A Study of Blood Ascorbic Acid in Leprosy[1]

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The importance of ascorbic acid (vitamin C) in a wide variety of clinical conditions has been emphasized in recent years ([1, 5]). It is reported that deficiency of ascorbic acid delays, and supplementation of it accelerates, the healing of pressure sores ([3, 9]). Trophic ulcer is one of the most serious complications of leprosy and also one of the chief causes for the social ostracism. As early as 1939, Conception, *et al.* ([2]) found low blood levels of ascorbic acid in leprosy patients and noted that intramuscular injection of the vitamin elevated the blood levels of ascorbate. Shionuma and Haruyama ([6]) reported a marked decrease in vitamin C in the aqueous humor in lepromatous cases. In two patients with secondary cataracts, the vitamin was absent or only a trace was found.

In view of the reported significance of ascorbic acid in infections and wound healing and the relative lack of recent study on this subject as it pertains to leprosy, the present work was undertaken to study a) the basal level of blood ascorbic acid in polar leprosy cases, b) the effect of dapsone (DDS) therapy on this level, and c) the effect of supplemental ascorbic acid therapy in the healing of trophic ulcers.

MATERIALS AND METHODS

Seventy cases with polar leprosy were selected from the leprosy wing of the S.R.N. Hospital in Allahabad, India. These cases were not associated with pyogenic bacterial and viral infections, diabetes mellitus, liver and gastrointestinal tract diseases, or respiratory and renal ailments.

Lepromatous leprosy (LL) cases. a) Twelve untreated patients, b) 15 cases on DDS therapy without erythema nodosum leprosum (ENL) attacks, c) 8 cases on DDS therapy with ENL attacks, and d) 8 cases on DDS therapy with trophic ulcers who were given supplemental treatment with 500 mg ascorbic acid daily for 60 days were studied.

Tuberculoid leprosy (TT) cases. a) Twelve untreated cases and b) 15 cases on DDS therapy were studied.

Controls. Twenty-five apparently healthy individuals from the same socio-economic status, relatives of patients living under similar conditions, were used as the control group.

Blood samples for ascorbic acid determinations were collected under fasting conditions. Ascorbic acid was determined by the colorimetric method of Roe and Kuether as described by Varley ([10]).

RESULTS AND DISCUSSION

The basal level of blood ascorbic acid was found to be significantly reduced in the lepromatous as well as tuberculoid leprosy patients compared to the control group (The Table). Interestingly, the level was found to be more reduced in the tuberculoid cases than in the lepromatous patients. The difference between untreated cases of both these forms of leprosy was statistically highly significant ($p < 0.001$). Practically no difference was observed between lepromatous cases with and without ENL attacks. No significant difference was found between untreated and treated cases of either the lepromatous or tuberculoid forms of leprosy. From these observations it is evident that there is a deficiency of ascorbic acid in leprosy patients and DDS therapy does not change its status. It is not clear whether the low level of ascorbic acid in leprosy patients is due to the adverse effect of the disease or

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THE TABLE. *Blood ascorbic acid levels (mg/100 ml) in different groups of leprosy patients.*

Group	No.	Ascorbic acid mean ± S.D. (range)
Controls	25	0.63 ± 0.20 (0.41–1.11)
Lepromatous		
Untreated	12	0.36 ± 0.05[a] (0.27–0.46)
Treated, without ENL	15	0.30 ± 0.15[a] (0.10–0.54)
Treated, with ENL	8	0.23 ± 0.13[a] (0.12–0.46)
Treated, with trophic ulcer	8	0.32 ± 0.12[a] (0.13–0.54)
Trophic ulcer cases after ascorbic acid treatment	8	0.59 ± 0.15 (0.36–0.83)
Tuberculoid		
Untreated	12	0.22 ± 0.07[a] (0.12–0.33)
Treated	15	0.17 ± 0.09[a] (0.10–0.35)

[a] $p < 0.001$, Student's *t* test, compared with controls.

