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# Stable Thiamine Pyrophosphate Solution (Cocarboxylase) in the Treatment of Diabetes

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*A study was made of the evolution of 94 diabetic patients who had been treated with either oral hypoglycaemics substances, insulin or both. Control of the complaint had been unsuccessful.*

*Glycaemic levels were then controled almost completely in less than a year through a pre-established pattern of treatment with stable thiamine pyrophosphate solution (TPP). The oral hypoglycaemic substances or the insulin of the study group were then discontinued or decreased.*

*This article proposes the control of diabetic patients through the use of stable TPP solution instead of oral hypoglycaemic substances or insulin, or for insulin to be reduced. TPP has no negative side-effects, and is essential for the metabolism of carbohydrates. It does not create hypoglycaemia, a cause of ischemia at the cerebral and vascular level.*

## Introduction

Diabetes[1,2,3] is one of Mexico's major health problems, since it is one of the main causes of death. The number of diabetics is now expected to increase following changes in the population pyramid with regard to the over 60s. A second major factor is diet. In recent years the general population has gradually increased its carbohydrate consumption. By constantly stimulating the beta cells in the pancreas, excess carbohydrate consumption causes deficiencies in the continuous secretion of insulin as a response to the frequent presence of glucose in the blood. This is especially so because one cause of hyperglycaemia is the loss of genic expression among these cells, which leads to reduced insulin production.[4,29]

Half the diabetic population develops major complications in the short or long term, specially at cardiovascular and renal levels. The one complication that leads to disablement is proliferative retinopathy which appears within five years of diagnosis. Within 10 years, 50% of diabetic patients develop retinopathy.[5,6]

Control of diabetic patients remains a common clinical problem, as much for insulin-dependents as for non-dependents.

The traditional therapy of oral hyperglycaemic substances and insulin does not control a large number of glycemias, and patients suffer side-effects such as cardiac alterations and insulin resistence.

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## Materials and method

A study was made of 94 diabetic patients who had received treatment at the Instituto de Investigaciones Científicas Hans Selye between January 1986 and November 1988. Both sexes were represented, and ages ranged between 12 and 90. Development of the illness had occurred in different ways.

The main symptoms exhibited by all were asthenia, adynamia, polyuria, polyfagia and polydypsia. Glycaemia levels were recorded before and after treatment.

The dosis of TPP was 3 ml (120 mg), given intramuscularly every day for two weeks, every third day for two weeks, three times a week for a month, and twice a week for the last month. Dosis was modified according to the results.

Patients were given a low (approximately 30% of the total) carbohydrate diet. Glycaemia levels were measured every month, ensuring that patients were fasting, that no insulin was administered before the test, and that oral hypoglycaemic substances were not taken the day before the study. Glycaemia levels were then compared with the original figure, and a progress curve was drawn for each patient. The following parameters were monitored in the group: 1) response time to TPP treatment; 2) duration of complaint; 3) discontinuation or reduction of hypoglycaemic substances and insulin, or both; and 4) glycaemia levels were measured before and after TPP therapy.

## Results

20.21% of the patients studied were insulin-dependent, and 79.79% were non-dependent (table 1).

Patients were divided by age into eight groups in ten-year blocks. More than 85% of patients were over 40 (table 2).

Table 3 shows the development of the complaint. This varies considerably from one month to 35 years. There was a greater incidence of patients with a history of one year.

Table 4 shows patient's response to insulin, with 57.90% discontinuing it altogether and 42.10% reducing the dosage.

Table 5 shows the response to hypoglycaemics substances; 61.33% of patients discontinued hipoglycaemic substances, 14.67% reduced their intake, and 24% followed-no treatment.

Table 6 shows the time of response; 75% of patients had recovered normal glucose levels within two months, and only 3.19% needed a year or more for this process (figure II).

No treatment was given to 19.5% of the study group, and the rest (80.85%) were treated with hypoglycaemic substances or insulin (table 7).

Two weeks after treatment, all patients were found to be assymptomatic. Table 1 shows that glycaemias returned to normal within at most two years and at least one week.

It is evident that glycaemia levels that were close to normal were not seen to decrease to the same extent as those that were higher (figure I).

T-test statistics were performed for glucose before and after treatment. It was shown that there were significant differences, with a 0.05 probability of error.

