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Reference Values for Electrolytes and Blood Gases in Wistar Rats with Permanent Cerebral Ischemia: The Effect of Treatment with Glycine on Gasometry and Electrolytes

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Abstract

Cerebral ischemia is a common neurological condition in people with hypoxia. Glycine is an inhibitory neurotransmitter that could protect neurons from hypoxia-induced toxicity. The aim of this study was to obtain reference values on gasometry and electrolytes and evaluate the effect of treatment with glycine on gasometry and electrolytes in Wistar rats with ischemic brain injury. Fifteen male Wistar rats (mean body weight, 340 g) were randomly allocated to the following three groups: G_0 rats underwent permanent left carotid occlusion and received treatment with a placebo; G_1 rats underwent a permanent left carotid occlusion and received treatment with glycine i.p 40mMol/kg post-surgery; G_2 rats with surgery received treatment with glycine i.p 40mMol/kg 5 days pre-surgery. Blood was obtained by cardiocentesis to determine reference values for electrolytes and blood gases. The results show some major alterations in acid base and electrolytes in G_0, and statistical significance in glucose levels for $G_{1,2}$. Glycine administered to Wistar rats with permanent left carotid occlusion limited changes in the acid base and electrolytes and increased glucose levels from the beginning of the ischemia, initiating brain protection by altering the cascade of events that lead to cellular death.

Keywords: gasometry, electrolytes, ischemia, glycine.

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Valores de referencia de electrolitos y gases en sangre de ratas Wistar con isquemia cerebral permanente: efecto del tratamiento con glicina sobre la gasometría y electrolitos

Resumen

La isquemia cerebral es común en la población que curso por un proceso de hipoxia. La glicina es un neurotransmisor que podría proteger las neuronas de la toxicidad inducida por hipoxia. Los objetivos del estudio consistieron en caracterizar los valores de referencia de electrolitos y gases en sangre de ratas wistar; y establecer la influencia de la glicina sobre la gasometría sanguínea y electrolitos en ratas con isquemia. Quince ratas Wistar (n=15) fueron sometidas a oclusión de la arteria carótida, y asignadas aleatoriamente en igual número a los Grupos 0, 1 y 2. G_0 Tratamiento placebo, G_1 Tratadas con glicina post-cirugía i.p. 40mMol/kg, G_2 Tratadas con glicina 5 días pre-cirugía i.p. 40mMol/kg. La sangre se obtuvo por cardiocentesis para determinar los valores de referencia para electrolitos y gases en sangre. Se detectaron alteraciones importantes en el equilibrio ácido base y electrolitos en el G_0, y significancia estadística en los niveles de glucosa en los $G_{1,2}$. La glicina administrada a ratas Wistar con isquemia cerebral limita los cambios en gasometría y electrolitos, aumentando la glucosa sérica desde el inicio de la isquemia iniciando la protección del cerebro al alterar la cascada de eventos que dan inicio a la muerte celular.

Palabras clave: gasometría, electrolitos, isquemia, glicina.

Introduction

A critical factor in developing a therapeutic strategy against focal ischemic cerebral damage is the therapeutic time window available. Isquemia cerebral is originated by the diminution of the sanguineous flow until a level sufficient to interfere with the function of the nervous system. This decrement is the result of the alteration of the balance of numerous hemodynamics factors and can lead to the appearance, in the neurons and glia, of a concatenated series of metabolic and biochemical alterations that will conclude in necrosis [24].

Now is widely accepted that the brain has an inbuilt ability to recover after such an event; recently, research has focused on the study of long-term recovery after a stroke. To investigate potential mechanisms involved in recovery from stroke, the use of animal models of focal cerebral ischemia, in particular rodent models, is essential [12].

Neuronal ischemia begins as an imbalance between energy supply and demand. The consequence of this energy imbalance is the depletion of ATP, which triggers the onset of numerous ischemia-induced cascades, each of which may lead to irreversible cell injury [14]. Cognitive and sensorimotor impairments are common both in humans and experimental animals [32]. Clinical and animal studies have indicated that cortical ischemia leads to functional impairments that substantially improve during the early period after the insult. It has been suggested that early motor improvement and the severity of chronic deficits are related to lesion size and lesion location [13].

