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Effect of Dapsone on Blood Lactic and Pyruvic Acids in Leprosy[1]

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Lactic and pyruvic acids are the two principal products of carbohydrate metabolism. Pyruvic acid is of major importance since it is further metabolized and provides energy for vital activities. The effect of leprosy on these important metabolites has not been well studied. Dapsone (DDS) is widely used in the treatment of this disease. Since leprosy involves various organs and their metabolic processes, the present work was undertaken to study the effect of leprosy and DDS therapy on the basal levels of blood lactic and pyruvic acids.

MATERIALS AND METHODS

Eighty-seven cases of lepromatous (LL) and 80 cases of tuberculoid (TT) leprosy were studied for basal levels of blood lactic and pyruvic acids. Out of 87 LL patients, 19 were untreated and 68 had had treatment with DDS for different durations. Similarly, in the TT group, 24 cases were untreated and 56 had had treatment. As controls, 30 apparently healthy subjects from the same socioeconomic status were also studied.

Blood lactic acid was determined by the colorimetric method of Barker and Summerson ([1]) and pyruvic acid by the method of Friedmann and Haugen ([3]). The blood samples were drawn under fasting conditions.

RESULTS

Lactic acid was found to be significantly raised in untreated cases of lepromatous as well as tuberculoid leprosy. The increase of lactic acid in tuberculoid cases was found to be relatively more than in lepromatous cases. In treated cases, lactic acid values showed a further increasing trend with the duration of therapy in lepromatous cases but not in tuberculoid cases (The Table). The differences in lactic acid levels between untreated and treated cases of each group were not statistically significant.

Pyruvic acid was also found to be raised in untreated cases of both these forms of leprosy. The increase was more marked in lepromatous leprosy and the values indicated a mild increase with the duration of the disease in this group. A further increase in pyruvic acid was found in both lepromatous and tuberculoid cases treated with DDS, but the values showed an increasing trend with the duration of therapy only in lepromatous cases.

DISCUSSION

Leprosy affects lactate and pyruvate metabolism. The blood levels of both these acids are significantly raised in untreated cases of lepromatous as well as tuberculoid leprosy. An increasing trend with the duration of the disease was seen in the lepromatous cases. Normally, in glycolysis, pyruvic acid is formed mainly under aerobic conditions, and lactic acid under anaerobic conditions. The simultaneous increase of both the metabolites in the present study indicates that the cause of their increase is independent of each other. The increase of lactic acid seems to be due to cellular hypoxia in leprosy. Interestingly, the increase of lactic acid in untreated tuberculoid cases was found to be slightly more than in untreated lepromatous cases, although the latter type of the disease is more severe and progressive. The reason for this is not clear. The data seem to suggest that in tuberculoid leprosy anaerobic conditions are more dominant. Lactic acid was also found to be

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THE TABLE. *Blood lactic acid and pyruvic acid in leprosy.*

Group	No. of cases	Lactic acid (Mean ± S.D. mg percent)	Pyruvic acid (Mean ± S.D. mg percent)
Healthy controls	30	8.53 ± 1.47	0.85 ± 0.14
Lepromatous			
Untreated			
<2 yr	7	10.44 ± 1.66[a]	1.15 ± 0.14[b]
2–4 yr	6	11.38 ± 1.63[b]	1.23 ± 0.09[b]
>4 yr	6	12.44 ± 1.19[b]	1.33 ± 0.10[b]
Treated			
<2 yr	23	10.86 ± 1.63[b]	1.35 ± 0.26[b]
2–4 yr	19	11.81 ± 2.0[b]	1.59 ± 0.24[b]
>4 yr	26	12.68 ± 1.85[b]	1.68 ± 0.28[b]
Tuberculoid			
Untreated			
<2 yr	10	11.52 ± 0.63[b]	1.00 ± 0.06[a]
2–4 yr	9	12.71 ± 1.13[b]	1.05 ± 0.08[b]
>4 yr	5	13.64 ± 1.87[b]	1.08 ± 0.09[a]
Treated			
<2 yr	24	11.75 ± 1.30[b]	1.12 ± 0.20[b]
2–4 yr	17	12.18 ± 1.79[b]	1.41 ± 0.18[b]
>4 yr	15	12.41 ± 2.46[b]	1.42 ± 0.18[b]

[a] $p < 0.01$, Student's t test, compared to healthy control subjects.
[b] $p < 0.001$, Student's t test, compared to healthy control subjects.

raised in treated cases of both forms of leprosy. The differences observed between untreated and treated cases of each group were not statistically significant, suggesting that DDS therapy was not effective in controlling the conditions responsible for the abnormal increases in lactic acid in leprosy.

Pyruvic acid was also found to be significantly raised in both forms of leprosy, although the increases were more marked in lepromatous cases. The higher bacterial loads and their metabolic activity in lepromatous leprosy could perhaps be responsible for this difference. The significant increase of pyruvic acid is suggestive of thiamine deficiency ([2]), but this cannot be said with certainty unless thiamine is measured directly. It is well known that in thiamine deficiency, the conversion of pyruvic acid to acetyl coenzyme A is hampered, resulting in the accumulation of pyruvic acid. Moreover, pyruvate is also formed by other metabolic pathways besides glycolysis which are concerned with the process of gluconeogenesis, transamination, and deamination. It is quite possible that these metabolic processes are also affected in leprosy, resulting in pyruvic acid.