Glycaemia averages and deviations for before and after treatment were:

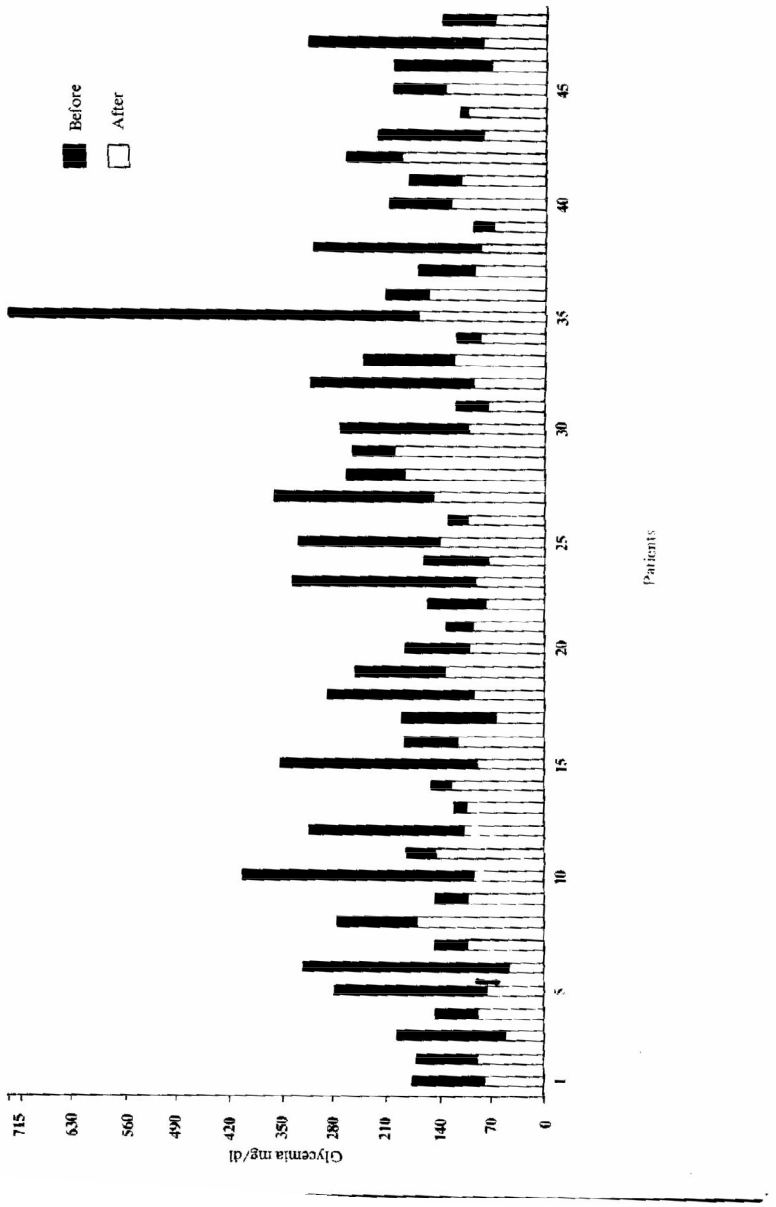
| | Before | After |
|---|---|---|
| Standard | 216.85 | 106.38 |
| Mean | 90.21 | 34.06 |
| Deviation | | |

## Discussion

We know that TPP is a transferase coenzyme (just like PTA). It transports phosphate groups and is an aldehyde group transporter. It is active in the decarboxylation of the alpha-cetoacids,[8,13] which participate in the metabolism of carbohydrates and have a place in the citric acid cycle. TPP unaided promotes the decarboxylation of pyruvic acid, which is the key to intermediate and therefore energy metabolism. Once the decarboxylation of pyruvic acid has occurred, the cycle is in a position to proceed, and produces adenosine triphosphate (ATP).

Diabetic energy process and respiratory rate insufficiencies are due to decreased glucose oxidation. Consequently, when the Krebs cycle operates correctly, energy metabolism improves and the side-effects of diabetes disappear as a result.[14,16] Clinical improvement —disappearance of asthenia,

**FIGURE 1**


Before
After
Glycemia mg/dl
715
630
560
490
420
350
280
210
140
70
0
1
5
10
15
20
25
30
35
40
45
Patients