Neurotoxicity of glutamate and other excitatory amino acids is the result of excessive activation of postsynaptic N-methyl-D-aspartate (NMDA) receptors [10]. Activation of NMDA receptors by glutamate, in particular, lead to a cellular influx of calcium ions. Concurrent activation of α-amino- 3-hydroxy-5-methyl-4-isoxazolepropionate receptors facilitates the incorporation of sodium ions into the cell. Intracellular accumulations of both ions give rise to edema and neuronal necrosis. A key factor in recognizing the importance of excitatory amino acids is the therapeutic potential of reducing neuronal injury by use of

drugs that antagonize the transmission of these amino acids [1].

Glycine is the simplest amino acid, with just an amino group, a carboxyl group, and two hydrogen atoms all bound to one carbon atom. Is taken up by cells via a variety of glycine transporters; typically by a secondary active transport coupled to hydrogen, sodium and/or chloride ion uptake [31]. In adition to its fundamental role in metabolism, glycine is an inhibitory neurotransmitter in the adult central nervous system (in the brainstem and spinal cord), and it also plays a critical role as a modulator of NMDA receptors. Glycine protected neurons from hypoxia-induced toxicity in cortical neuron cultures. Recently, several antagonists at the glycine site of the NMDA receptor have been developed, and their neuro protective effect was reported in an experimental stroke [7, 8]. Recently was determined that in experimental animals a low dose of glycine triggers a protective mechanism against ischemia in various tissues [19].

In normal conditions, receivers NMDA are implied in processes of synaptic plasticity, learning and memory, but an excess of ionic calcium (Ca^{2+}) intracellular, caused by hyperstimulation of the receiver, can be excitotoxic and to inhibit the maturation of the neurons developing [20]. Today, blood samples are taken from guinea pigs under anesthesia in order to help immobilize them and minimize stress, guaranteeing more reliable results, especially when working with blood gas samples [18]. Measurement, knowledge and interpretation of blood gas are complemented with electrolyte, glucose, lactate and hematocrit values providing essential clinical information on the state of the patient and can help clinicians and investigators in evaluation, handling and care of the patient in order to make therapeutic decisions and avoid putting the patient animals under study at risk [26]. The objectives of this study was to establish the reference values of electrolytes and blood gases of wistar rats and to determine the effect of treatment with gycine on gasometry and electrolytes in permanent cerebral ischemia of wistar rats.

Materials and methods

Fifteen male Wistar rats of 60 days old were used. They were fed with a standard chow diet (Purina, México City) and drink water *ad libitum*. The animals were maintained under controlled conditions at a temperature of 25°C, relative humidity of 40% and photoperiodicity of a 12-h light-dark cycle, with the light on at 08:00 h. The rats were housed in acrylic cages with five animals per cage until they were treated with each experimental condition. The use of animals for all experiments was approved by the Research Committee of the National Institute of Rehabilitation, SSA México. The rats were treated according to the Guide for the Care and Use of Experimental Animals [17]. And fulfilling with NOM-062-ZOO-2001 [16] which refers to techniques for the production, care and use of laboratory animals.

The rats were divided into three groups: Occlusion of the left common carotid artery (OCC) was performed to animals in all groups. Animals in G_0: Rats (n = 5) They don't received any drug for treatment or pretreatment. G_1: Rats (n = 5) They received a dose of 40 mMol/kg body weight of glycine (Sigma) i.p. dissolved in 0.9% saline solution post surgery every 20 minutes. G_2: Rats (n = 5) They received a dose of 40 mMol/kg body weight of glycine i.p. dissolved in 0.9% saline solution 5 days previously at the surgery at the same hour. Glycine was purchased commercially and under aseptic conditions (sigma-Aldrich Quimica S.A. de C.V.; Toluca, México City) was disolved in 0.9% normal saline and administered intraperitoneally (i.p.) to animals.

Surgical procedure

The morning of the surgery, animals were anesthetized with i.p. administration of ketamine (50 mg kg^{-1}) and xylazine (5 mg kg^{-1}). The animals were placed in dorsal position and their extremities were fixed; the skin was clamped and exposed by a gentle traction of the clamps; an incision of approximately 2.5 cm long was performed in the mean anterior line of the neck, at approximately 3 cm distal to the sternum. Using the omohyoid and sternocleidomastoid muscles as references, we located and dissected the vascular package. We identified the internal jugular vein, the CCA (pulsating), and the vague nerve.