is associated with nutritional factors. Nutritional factors in general have been found to be partially responsible for the deficiency of vitamin C in a number of known clinical conditions. Moreover, it has long been noted that the prevalence of leprosy diminishes with a rising standard of living. Some workers ([8]) presumed that increased vitamin C availability with improved nutritional status under these circumstances may have been an influencing factor. The leprosy patients studied generally belonged to such a socio-economic level that nutritional factors were more likely to be responsible for the low level of ascorbic acid. However, the disease may also be responsible for the deficiency of ascorbic acid because it is known that increased losses of vitamin C accompany infections and fevers, and the vitamin plays a role in the reaction of the body to stress.

In cases with trophic ulcers, after supplementary treatment with 500 mg of ascorbic acid daily for 60 days, the ascorbic acid level was found to be close to that of the control group. A marked improvement in the healing of ulcers was also observed clinically. This suggests that supplementation with ascorbic acid raises its level and provides a beneficial effect on the healing process.

Dunphy, *et al.* ([3]) and Taylor, *et al.* ([9]) have reported that deficiency of ascorbic acid delays, and supplementation with ascorbic acid accelerates, the healing of pressure sores. They reported that the basic defect of repair in ascorbic acid deficiency appears to be one of collagen synthesis. Ascorbic acid is known for its specific role in collagen synthesis with special reference to the synthesis of hydroxyproline from a proline precursor. They presented evidence that this defect is corrected within 24 hours following the intramuscular administration of ascorbic acid.

Skinsnes and Matsuo ([8]) reported a marked regression and localization of *Mycobacterium lepraemurium* infections in mice by the administration of high doses of vitamin C. They also studied a single case of lepromatous leprosy receiving 1.5 gm of vitamin C per day without concomitant specific leprosy therapy and observed remarkable histopathologic evidence of lesion regression in 4.5 months. Matsuo, *et al.* ([4]) also reported growth suppression of *M. leprae* by ascorbic acid therapy. These reports corroborate our observation that ascorbic acid supplementation accelerates the healing of trophic ulcers. However, the positive role of ascorbic acid in the early healing of ulcers should not be overemphasized from the present study of only a few cases. A detailed investigation is warranted.

In our previous work ([7]) we reported that blood lactic and pyruvic acid levels were significantly raised in polar leprosy. The increase in lactic acid was suggested to be due to infectious conditions, and the increase in pyruvic acid probably was due to thiamine deficiency. DDS therapy was found to cause further increases in these acids, indicating that DDS somehow disturbs lactate and pyruvate metabolism, the mechanism of which is not clear. In our present work, these acids were also measured along with ascorbic acid and our findings were the same as reported earlier. An interesting observation was made from our present study regarding the effect of ascorbic acid supplementation on blood lactic and pyruvic acids. In trophic ulcer cases, these acids were significantly raised but after supplemental ascorbic acid therapy their values became close to the control value. This clearly indicates that ascorbic acid therapy plays a role in controlling the conditions responsible for the rise of lactic

and pyruvic acids, such as infection and possibly thiamine deficiency. This also indicates that the disturbance caused by DDS on lactate and pyruvate metabolism was also somehow checked. On the basis of these observations, it was felt that supplemental ascorbic acid might prove effective in controlling some of the known toxic effects of DDS therapy. Our present study suggests that the supplement of ascorbic acid with DDS may have a beneficial effect on the general condition of leprosy patients and on the healing of trophic ulcers.

SUMMARY

The basal level of blood ascorbic acid was studied in 70 cases of polar leprosy. The level was found to be significantly reduced in both polar types, more so in tuberculoid. In untreated cases of these two polar forms, the differences were highly significant. No significant differences were found between untreated and treated cases of either form of leprosy, indicating that dapsone (DDS) has no effect on the ascorbic acid level. In lepromatous leprosy, the level was not affected by erythema nodosum leprosum (ENL). The deficiency of ascorbic acid in leprosy might be due to the disease per se and/or associated with nutritional factors. In trophic ulcers after supplement therapy for 60 days, the low level of ascorbic acid became close to the control group with marked improvement in the healing of the ulcers clinically.

