

# Beneficial Effects of Glycine on Spasticity in the Human

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**Abstract**— The glycine was administered to 50 patients male and female with spasticity diagnosis (caused by vascular disease or traumatic brain injury) with 46 years average, during 360 days. Was determined their weight before and after of treatment, observed an increased of 11% in the corporal weight. The muscular clinic examination showed a significant increased ( $p < 0.05$ ) of 75% in the Ashworth Scale. The dynamic electromyography showed a significant increased ( $p < 0.05$ ) in the motor active units per second in all muscles of superior extremity like biceps before treated an mean  $106.58 \pm 23.11$ , at 360 days the mean was  $229.4 \pm 15.1$ . In lower extremity the anterior tibialis muscle at the start presented a value of  $92.16 \pm 25.01$ , the mean at 360 days was  $180.2 \pm 15.3$ . However, such activity did not reach the values of the negative controls. Was determined glucose, creatinine, cholesterol, triglycerides and seric calcium concentrations and we did not observe significant changes ( $p < 0.05$ ) in the 50 patients. The pH and the urinary density did not present significant changes. It is concluded that glycine has a beneficial effect on muscle mobility, because increase the motor units active of all patients during treatment. In addition, all patients tolerated the doses administered, without undesirable effects.

**Index Terms**— Brain injury, biochemicals analysis, dynamic electromyography, glycine, motor units, spasticity, vascular cerebral event

## 1 INTRODUCTION

Spasticity is an alteration of the descending motor nerve pathways, corticospinal, vestibulospinal, rubrospinal, due to injuries due to craniocerebral trauma, cerebrovascular or cardiovascular disease, degenerative diseases such as multiple sclerosis, the neonatal hypoxia that due to these injuries, occur synaptic degeneration or plastic changes, which can alter the mechanisms controlling the release of the inhibitory neurotransmitter from presynaptic fibers [1], presenting excitability changes in the membrane and release of the excitatory neurotransmitter from input terminals or presynaptic inhibition, which is controlled by GABA inhibitory neurotransmitters and mainly in spinal cord this effect is controlled by glycine, this alteration results in skeletal muscle spasticity [2].

### 1.1 Clinical Diagnostic

Spasticity is a change in muscle tone; the diagnosis is made by clinical history of the patient, by trauma or cerebral hemorrhage and the clinical muscle test, where the muscle movements are diminished or absent.

In this type of patients the muscle tone is increased, characterized by the feeling of resistance when handling the joint range of motion (hyperreflexia and paresis) and with difficulty for muscular relaxation [3].

### 1.2 Electromyography Diagnostic

In an incomplete paralysis the motor unit exhibits normal behavior, the interference pattern is reduced with decreased speed and interruption between potentials of individual motor units. Showing degeneration of the descending motor pathways, recorded in the cells of the anterior horn (Alpha motoneurons), this activity resulting in a reduced number of activities of potentials of motor units in both muscles, agonists and antagonists [4].

### 1.3 Treatment

Pharmacological treatment aims to increase inhibitory effects of 2 important amino acids in the central nervous system through stimulation of receptors for GABA, with baclofen or diazepam, these drugs have the drawback of producing drowsiness, situation in which the patient does not learn physical or occupational therapy, decreasing thus its time recovery [2].

Glycine is a non-essential amino acid, its synthesis takes place in the cytosol of the hepatocyte, which contains glycine-transferase, this enzyme catalyzes the synthesis of glycine to glyoxylate, glutamate and alanine. Glycine is the amino acid with inhibitory neurotransmitter activity, it is located in the gray matter of spinal cord ventral quadrant, also in neurons interlayer spinal [6], studies conducted in marrow of cat and rat, showing two types of alpha and beta receptors, that open channels of chlorine, and its activation resulting in a hyperpolarization [7, 8, 9, 10].

### 1.4 Objective

Evaluate the effect of glycine on the spasticity, caused by cerebral vascular event and traumatic brain injury.