The OCC was dissected, occluded with silk suture and sectioned. For the purpose of standardizing the surgical procedure, occlusion was always performed to the left CCA. The sectioned segment was analyzed histopathologically in order to confirm that the proper vessel was occluded.

Blood samples

The animals included in this study were handled gently and orderly. The rats were anesthetized with 8 mg/Kg xylazine (Rompun vet®, Bayer S. A.; Mexico) and 80 mg/Kg ketamine (Ketalar®, Pfizer, Mexico) simultaneously and intraperitonealy. Afterwards they were placed in sterilized polycarbonate cages while waiting for the anesthesia to take effect. The thoracic area was then disinfected with iodine solution and the excess was removed with sterilized

gauze. The animals were carefully immobilized by all 4 extremities and placed in a prone position on a veterinary operating table. Once absences of reflections were confirmed, the thoracic area was shaved with an electric shaver (Wahl, precision WAHL®, USA).

After the anesthesia was applied the blood sample was taken using a (4-5 cm) 23 gauges, Gx1 long sterile syringe. The process was carried out by inserting the syringe behind the xiphoid with the needle pointing cephalad in order to access the heart and obtain 200 μL of blood. Part of the blood obtained was transferred to a 150-μL heparinized microcapillary tube (lithium) and then processed by analyzing the gases and electrolytes in the blood, through a third generation critical blood gas-meter (GEM Premier 3000, Instrumentation Laboratory Diagnostics, USA and Italy). Two minutes later the following parameters were obtained: pH, partial CO_2 pressure and O_2 (mmHg), serum electrolytes: Na^+, K^+ and Ca^{2+} (mmol/L); substrates: glucose (mg/dL) and lactate (mg/dL), hematocrit (%), and total blood calculated parameters [carbonate (HCO_3^-), (tCO_2), calculated oxygen saturation (SO_2c), (thbc)]. Blood samples were taken at four different times: first, basal register previously at the surgery of Left common carotid artery occlusion, and the second at 1, 5, 10, 20 minutes after the surgery; the number of serial bleeds did not exceed 1% of the rat's body weight.

Statistical analysis

Descriptive statistics were taken for each group in the study: dispersal measurement: standard deviation, variation and coefficient, mode, minimum and maximum. With the objective of finding differences between strains, that data was consolidated as mean ± standard deviation and were compared between groups by a Student t test, and ANOVA assuming equality in variances with (SPSS for windows, release 10.0). In all cases, the probability of error less than 0.05 were selected as the criterion for statistical significance from control values.

Results

Initially descriptive statistic was made to obtain normal values average in the gasometry and obtained serum electrolytes of a sanguineous sample taken intracardiac in rates from weight average of 340 grams.

Table 1, shows basal values electrolyte and arterial blood and substrates in adult Wistar rats; in relation to the levels of electrolytes, was identified as normal Na^+ 150.50 (mmol/L), K^+ 3.45 (mmol/L), Ca^{++} 0.85 (mmol/L), glucose 217 (mg/dL) and lactate 0.96 (mg/dL) These reference values permit the correct interpretation of the hemodynamic changes after the effect of the drug or circumstances of the animal under study.

Table 2, shows basal values arterial blood gas of adult Wistar rats, in relation to these values are considered normal pH 7.33, pCO_2 39.18 (mmHg) 31.25 pO_2 (mmHg), HCO^{3-}20.85 (mmol/L), HCO^3std 20.06 (mmol/L) and –4.73 BE (mmol/L), this allows the correct interpretation of the hemodynamic changes after the effect of the drug or circumstances of the the individual under study.

Therefore, in the G_0 we compared the averages of the basal sample with the sample taken to the minute after ischemia finding significant differences in the values of BE (excess of bases) to expenses of an increase of these in the minute. To the five minutes = 0,040 diminished the levels of Calcium p, to the ten minutes diminished bicarbonate with a value of p=0.005, to the 20 minutes the values of HCO^{-3}, and equal BE of low stayed in that to the 10 minutes (Table 3 and 4). In the G_1 was observed without changes in all the measured parameters when comparing

Table 1. Normal electrolytes, glucose and lactate values and parameters calculated in the total blood of wistar rats.