A further increase of pyruvic acid was observed in both forms of leprosy treated with DDS. The values showed an increasing trend with the duration of therapy in lepromatous cases. Bharadwaj, *et al.* ([2]) in their study of the effect of DDS on blood lactic and pyruvic acids in lepromatous cases, with and without neuritis, also observed increases in pyruvic acid after DDS therapy. These observations clearly show that DDS brings about a derangement of pyruvate metabolism. It is not clear whether DDS creates a further deficiency of thiamine or affects pyruvate balance in some other way. Williams and Bradley ([4]) studied the enzymes of the glycolytic pathway, i.e., glucose-6-phosphate dehydrogenase, phosphofructokinase, pyruvate kinase and aldolase, in guinea pigs on toxic doses of DDS and found the levels of these enzymes to be within normal limits. These observations suggest that the production of pyruvate was normal and the abnormal, increased levels of pyruvate after DDS therapy could be explained only if there occurred a disturbance beyond pyruvate production. An elaborate study of the various related metabolic pathways is obviously needed to understand the underlying mechanism of the deranged pyruvate metabolism caused by DDS.

The clinical manifestations of the progressive accumulation of lactic and pyruvic acids in leprosy patients are also not well studied. One of the effects may be the general weakness usually felt by leprosy patients in spite of a normal diet. It may be that pyruvate, which is normally metabolized and serves as a source of energy in the body, is not being utilized at a normal rate in leprosy patients. It is also not clear whether some of the reported DDS toxicities are caused by the drug itself or are the result of the adverse effects of accumulated lactic and pyruvic acids.

SUMMARY

The effect of leprosy and dapsone (DDS) on the basal levels of blood lactic and pyruvic acids has been studied. In untreated tuberculoid and lepromatous leprosy patients both of the acids were found to be significantly raised. The rise in lactic acid was relatively more in tuberculoid patients; whereas pyruvic was relatively more elevated in lepromatous cases. Both the acids showed a tendency to increase with the duration of the disease in lepromatous leprosy. Statistically no significant differences were observed in lactic acid levels between untreated and treated cases of both forms of leprosy, suggesting that DDS was not effective in controlling the conditions responsible for the increased lactic acid. On the other hand, pyruvic acid showed a further increase in cases who were on DDS therapy, particularly in lepromatous cases. This indicated that DDS affects pyruvic acid metabolism. Whether DDS disturbs the normal degradative pathway of pyruvic acid or affects pathways of pyruvic acid production is not clear.

RESUMEN

Se estudió el efecto de la lepra y la dapsona (DDS) sobre los niveles basales de los ácidos láctico y pirúvico en sangre. Tanto en los pacientes tuberculoides como en los lepromatosos no tratados se encontraron niveles significativamente elevados de ambos ácidos. Sin embargo, mientras que la elevación del ácido láctico fue relativamente mayor en los pacientes tuberculoides, el ácido pirúvico estuvo más elevado en los lepromatosos. Ambos ácidos mostraron una tendencia a incrementar que fue paralela a la duración de la enfermedad cuando ésta fue del tipo lepromatoso. No se encontraron diferencias significativas en los niveles de ácido láctico entre los casos tratados y los no tratados de ambas formas de lepra sugiriendo, que el DDS no tuvo efecto en el control de las condiciones que determinaron el incremento en ácido lático. Por otro lado, el ácido pirúvico mostró un mayor incremento en los casos que estuvieron bajo terapia con DDS, particularmente en los casos lepromatosos. Esto indicó que el DDS afecta el metabolismo del ácido pirúvico. No está claro si el DDS altera el catabolismo o el anabolismo del ácido pirúvico.

RÉSUMÉ

L'action de la lèpre et de la dapsone (DDS) sur les taux de base des acides lactique et pyruvique du sang ont été étudiées. Chez les malades atteints de lèpre lépromateuse tuberculoïde non traitée, on a observé une augmentation significative des taux de l'un et l'autre de ces acides. L'augmentation du taux d'acide lactique était relativement plus prononcée chez les malades tuberculoïdes. Par contre, les taux d'acide pyruvique étaient relativement plus élevés dans les cas de lèpre lépromateuse. On a relevé une tendance à une élévation des taux des deux acides dans la lèpre lépromateuse, en association avec la durée de la maladie. Aucune différence statistiquement significative n'a été observée dans les taux d'acide lactique chez les malades traités et chez les malades non traités, tant dans la forme lépromateuse que dans la forme tuberculoïde, ce qui suggère que la dapsone est dépourvue d'action pour contrôler les conditions qui déterminent l'augmentation du taux d'acide lactique. Par ailleurs, l'acide pyruvique a montré une augmentation plus prononcée dans les cas qui étaient sous traitement à la dapsone, et ceci particulièrement dans les cas lépromateux. Ces résultats indiquent que la dapsone affecte le métabolisme de l'acide pyruvique. Il n'est cependant pas clair si cette action est exercée par le truchement d'une modification dans les voies normales de dégradation de l'acide pyruvique, ou d'une altération des voies de production de cet acide.

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