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## 2 MATERIALS AND METHODS

### 2.1 Description

Glycine was administered at dose of 3-4 g/day, was given orally to 50 patients from the National Institute of Rehabilitation (INR), average age 46 years (35 women and 15 men), diagnosed with spasticity (hemiparesis left or right), by cerebrovascular (stroke) source (34 patients), and traumatic brain injury (16 patients), during 360 days, their body weight were determined before and every 3 months during treatment, as well as also was performed dynamic electromyography (electromyography Nicolet, monopolar needle) on the muscles of upper limb deltoid, biceps, triceps, first radial external flexor of right and left hand, and muscles of lower limb as the vast external, tibiae anterior, gastrocnemius, before (control) and every 3 months during treatment. In addition, a healthy control group was formed. The results were analyzed for their statistical significance with Student's t test.

The serum concentration of glucose, creatinine, cholesterol, triglycerides and calcium, were determined before to treatment (control) and then every 3 months in all patients, with the colorimetric method standardized, (photometer 4010 of Lakeside, reagents of Diagnostica Merck), the results were analyzed with the Student's t test to verify their statistical significance.

It was assessed before and after every 3 months of treatment the effect of the administration of glycine on the pH and the density of urine by the standardized method of the Combur<sup>10</sup> Test Strip, the results were analyzed for their statistical significance with the Student's t test.

## 3 RESULTS

### 3.1 Body Weight

The body weight in all patients who were administered glycine increased significantly ( $p < 0.05$ ) at an average of 11.70% in men and 11.75% in women during the 360 days of treatment. It is important to mention that the patients tolerated the doses administered without any side effects during treatment (table 1)

Table 1: Body weight of patients treated with glycine for 360 days

Group	begin Mean±DE	90 days Mean±DE	180 days Mean±DE	270 days Mean±DE	360 days Mean±DE	% increase
Healthy witness (men)	71.5 1.8	72.1 1.1	72.0 1.4	73.3 1.9	74.5 2.2	10.4
Healthy witness (woman)	65.4 1.7	66.1 1.2	65.2 1.3	64.3 1.4	66.1 1.5	10.01
Treatment with glycine (men)	72.2 1.4	75.3 1.9*	79.4 1.4*	79.6 1.3*	84.5 2.2*	11.70
Treatment with glycine (woman)	66.5 1.4	67.3 1.2	72.4 2.1*	74.7 1.8*	78.2 2.1*	11.75

\*Statistically significant difference with respect to the control value, ANOVA and Student's t-tests ( $P=0.05$ ). (men: n = 35) (women n = 15)

### 3.2 Muscle clinical examination (Ashwort Scale)

All patients showed improvement in muscle clinical examination (Ashwort Scale), observing a decrease in the scale. The patients did not present resistance when executing the movements.

In addition, the clonus and hyperreflexia decreased. On the scale, men had an average between  $3 \pm 0.2$  and  $4 \pm 0.5$ , and for 360 days was  $2 \pm 0.4$ . In the group of women, values between  $3 \pm 0.3$  and  $4 \pm 0.3$  were obtained at the start, while at the end of treatment was  $2 \pm 0.2$ . The results showed a significant increase in both groups ( $p < 0.05$ ) of 75% in all patients treated with glycine (both doses). In the activities of daily living, all the patients were more independent. These same results when compared with the negative witnesses, failed to normal levels of 0 on the scale (table No.2).

Table 2. Activities of daily living and dependence in patients treated with glycine

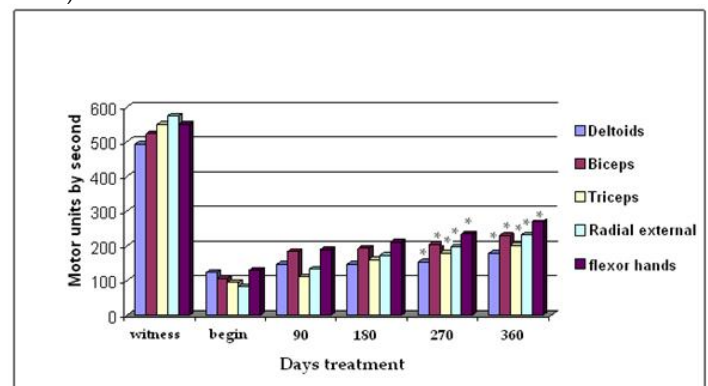
Group	begin	90 days	180 days	270 days	360 days
Healthy witness (control)	0	0	0	0	0
Men treated	3 a 4	3	3 - 2	2 - 1*	2 - 1*
Women treated	3 a 4	3	3 - 2	2 - 1*	2 - 1*