	Na^+ (mmol/L)	K^+ (mmol/L)	Ca^{++} (mmol/L)	Glucosa (mg/dL)	Lactato (mg/dL)
Median	150.5	3.45625	0.8525	217	0.96875
Min	142	2.6	0.27	111	0.4
Max	163	4.3	1.26	359	2.2

Table 2. Normal gas values in the groups, calculated in the total blood of wistar rats.

	pH	pCO_2 (mmHg)	pO_2 (mmHg)	HCO_3- (mmol/L)	HCO_3std (mmol/L)	TCO_2 (mmol/L)	BE(B) (mmol/L)	SO_2c (mmol/L)
Median	7.333125	39.1875	31.25	20.85625	20.06875	22.05	–4.73125	46.8125
Min	7.25	26	12	12.2	13.6	13	–13.3	10
Max	7.38	54	58	25.4	22.6	27.1	–1.2	89

Table 3. Effect of the glycine on gas, electrolytes and substrates values, parameters calculated in the total blood of the Wistar rats under anesthesia with 50 mg/Kg of ketamine and 5 mg/Kg of xylazine.

Parameters	Time	Group 0 Control Mean±SEM	Group1 Glycine post cerebral ischemia Mean±SEM	Group2 Glycine pre cerebral ischemia Mean±SEM	t Student between group 0 and 1	t Student between group 0 and 2
pH	0	7.36±0.012	7.28±0.011	7.35±0.007		
	1	7.33±0.017	7.28±0.02	7.33±0.007	0.147	0.919
	5	7.33±0.011	7.28±0.007	7.33±0.015	0.003*	1.00
	10	7.34±0.021	7.22±0.20	7.33±0.012	0.003*	0.643
	20	7.31±0.012	7.23±0.02	7.34±0.013	0.017*	0.086
pCO_2 (mmHg)	0	38.4±1.74	40.4±5.31	39.4±2.33		
	1	35.4±1.66	44.2±3.35	43.6±1.32	0.047*	0.005*
	5	38±2.23	39±2.96	39±1.87	0.795	0.740
	10	34.2±4.23	41.4±4.63	38.2±2.39	0.285	0.435
	20	36.4±3.04	39.6±4.86	39.2±2.7	0.592	0.511
pO_2 (mmHg)	0	31±4.54	23±3.67	34.4±5.84		
	1	27.4±5.61	30.4±7.07	27.6±3.5	0.748	0.977
	5	23.8±5.52	29.2±5.77	41.2±6.85	0.518	0.084
	10	30.8±4.40	30.6±1.40	39.4±7.56	0.967	0.355
	20	35.6±4.98	26.2±6.85	40.4±6.74	0.300	0.583
HCO^-_3 (mmol/L)	0	21.66±0.78	19.22±2.71	21.7±1.06		
	1	19.16±0.84	20.88±0.76	23.4±0.70	0.169	0.005*
	5	20.64±0.91	18.4±1.60	20.8±0.75	0.261	0.896
	10	18.44±1.32	17.06±1.65	20.3±0.76	0.534	0.250
	20	18.36±1.49	16.8±2.10	21.4±0.97	0.562	0.124
tCO_2 (mmol/L)	0	22.82±0.829	20.46±2.88	22.9±1.14		
	1	20.2±0.864	22.2±0.83	24.76±0.74	0.128	0.004
	5	21.8±0.98	19.6±1.69	22±0.78	0.293	0.878
	10	19.48±1.45	18.4±1.79	21.5±0.84	0.664	0.255
	20	19.5±1.57	18±2.24	22.62±1.06	0.600	0.140
BE (mmol/L)	0	–3.48±0.71	–7.24±2.42	–3.64±0.81		
	1	–6.4±0.93	–5.62±0.75	–2.5±0.62	0.535	0.008*
	5	–4.6±0.62	–7.82±1.45	–4.64±0.74	0.076	0.968
	10	–6.4±0.71	–10.02±1.40	–5±0.47	0.051	0.142
	20	–7.2±1.28	–10.14±2.01	–3.9±0.62	0.254	0.050*
SO_{2c} (mmol/L)	0	42.2±9.1	32.2±7.8	57.6±11.16		
	1	49.8±10.27	43.2±11.8	45.2±7.12	0.648	0.723
	5	25±3.13	44.4±11.8	65.6±11.68	0.152	0.010*
	10	53.2±9.86	44.8±3.83	62.4±11.26	0.450	0.556
	20	58±8.67	37.8±13.4	65.6±11.58	0.241	0.614

Table 4. Effect of the glycine on electrolytes, substrates, hematocrit values and parameters calculated in the total blood of the Wistar rats under anesthesia with 50 mg/Kg of ketamine and 5 mg/Kg of xylazine.