In addition, lactic and pyruvic acids were also measured and found to be significantly raised. After ascorbic acid supplement, the levels fell to near the control values, indicating that ascorbic acid played a role in controlling the infection as well as possible thiamine deficiency and also checked the disturbance caused by DDS on lactate and pyruvate metabolism. The present study suggested that supplementing DDS therapy with ascorbic acid might provide a beneficial effect on the general condition of the leprosy patients and the early healing of trophic ulcers.

RESUMEN

Se estudió el nivel basal de ácido ascórbico en la sangre de 70 casos de lepra polar. El nivel basal se encontró significativamente disminuído en ambos tipos polares, pero más en el tuberculoide. Las diferencias entre los casos polares no tratados fueron altamente significativas pero no hubieron diferencias importantes cuando se compararon los pacientes tratados con los no tratados dentro de cada forma de lepra. Esto indica que la dapsona (DDS) no tiene efecto sobre el nivel del ácido ascórbico. En la lepra lepromatosa, el nivel no fue afectado por el eritema nodoso leproso (ENL). La deficiencia de ácido ascórbico en la lepra puede ser debida a la enfermedad per se, puede estar asociada a factores nutricionales, o pueden suceder ambas cosas. Los niveles de ácido ascórbico en los casos con úlceras tróficas tratados por 60 días con terapia suplementaria llegaron a ser similares a los del grupo control y ésto correlacionó con una marcada mejoría clínica de las úlceras.

También se encontraron significativamente elevados los niveles de los ácidos láctico y pirúvico. Después del suplemento con ácido ascórbico, los niveles de estos ácidos decayeron a valores cercanos a lo normal. Esto indica que el ácido ascórbico además de controlar el posible efecto del DDS sobre el metabolismo del lactato y del piruvato, participa de alguna manera controlando la infección y la posible deficiencia en tiamina. El presente estudio sugiere que suplementando con ácido ascórbico la terapia con DDS se puede propiciar un efecto benéfico sobre las condiciones generales de los pacientes con lepra y una curación más temprana de las úlceras tróficas.

RÉSUMÉ

Chez 70 malades atteints de lèpre polaire, on a étudié les niveaux de base de l'acide ascorbique dans le sang. On a observé que ce niveau était significativement réduit dans les deux types polaires, mais encore davantage dans le type tuberculoide. Dans les cas atteints de ces deux formes polaires, mais non traités les différences étaient fortement significatives. Aucune différence significative n'a été relevée entre les cas traités et non traités, et ceci quelle que soit la forme de lèpre. Cela indique que la dapsone (DDS) n'a pas d'effet sur le niveau d'acide ascorbique. Dans la lèpre lépromateuse, le niveau n'était pas affecté par l'érythème noueux lépreux (ENL). La carence en acide ascorbique dans la lèpre peut être du à la maladie en soi, ou bien être associée avec des facteurs nutritionnels, les deux causes pouvant se combiner. Dans les ulcères trophiques, le faible niveau d'acide ascorbique revient, après une thérapeutique de 60 jours, à des tau qui se rapprochent de ceux du groupe témoin, ceci étant accompagné par une amélioration dans la guérison clinique de ces ulcères.

On a, de plus, mesuré les niveaux d'acide lactiques et pyruvique, qui se sont révélé significativement élevés. Après une thérapeutique par l'acide ascorbique, ces taux sont retombés à des niveaux proches de ceux observés chez les témoins, ce qui indique que l'acide ascorbique joue un rôle dans le contrôle de l'infection, tout autant qu'une carence éventuelle en thiamine; l'acide ascorbique contrôle également les troubles causés par la DDS sur le métabolisme du lactate et du pyru-

vate. Cette étude suggère qu'en additionnant de l'acide ascorbique à la thérapeutique par la DDS, on peut obtenir un effet bénéfique sur la condition générale des malades de la lèpre et sur la guérison précoce des ulcères trophiques.

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