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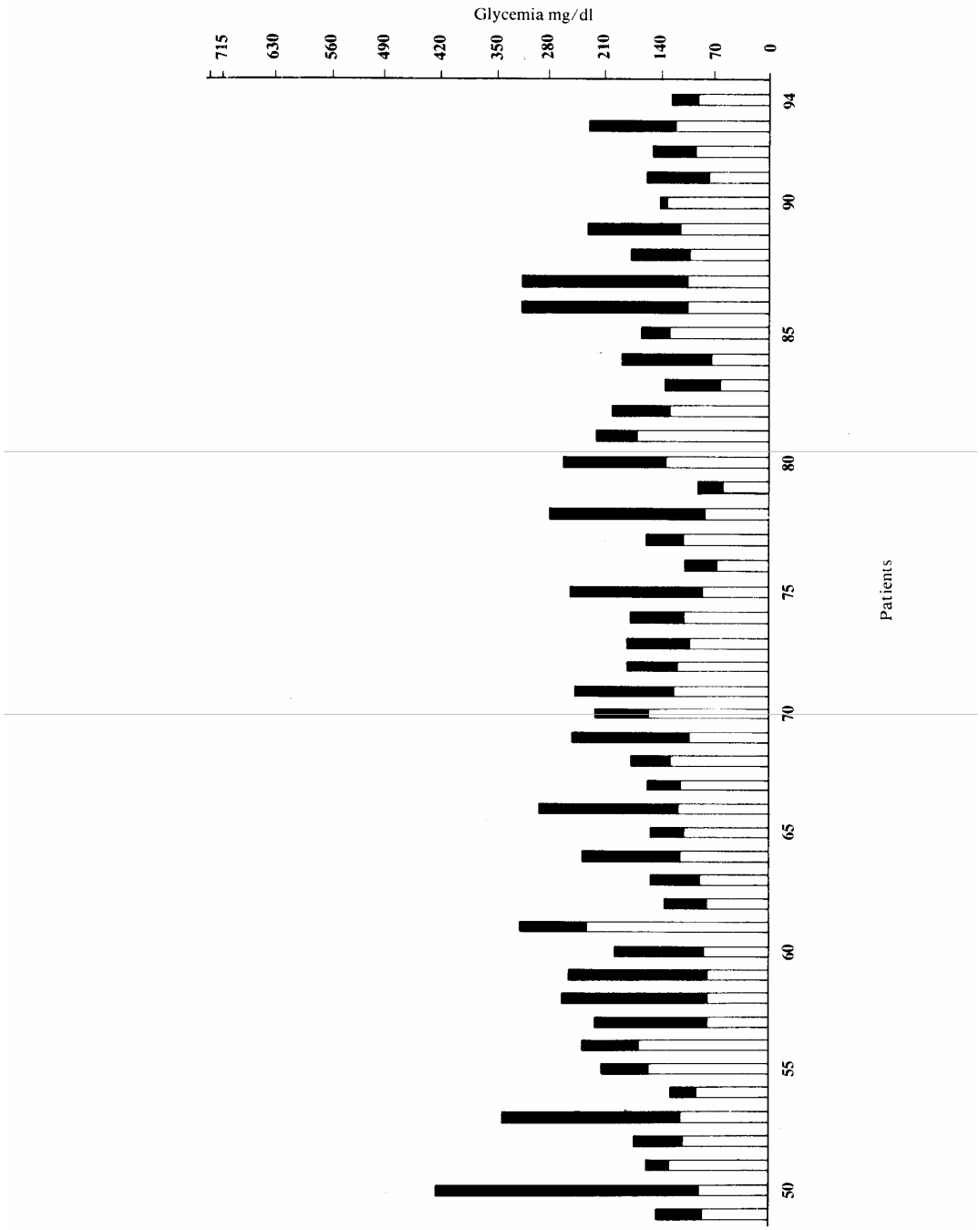
Glycemia mg/dl
715
630
560
490
420
350
280
210
140
70
0
94
90
85
80
75
70
65
60
55
50
Patients

TABLE 1

| Diabetes | Number of cases | % |
|---|---|---|
| Type I | 19 | 20.21 |
| Type II | 75 | 79.79 |
| Total | 94 | 100.00 |

TABLE 2

| Age (years) | Number of cases | % |
|---|---|---|
| 20 | 4 | 4.26 |
| 20-29 | 3 | 3.19 |
| 30-39 | 7 | 7.45 |
| 40-49 | 16 | 17.02 |
| 50-59 | 23 | 24.46 |
| 60-69 | 25 | 26.60 |
| 70-79 | 15 | 17.02 |
| 79 Or over | 1 | 1.06 |
| Total | 94 | 100.00 |

adynamia, polyphagia, polydipsia and polyuria— is noticeable in a considerably short time, indicating a more regular metabolism.

On the strenght of more than 20 years of our clinical experience, and of the observations contained in this paper, the use of our treatment is suggested upon the appearance of diabetic signs and symptoms; whenever there is a family history of diabetics, and in cases of stress (emotional, surgical intervention, infection, and so forth); and as a prophylaxis against the effects of adrenalin on the beta cells in the pancreas.

