

Bangladesh Med Res Counc Bull 1984 June; 10  
(1): 24-8. PMID: 6466264

## EFFECT OF ASCORBIC ACID IN THE TREATMENT OF TETANUS

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### SUMMARY

The effect of daily intravenous administration of 1000 mg ascorbic acid (AA) in tetanus patients aged 1-30 years was studied. In the age group of 1-12 years, 31 patients were treated with AA as additional to antitetanus serum, sedatives and antibiotics. It was found that none of the patients died who received AA along with the conventional antitetanus therapy. On the other hand, 74.2 per cent of the tetanus patients who received the conventional antitetanus therapy without AA (control group) were succumbed to the infection. In the other age group of 13-30 years, there were 27 and 38 patients in the treatment and control groups respectively. The mortality in the AA and control groups were 37 percent and 67.8 percent respectively.

These results suggest that AA might play an important role in reducing the mortality of tetanus. This was supported by the fact that AA was found to mitigate the toxic effects of strychnine producing tetanus like condition in young chicks in the present study.

### INTRODUCTION

While tetanus is no longer a problem in advanced countries as almost every body is immunised, it has remained a dreaded disease and a major killer in countries like Bangladesh. The neonatal death rate due to tetanus is estimated to be 24.05 per thousand live births and accounts for 26.20 per cent of all infant deaths (Islam, 1983). Considerable cases are also seen in older children and adults arising out of injuries while playing or working in the fields. There are incidents of the disease due to circumcision or surgical procedures where sterile condition is not maintained. However, the mortality of tetanus is high in rural areas where adequate treatment is hardly available. Even in the urban hospitals, mortality due to tetanus neonatorum is believed to be 80 to 90 per cent and in adult cases it is over 60 per cent (Infectious Disease Hospital Record, 1983). The conventional antitetanus therapy includes antitetanus serum, sedatives, antibiotics, muscle relaxant and sometimes steroids. But the role of AA in the therapy of tetanus has not been previously investigated.

It has been observed that  $\beta$ -N- $\beta$  oxalyl diaminopropionic acid (ODAP) isolated from lathyrus sativus (known as Khesari in local language) (Rao et al. 1964) was found responsible for neurolathyrism (Sarma and Padmaban, 1969). It was also observed that

in both tetanus and in neurolathyrism some common characteristics such as spastic paralysis and neuroexcitation are seen. Both ODAP and tetanus toxin find their way to the central nervous system (CNS) to get themselves attached to the synaptosomes (Lakshmanan and Padmanaban, 1977). Glutamic acid also under certain circumstances has been found to affect the CNS in the way ODAP does (Olney et al. 1976). Both ODAP and glutamate are considered to have common receptors (Lakshmanan and Padmanaban, 1977). It was found that biological effect of ODAP as well as glutamate was related to the serum level of AA and in fact both neurolathyrism and glutamate toxicity could be prevented by administration of AA (Ahmad and Jahan, 1983).

On the basis of the above fact, it was considered that AA might have some beneficial effects in the treatment of tetanus. The present study was therefore, undertaken to validate the above concept.

## MATERIALS AND METHODS

A total number of 117 tetanus patients admitted into the Infectious Disease Hospital, Mohakhali, Dhaka were studied. They were divided into two different age groups. In the age group of 1-12 years, there were 31 patients in the treatment group who received 1000 mg. AA daily in addition to conventional antitetanus therapy which included antitetanus serum, sedatives, antibiotics and muscle relaxant etc. There were also 31 patients in the similar age groups who received only the conventional antitetanus therapy but no AA and this group served as control. In the other age group of 13-30 years, there were 27 and 28 patients in the treatment and control groups respectively and they were treated in a similar manner as in the age group of 1-12 years.