\*Statistically significant difference with respect to the control value, ANOVA and Student's t-tests, ( $P=0.05$ ). (men: n = 35) (women n = 15)

### 3.3 Dynamic Electromyography

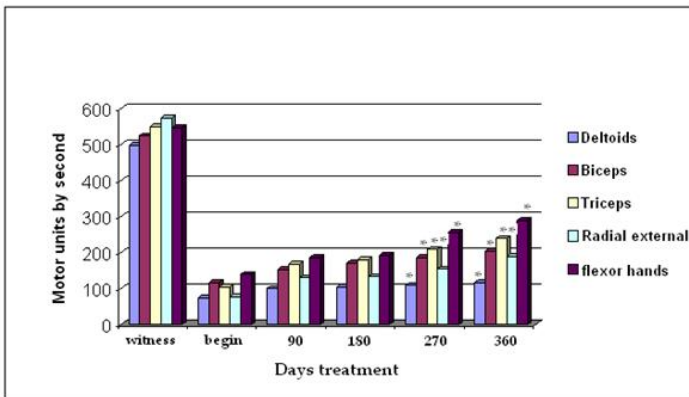
The activity of the motor units per second of deltoid muscle before the treatment presented an average of  $122.8 \pm 17.4$ . At 360 days of the administration of Glycine from the dose of 3 g/day, their average increased significantly ( $p < 0.05$ ) to  $178.5 \pm 13.6$ . At the beginning, the average of the biceps muscle was  $106.58 \pm 23.11$ , at 360 days of treatment the number of motor units increased significantly ( $p < 0.05$ ) to an average of  $229.4 \pm 15.1$ .

The muscles of the lower limb, the anterior tibialis muscles, presented at the beginning an average of  $92.1 \pm 25.0$ , and at 360 days increased significantly ( $p < 0.05$ ) their average to  $180.2 \pm 15.3$  of motor units per second. The gastrocnemius muscles recorded an average  $15.2 \pm 8.3$  before treatment, at 360 days was  $122.4 \pm 15.9$ . The control group presented an average of number of motor units per second of  $494.15 \pm 17.01$  in the deltoid muscle, the biceps muscle recorded an average of  $523.10 \pm 15.47$ . The anterior tibialis muscles of the control group, recorded an average of  $603.84 \pm 23.69$  and the gastrocnemius had an average of  $586.26 \pm 11.31$  (Pictures 1, 2, 3 and 4).

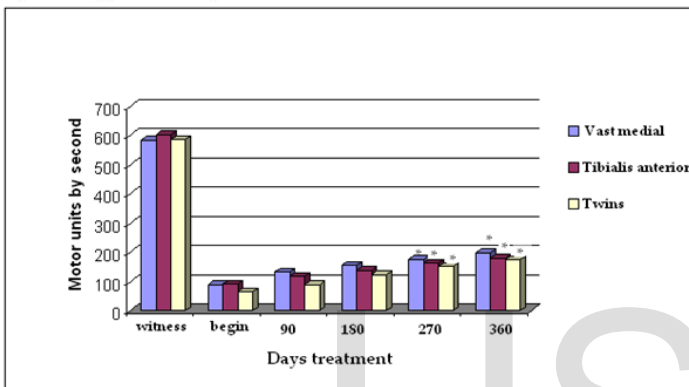


Picture 1. Right upper limb muscle electromyography. The activity of the motor units per second before the treatment and during 360 days of the administration of Glycine.