The use of stable TPP solution is also suggested since it acts directly on the carbohydrate mechanism —the main problem with diabetes— fulfilling its function as a coenzyme. One of the key functions of TPP is the oxydic decarboxylation of pyruvate to acetyl coenzyme A. Without this reaction, pyruvic and lactic acid accumulate. It is active in the pentose cycle, as a co-factor of the transcetolase enzyme. In the Krebs cycle, it is essential for the oxydic decarboxylation of alphacetoglutarate to succinate. It is essential for glycogen synthesis and the transformation of glycids into lipids. It is quite possible that neurological signs occurring due to the lack of the coenzyme may be secondary to disorders of the carbohydrate metabolism or to an insufficient formation of active acetate which is needed for the synthesis of acetylcolin, an indispensable substance for the transmission of nerve impulses at the synapse level. It helps to maintain the normal permeability of nervous tissue membrane. There are 24 enzymes known to contain TPP as a coenzyme.[9,11]

Upon decarboxylating the pyruvic acid, the TPP unblocks the Pasteur effect, and oxydic phosphorylation can proceed. When the oxygen molecule is completely reduced and two molecules of water are formed, the production of free radicals is avoided by accepting the 4 hydrogen molecules from the respiratory chain. These appear when oxygen is partially reduced accepting only two electrons, and the product is hydrogen peroxide. If the oxygen accepts only one electron, the product will be superoxide radical. Both hydrogen peroxide and superoxide attack the

TABLE 3

| Clinical Evolution | Number of cases | % |
|---|---|---|
| 1 month | 7 | 7.45 |
| 2 months | 2 | 2.13 |
| 3 months | 1 | 1.06 |
| 5 months | 2 | 2.13 |
| 7 months | 1 | 1.06 |
| 8 months | 2 | 2.13 |
| 1 year | 11 | 11.70 |
| 1.5 years | 1 | 1.06 |
| 2 years | 5 | 5.32 |
| 3 years | 3 | 3.19 |
| 4 years | 4 | 4.26 |
| 5 years | 3 | 3.19 |
| 6 years | 2 | 2.13 |
| 7 years | 4 | 4.26 |
| 8 years | 1 | 1.06 |
| 9 years | 3 | 3.19 |
| 10 years | 6 | 6.38 |
| 11 years | 3 | 3.19 |
| 12 years | 1 | 1.06 |
| 13 years | 1 | 1.06 |
| 14 years | 3 | 3.19 |
| 15 years | 4 | 4.26 |
| 16 years | 3 | 3.19 |
| 17 years | 3 | 3.19 |
| 18 years | 4 | 4.26 |
| 20 years | 6 | 6.38 |
| 23 years | 1 | 1.06 |
| 24 years | 2 | 2.13 |
| 25 years | 1 | 1.06 |
| 27 years | 1 | 1.06 |
| 28 years | 1 | 1.06 |
| 30 years | 1 | 1.06 |
| 35 years | 1 | 1.06 |
| Total | 94 | 100.00 |

unsaturated fatty acids present in the lipids of the membrane and alter their structure, which makes them toxic to the cell.[18]

Colaterally, when glucose is not kept within normal limits —in diabetes for example— it is not properly metabolised. This creates the conditions for the glucose to act as a free radical and join the protein and hemoglobin and form the advanced glycolization products (AGE). Once these AGE unite with other proteins, they lead to the formation of interlinked chains, to be found in diabetic and senescent patients.[19]

Low carbohydrate diet is suggested in this and similar cases, since one cause of diabetes type 2 is the relative exhaustion of the beta cells in the pancreas. A reduced carbohydrate diet enables the endogenous insulin to reduce the work of these cells. The lower the carbohydrate consumption, the less insulin is secreted.

With therapy bases on TPP and the above diet, the use of exogenous medication is also avoided. In the short and long term, such medications produce side-effects such as the well-known cardiovascular effect caused by hypoglycaemias (The University Group Diabetes Program, 1970).

It is important to note that TPP does not act like a hypoglycaemic substance, as testified by clinical developments and results.