In view of the recognised similarity between the mode of action of tetanus toxin and strychnine, (Heyningen et al, 1971) an animal experiment was conducted in the Institute of Nutrition and Food Science, University of Dhaka to investigate whether AA could mitigate the toxicity induced by strychnine. Two-days old chicks weighing 32-35 gm were divided into four groups with 15 birds in each group. Birds of group I were received 5  $\mu$ g of strychnine sulphate only and those of in group II received strychnine sulphate in the same dosage along with 30 mg AA 10 minutes before strychnine. Birds of group III were administered strychnine in a higher dosage of 10  $\mu$ g only and the group-IV received both strychnine (10  $\mu$ g) and AA 30 mg. Both the drugs were administered intraperitoneally in aqueous solutions.

## RESULTS

The effect of AA in the treatment of tetanus was shown in Table I. In the age group of 1-12 years, there was no mortality in patients who received 1000 mg AA daily (i.v.) in addition to conventional antitetanus therapy. On the other hand, in

the control group i.e. the patients who had not received AA along with antitetanus therapy, the mortality rate was 74.2 per cent (Table-I). In another age group of 13-30 years, addition of AA to the conventional antitetanus regimen caused a marked reduction in the mortality. In the treatment group (i.e. patients that received both AA and antitetanus therapy), the mortality was only 37 percent as opposed to 67.8 per cent in patients who had not received AA (Table-I).

The results of animal experiments are shown in Table-II. Administration of AA protected the chicks from strychnine toxicity and the chicks who received AA and strychnine did not develop the signs of strychnine toxicity indicating that AA mitigated the same.

Table-I Studies on the effect of daily administration of (i.v.) of 1000 mg of AA as supplement to conventional treatment on the recovery of tetanus patients.

Age group (years)	Patients receiving ascorbic acid			Patients not receiving ascorbic acid		
	No. of patients	Patients that recovered	Mortality	No. of patients	Patients that recovered	Mortality (Percentage)
1-12	31	31	00%	31	8	74.2
13-30	27	17	37%	28	9	67.8

Table II—Effect of AA on the toxicity of strychnine sulphate (SS) in chicks

Groups	Dose of SS per chick ( $\mu$ g)	Dose of AA per chick (mg)	Observation
I	5	—	Wings of all birds stretched. Some walked on toes, other kept jumping and they could not walk.
II	5	30	No symptoms.
III	10	—	Extensor paralysis of legs, opisthotonus and severe convulsion. All but three died.
IV	10	30	Extensor paralysis in 3 chicks. No neurological symptoms in others. The affected birds recovered in about 30 minutes after the appearance of the symptoms.

The number of birds were 15 in each group.

## DISCUSSION

The results of the present study indicate that AA acts in some way to mitigate the toxicity of tetanus toxin so that in the age groups of 1-12 years none of the patient receiving AA succumbed to the toxinosis of tetanus as opposed to the corresponding control groups. In the another age group of 13-30 years, although some succumbed but there was substantial reduction in mortality due to the addition of AA. Even though several variable such as site injury, status of infection before start of treatment nutritional status of the patients and exposure to risks of secondary infection must also have acted as determinants of mortality amongst tetanus patients, the beneficial effect of AA as seen in this study appears significant.

During the course of study, it was noticed that patients succumbed to tetanus even three to four weeks after admission. This is contrary to the literature report that death if it occurs follows relatively soon after the appearance of symptoms, the dictum of Hippocrates, such persons as are seized with tetanus die within four days or if they pass those they recover, still stands (cited by Burrows, 1968). In many instances it would appear that these patients had almost recovered when fresh wave of convulsions would overtake bringing the end.

The studies on human patients of tetanus and the studies on strychnine toxinosis in chicks indicate that AA interacts with tetanus toxin as well as strychnine to reduce their toxic effect although the mechanism of this interaction is yet to be understood.

## ACKNOWLEDGEMENTS

The authors acknowledge the cooperation and management of the clinicians of the Infectious Disease Hospital during the course of this study. The authors are also thankful to Professor Nurul Islam, Director and Professor of Medicine, Institute of Postgraduate Medicine and Research, Dhaka for encouragements.

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