Parameters	Time	Group 0 Control Mean±SEM	Group1 Glycine post cerebral ischemia Mean±SEM	Group2 Glycine pre cerebral ischemia Mean±SEM	t Student between group 0 and 1	t Student between group 0 and 2
Na^+ (mmol/L)	0	148.6±2.06	154.4±3.21	149.4±1.86		
	1	151±2.04	150.6±1.96	147.2±1.93	0.891	0.214
	5	152±0.89	151.8±2.15	147.8±2.35	0.934	0.134
	10	147±1.98	151.8±3.16	149±1.34	0.294	0.576
	20	140±1.00	151.8±3.99	146.6±1.63	0.516	0.245
K^+ (mmol/L)	0	3.58±0.16	3.42±0.35	3.32±0.18		
	1	3.20±0.20	3.54±0.26	3.62±0.24	0.343	0.228
	5	3.30±0.13	3.4±0.26	3.48±0.21	0.747	0.495
	10	3.80±0.24	3.86±0.35	3.24±0.09	0.893	0.068
	20	3.84±0.14	3.52±0.42	3.96±0.25	0.496	0.690
Ca^{2+} (mmol/L)	0	0.876±0.047	0.75±0.19	0.84±0.09		
	1	0.754±0.09	0.90±0.11	0.96±0.10	0.344	0.164
	5	0.73±0.03	0.74±0.11	0.86±0.087	0.937	0.189
	10	0.78±0.074	0.77±0.14	0.84±0.03	0.954	0.510
	20	0.77±0.07	0.77±0.16	0.97±0.08	0.967	0.120
Glucose (mg/dL)	0	218.6±33.8	214.8±44.4	202.4±12.15		
	1	229.2±33.69	251±27.4	236.2±10.04	0.629	0.847
	5	167.4±4.24	239.4±27.53	230.4±22.74	0.032*	0.026*
	10	242.4±41.85	274.4±49.67	237.8±8.72	0.635	0.917
	20	265.8±30.54	249.6±45.4	276.8±18.87	0.774	0.767
Lactate (mg/dL)	0	1.28±0.33	0.84±0.13	0.68±0.11		
	1	1.06±0.25	1.28±0.21	0.60±0.03	0.529	0.115
	5	1.82±0.23	0.98±0.14	0.60±0.054	0.017*	0.001*
	10	1.28±0.23	1.58±0.39	0.62±0.02	0.531	0.025*
	20	1.22±0.33	1.36±0.39	0.68±0.06	0.793	0.150
Hematocrite (%)	0	38.2±3.83	35±5.31	40.8±1.59		
	1	33.8±4.35	38.4±1.69	43±1.78	0.353	0.086
	5	36±0.44	32.8±3.99	39.6±1.4	0.449	0.04*
	10	37.4±1.69	31±4.61	40.2±0.48	0.229	0.15
	20	35.2±2.31	33.8±3.83	40.2±1.46	0.763	0.105

the basal values and the values obtained to the minute, 5, 10, 15 and 20 minutes. In the G_2 treatment with glycine during 5 days previous to ischemia, it was observed that when comparing the basal parameters with obtained to the other times did not present display changes, except the glucose levels with increment and statistical significance. Finally, all the obtained values of the group were compared control (to minutes 1, 5, 10 and 20); with the group with treatment post ischemia being significant differences to the minute in pCO_2 with p=0.047, to the 5 minutes was increased to the glucose p=0.032, and diminished lactate p=0.017 (Table 3 and 4).

When comparing the group control with the group with treatment post ischemia to the minute we found that pCO_2 increased p=0.005, HCO_3^- increase p=0.005, TCO_2 increased p=0.004 and the BE diminished p=0.008. To the 5

minutes p=0.026 increased to the glucose, diminished lactate p=0.06 and increase the oxygen saturation p=0.010. To the 10 minutes 3std continued diminishing the HCO_3^- p = 0,020 and it stayed equal to the 20 minutes.

Discussion and conclusions

The present study found that administration of glycine in an animal model of brain ischemic injury prevent cell damage. Glycine is normally found in the interstitial space of a brain concentration of 4 mol L^{-1} in the cortex [1, 8], and is a well-recognized major inhibitory neurotransmitter in the spinal cord and it plays an important role as a coagonist of NMDA subtype receptors [20, 26].

