were not statistically significant ($p > 0.01$) which is consistent with the results shown by Tsai K who showed that the levels of vitamin E are largely unaffected in the cases of oxidative stress induced by excess of neutrophils (2). But there was a statistically significant fall in the levels of vitamin E when the samples at 48 hours after the admission were compared to the samples at 7 days after the admission.

The second part of the study was to evaluate the correlation between the levels of vitamin C and vitamin E and the severity of the disease according to the Ranson's score. Since the value of correlation coefficient was non-

significant at the time of admission, 48 hours and seven days for both vitamin C and vitamin E, so we may conclude that levels of vitamin C and vitamin E have no prognostic significance in the cases of acute pancreatitis with respect to the severity of the disease. This is in contrast to the results shown in the study which showed that oxidative stress markers are highly correlated with the severity of pancreatitis but are not as useful as Modified Glasgow Criteria in predicting the severity (13).

Conclusion

Hence we conclude from our study that there is an initial fall in the levels of vitamin C with the rising trend towards the end of the 7 days period. The levels of the vitamin E have rising trend towards the end of the 7 days but no statistically significant initial fall in the levels as compared to the control group. Levels of vitamin C and vitamin E have no prognostic significance in the cases of acute pancreatitis.

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