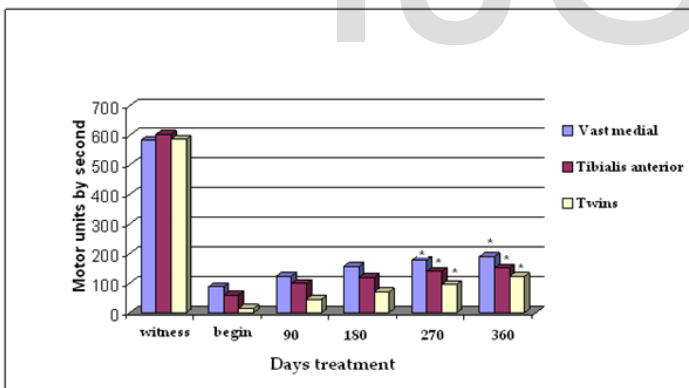
\*Statistically significant difference with respect to the control value, ANOVA and Student's t-tests ( $P=0.05$ ). (men: n = 35) (women n = 15)



**Picture 2.** Left upper limb muscle electromyography. The activity of the motor units per second before the treatment and during 360 days of the administration of Glycine. \*Statistically significant difference with respect to the control value, ANOVA and Student's *t*-tests ( $P=0.05$ ). (men: n = 35) (women n = 15)



**Picture 3.** Member right pelvic muscle electromyography. The activity of the motor units per second before the treatment and during 360 days of the administration of Glycine. \*Statistically significant difference with respect to the control value, ANOVA and Student's *t*-tests ( $P=0.05$ ). (men: n = 35) (women n = 15)



**Picture 4.** Member left pelvic muscle electromyography. The activity of the motor units per second before the treatment and during 360 days of the administration of Glycine. \*Statistically significant difference with respect to the control value, ANOVA and Student's *t*-tests ( $P=0.05$ ). men: n = 35) (women n = 15)

### 3.4 Blood chemistry analysis

Serum glucose: the average initial concentration was  $91.82 \pm 3.22$  mg/dl, at 360 days did not record significant changes ( $p < 0.05$ ) among the patients themselves, the average level was of  $91.4 \pm 2.6$  mg/dL at the end of the treatment. Compared with the values of healthy witnesses with an average of  $82.2 \pm 3.1$  mg/dL, there has been a significant increase, however, the reference values had an average of 60 to 120 mg/dL and the results obtained from the patients were within normal limits.

Serum creatinine: the concentration at the start of treatment was

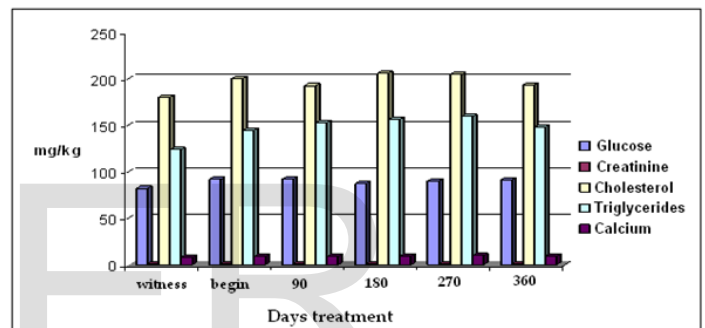
on average of  $1.26 \pm 0.2$  mg/dL, at 360 days of treatment with glycine his average was  $1.02 \pm 0.03$  mg/dL

Serum cholesterol: presented an average value of  $200.2 \pm 12.4$  mg/dl on zero time of treatment and at 360 days was assessed  $193.5 \pm 10.4$  mg/dl, results that were not significant ( $p < 0.05$ ). The control group presented values averages of  $180.2 \pm 11.4$  mg/dl, being less than 250 mg/dl reference values.

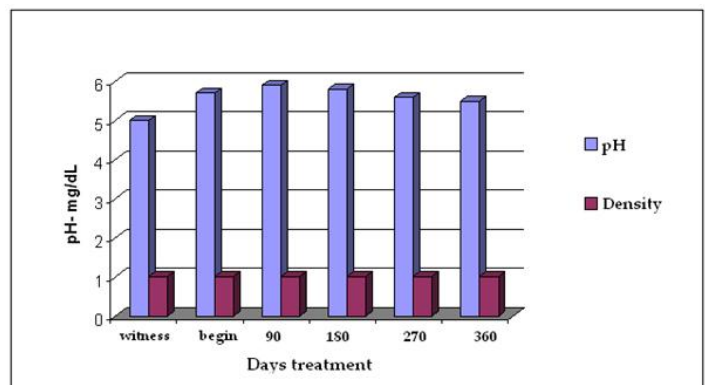
Serum triglycerides: The initial concentration was  $144.6 \pm 12.8$  mg/dL, at 360 days was of  $147.8 \pm 15.5$  mg/dL, data referring us not significant changes ( $p < 0.05$ ). Healthy witnesses' mean values were  $123.8 \pm 14.9$  and the reference value was less than 150 mg/dL.