Blood pH less than 7.0 (>100 nmol/L de H^+) or greater than 7.7 (<20 nmol/L de H^+) may cause death, for which blood pH is regulated inside the physiological limits [15]. Normally, values below 7.32 indicate intracellular acidosis reflecting inadequate liberation of oxygen [4].

Lactate is metabolized by the liver and kidney though oxidant and non oxidant routes, mainly glycogenolysis [32, 19].

According to Schwenke and Cragg [22], the pO_2 value for guinea pigs without anesthesia is 98 ± 2 mmHg. These investigators mention that the use of combined xylazine-ketamine decreases pO_2 17%, due to diminishing respiratory frequency. It is well known that alveolar hyperventilation is reflected by falling pO_2 accompanied by an increase in pCO_2 [29]. Anesthesia is one of the factors that reduce breathing by diminishing the supply of oxygen to organs and tissue [2]. Xylazine can induce cardiovascular alterations, atrioventricular blocking and diminished demand for O_2 by myocardium [27]. On the other hand, ketamine induces cardiovascular stimulation and increases oxygen consumption but in some cases causes slight respiratory decrease [30].

The elevated levels of calcium could be related to a probable increase in the parathyroid hormone. Increase in this hormone initiates a skeletal calcium mobilization; this way an increase in the calcium levels could be involved in the defense mechanism responding to stress [25].

The importance of HCO_3^- is rooted in its function as a system buffer that avoids drastic changes in blood pH. When there is an increase acid on a corporal level, the first reaction is a chemical spring through the HCO_3^- that combines with hydrogenions as a result of metabolism producing carbonic acid which separates into $CO_2 + H_2O$, the CO_2 is eliminated by the respiratory system and the water serves to maintain the homeostasis in the different compartments [11]. Acid-base balance requires the integration of three organic systems: liver, lungs and kidney. The liver metabolizes the proteins producing hydrogenions, the lungs eliminate the CO_2 and the kidney generates HCO_3^- [29].

The presence of hypoglycaemia marked produces functional and structural alterations in the central nervous system; 20 inferior concentrations to mg/dL of glucemia originate confusion, and the coma appears below the 10 mg/dL. While the brain consumes the little glucose deposits and glycogen, the situation is reversible, without neurological sequels. After some time, the brain begins to metabolize other substances and appear structural injuries that they consist of a selective cortical neuronal necrosis, with preservation of the glial weave [23]. In our investigation, hyperglycemias in the group with treatment with later glycine to ischemia appeared, which we could think that it influences like a beneficial factor to protect the cerebral damage [28].

Edema that appears during ischemia cerebral is the result of the accumulation of liquid inside the cells, of the cellular interstice or both. In the first case, it receives the cytotoxic name of edema and in the second, of edema cerebral vasogenic [9, 19]. Edema aggravates the initial cerebral ischemic process by several mechanisms: it interferes in the homeostasis of the water and electrolytes in cerebral parenchyma, it alters myelinized fibers, and it has a volumetric effect that causes compression of the microcirculation, elevates intracerebral the intracranial pressure and originates hernias. These factors are responsible for the progression of edema and the initial cerebral damage that, in extreme cases, can get to originate one ischemia global and cerebral death [6]. In the group two in which there were no changes in pH and electrolytes, it is of great importance because when not existing changes it helps us to that cytotoxic or vasogenic injuries do not appear and this with treatment with glycine previously the surgery [21].

Glycine plays two important roles in the central nervous system: that of an inhibitory neurotransmitter and that of a modulator of excitation at the NMDA receptor [10]. Studies have shown that NMDA open channel blockers are more effective than competitive receptor antagonists in alleviating the damage caused by excessive levels of glutamate [5]. Finally, the important thing is the effect of the glycine on the receivers NMDA since when modulating their effects allow us to avoid the cascade beginning of chemical reactions, which cause the irreparable damages in ischemia cerebral. Is important the development of effective and safe drugs preventing NMDA overactivation after cerebral ischemia, like glycine to minimize the ischemia effects in brain [3].

In conclusion, glycine administered i.p. to rats with permanent left carotid occlusion limited the changes in the acid base and electrolytes like consequence the ischemic brain damage, probably by increasing the neurological availability of glycine concentration enough to prevent the desensitization of NMDA receptors and increment glucose levels since ischemia beginning protecting the brain and consequently altering the cascade of events that lead to cellular death.

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