**TABLE 4**

| Diabetes Type I | Number of cases | % |
|---|---|---|
| Discontinued insuline | 11 | 57.90 |
| Disminished insuline intake | 8 | 42.10 |
| **Total** | 19 | 100.00 |

**TABLE 5**

| Diabetes Type II | Number of cases | % |
|---|---|---|
| Discontinued hypoglycemiants | 46 | 61.33 |
| Disminished hypoglycemiants | 11 | 14.67 |
| No pharmacological treatment | 18 | 24.00 |
| **Total** | 75 | 100.00 |

**TABLE 6**

| Time of response to treatment | Number of cases | % |
|---|---|---|
| 1 month | 27 | 28.73 |
| 1 month | 25 | 26.61 |
| 2 months | 19 | 20.21 |
| 3 months | 3 | 3.19 |
| 4 months | 6 | 6.38 |
| 5 months | 5 | 5.32 |
| 6 months | 3 | 3.19 |
| 9 months | 1 | 6.38 |
| 10 months | 1 | 1.06 |
| 11 months | 1 | 1.06 |
| 1 year | 2 | 2.13 |
| 2 years | 1 | 1.06 |
| **Total** | 94 | 100.00 |

**TABLE 7**

| Treatment | Number | % |
|---|---|---|
| Yes | 18 | 19.15 |
| No | 74 | 80.85 |
| **Total** | 94 | 100.00 |

Patients can continue the treatment indefinitely and it will not lead to hypoglycaemia. This treatment has been used with normal subjects, young and old, both as a prophylaxis and in patients with other complaints.

Patients from this study who have not yet attained normal glucose levels have simply not yet been able to suspend their insulin or oral hypoglucemic substances; and upon continuation of the treatment, the same success as that of other patients should be attained (72.34%).

Parallely, another study was made comparing diabetic patients with healthy individuals,[20] *in vivo* and *in vitro*. Research is underway at present into the following studies: 1) the molecular action of TPP on glucose; 2) the study and in-depth diagnosis of diabetic patients and the application of TPP solution; 3) the use of TPP in diabetic rats; and 4) a long-term clinical and experimental study of the prevention and reduction of the complications of diabetes, also using TPP.

Since 1937, the work of Dr. Siliprendi[21] and others[22-28] into the use of TPP in diabetes has been well-known. Results have been good, in spite of using a cocarboxylase that was not stable in solution.

Studies made of a further possible treat-

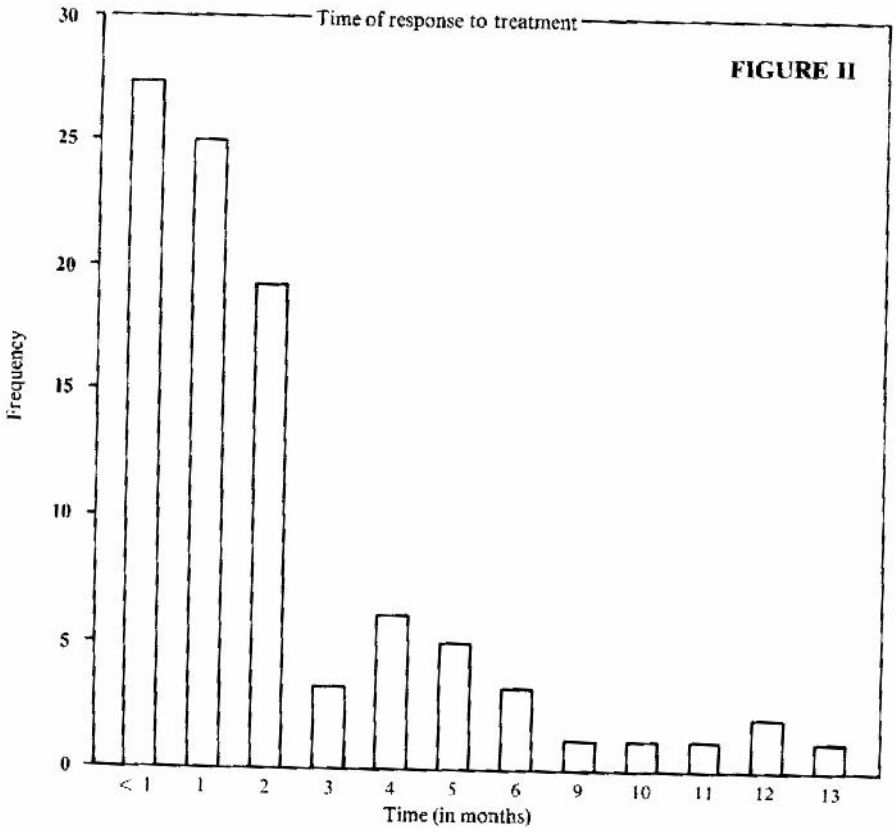


**FIGURE II**

ment for diabetes have even contemplated regulating the genic expression; but with poor results.[29] Likewise, attempts to decrease or prevent complications in the long term have also been unsuccessful, since present treatment does not completely restore the metabolic homeostasis of diabetes.[30-33]

The essential and central biochemical mechanism for the metabolism of carbohydrates has so far been ignored.

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