Serum calcium: their initial mean values were of  $9.0 \pm 0.14$  mg/dL and at 360 was of  $9.1 \pm 0.12$  mg/dL, values that were not significant ( $p < 0.05$ ), healthy witnesses resulted from  $8.2 \pm 0.17$  mg/dL, being baseline of 8.1 to 10.4 mg/dl (Picture No.5).

The density and the urinary pH as they were observed in the graph number 1 did not show significant changes ( $p < 0.05$ ) with regard to the healthy controls (Picture 6).



**Picture 5.** Sanguine chemistry of patients treated with glycine. \*Statistically significant difference with respect to the control value, ANOVA and Student's *t*-tests ( $P < 0.05$ ). (Men n = 35) (Women n = 15)



**Picture 6.** Density urinary and pH of patients treated with glycine. \*Statistically significant difference with respect to the control value, ANOVA and Student's *t*-tests ( $P < 0.05$ ). (Men: n = 35) (Women n = 15)

## 4 DISCUSSION AND CONCLUSION

With regard to body weight, an increase with Glycine was observed from the second administration, study that has not been reported in humans with a diagnosis of spasticity, however, there are studies by Srivastava et al. (1992) [11], where he showed that glycine (250 mg/kg) administered to normal mice with muscular dystrophy increased their body weight. Other research by Fleck (1992) [12], which administered glycine (1 g/kg) to born newly

Wistar rats and adult, they observed that the adult rat presented a greater body weight compared with rat newly born, since glycine is reabsorbed by active transport through the kidneys, the blood concentration of amino acid in adult rats is greater than the newborn rat, at this stage the animals have deficiency in the active transport.

The clinical improvement that the patients presented in muscular clinical examination when administered Glycine from the dose of 3 g/day, to increase mobility, produce less hyperreflexia and decrease in clonus, reducing the hemiplegic of the affected limb. In connection with our results is Nuño et al. (1996) [13], report they showed electromyography records an increase in the activity of the antagonistic muscles in intensity and speed. Other studies by Whesley et al. (1992) [14], in the salamander observed powered higher by managing Glycine, N-methyl-D-aspartate in the records of its walk.

Electromyography showed an increase in the activity of the motor units in both agonist and antagonist muscles of upper left or right and left and right pelvic limb, reflecting thus the clinical improvement that showed patients treated with glycine, this amino acid has been studied and it is known to be released in the spinal cord through the interneuron that inhibit antagonist muscles, causing the output current of chlorine in the synapse (Schwartz et al., 1996) [15].

The results of blood chemistry showed that glycine does not alter these parameters do not increase or decrease its concentration. Above all, a special study was conducted on the concentrations of cholesterol and triglyceride, results showing that those concentrations are not affected, although patients had an increase in weight. It is worth mentioning that there are no previous studies on this research.

With respect to pH and urine density, the amino acid not produced significant changes. There are studies showed that glycine is reabsorbed in the proximal tubule in kidney of rats treated [16, 17]. In addition, there are studies that show the glycine cytoprotective effect when administered together with a substance nephrotoxic as cisplatin, showing that the amino acid increases renal flux.

Glycine to the administered doses was well tolerated by patients, but had to adjust the dose-response concentrations in each of the patients; with respect to the tolerance and toxicity of this amino acid, tests have been conducted to genotoxicity. In studies conducted by Reyes et al. [18], in mice of CD-1 strain, they used doses equal to those used in humans; they reported that glycine is not genotoxic in micronucleus tests and sister chromatid exchange tests.

Therefore it is concluded that glycine exerts beneficial effects on patients who are studying with the diagnosis of spasticity by different etiology, it is suggested to conducting studies using higher doses, to evaluate dose response.

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