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CONSISTENT THERAPEUTIC OF THE DEPAKINE AND THE TEGRETOL AT THE EPILEPTICS BY THE DOSAGE OF THE CARBAMAZEPINE AND THE ACIDIC VALPROIQUE

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ABSTRACT

The objective of our survey was to determine the concentrations plasmatic of the carbamazépine and the acidic valproïque respectively at the epileptics under treatment of Tégrétol and the dépakine and to value their concentrations plasmatic in relation to their therapeutic minimal concentrations in plasma. The concentrations middle plasmatic of the carbamazépine and the acidic valproïque that we got was respectively of 1,60 mg/l and 80,70 mg/l. In polythérapy the carbamazépine interacts with many medicines that make it inefficient or toxic. In polythérapie, the dépakine becomes inefficient or toxic insofar as the posology is not respected, but especially it enters in competition with the activation of the fatty acids in the transportation transmitochondrial. The addition of the carnitine to the epileptic treatment by the dépakine is a necessity to take in account and the dosage of the acidic valproïque and the carbamazépine.

KEYWORDS: Consistent therapeutic, epilepsy, tegrétol, dépakine, carbamazépine, Valproïque acidic.

I. INTRODUCTION

The nervous system is the center of regulation and communication of the organism, our thoughts, actions, and our evidence emotion. its activity, its cells communicate by means of fast and specific electric signals that nearly bring some immediate answers.

The nervous system fills closely bound three functions first, through the intermediary of its millions of sensory receptors, it receives information on the alteration that occur inside and outside of the organism. These alterations are called stimulus and the introverted information carries the name of sensory information, second, it treats and interpret the sensory information and determine the action to undertake at all times, what constitutes the process of integration. Third, it provides a motor answer that activates the muscles or the glands (MARIEB, 2008, MURRAY and call, 2012).

The neurons are fundamental units, morphological and functional of the nervous tissue constituted by the cellular substance and its extensions (axons and dendrites) the neurons drive and transmit the nervous impulse through the intermediary of their axons (QUEVAULLIERS and coll, 2007).

The pathologies of the nervous system are multiple and have various reasons, among these pathologies; there is the epilepsy that is a chronic affection characterized by repetition of paroxysms due to epileptic discharges, that is to say the sudden simultaneous and abnormally intense activation of a big number of cerebral neurons.

These paroxysms result clinically in epileptic crises these still have the variable clinical aspects going from the generalized crises, to the partial vises and their absence (DE LA MARE and coll, 2012).

The treatment of the epilepsy rests on the classic medicine anti-epileptic (phenobarbital) valproate of sodium, benzodiazepine and phenytoine) the tegrétol (carbamazépine) is am anticonvulsant derivative non barbiturate of the dibenzodiazepine and endowed of anti-epileptics properties, neurotropes and psychotropics it acts mainly on the voltage sodiques reliant duct otherwise the reduction of the discharge of the glutamate and the stabilization of the neural membranes can explain the essential of its effects anti epileptics. The properties anti maniac of the carbamazepine seem to be due to the depressive effect on the regeneration of the dopamine and the noradrenaline (LOICHOT and GRIMA, 2004).

The dépakine (valproïque acidic) is a medicine belonging to the family of the anti-convulsivants non barbiturates and that commercialize itself as tablets of 200 mg and 500 mg or in syrup (small bottle of 150ml) with as an active principle: valproate of sodium and acidic valproïque, it is used in the treatment of the epilepsy, only or in association with another anti-epileptic. The valproïque acidic is a major anti-epileptic to a very large specter and to a complex action mechanism: effect gabamimetique, antagonistic effect of the glutamate and inhibition of the voltage sodique dependant dust (ROYER MORROT, 2005).

The objective of this survey was to determine the concentration plasmatics of the carbamazepine and the valproïque acidic at the epileptics under treatment, respectively of tegrétol and the dépakine and to value their plasmatics concentrations in relation to their therapeutic minimal concentrations in plasma.

II. ENVIRONMENT, MATERIAL AND METHOD

II.1. Environment

our investigations have been done to the academic clinics of Lubumbashi, at the neuro psychiatric center doctor Gislain and at the medical laboratory dee services. administrative centre of the province of Haut-Katanga, Lubumbashi, is situated to 11°40' of latitude south, 27°28 of longitude easterm and to 1268 meters of altitude. The climate is characterized by two seasons 6 months in the dry season 6 months and in the rainy season as well the middle temperature is 21°c (LE BLANC and MALAISE, 1978).

II.2. Material

A) Patient

We considered like patient, all person suffering from the epilepsy, under treatment of tegrétol (carbamazepine) and the dépakine (valproïque acidic) in ambulatory or in hospitalization to the academic clinics of Lubumbashi and at the neuro psychiatric center doctor Gislain.

Our sampling has finally been constituted of 40 epileptic individuals to the al of which 20 individuals under treatment of the dépakine and 20 other under treatment of tegrétol en polytherapy.

We took like criterias of inclusion

- To be epileptic under treatment of tegrétol or dépakine
- Not to endure another pathology
- To accept to participate in our server voluntarily.

B) Material of with drawal of blood and laboratory

- Dry tubes, scorer, cotton wool (ouate) altered alcohol, syringes, centrifuge, micropipettes, portoir fridge, acorn, cryotubes, micropipettes, edge, automaton (AU 480) of MARK BECKMAN

C) Reactive

- Reactive of carbamazepine
- Reactive of the acidic valproique

III. Methods

We used the analytic prospective method, our sample of blood have been withdrewed without triangulation or garotte and it has been poured in the dry tubes without anti-coagulant immediately after the withdrawal of blood, the tube have been routed to the laboratory, then centrifuged to 2500 turn per minute during 10 minutes. The introverted serum was kept fresh to 4°C until the moment of the laboratory, dosages (carbamazépine and valproïque acidic) that made themselves the same day to the automaton by the colorimetric method, has the statistical analyses been done with the help of the T test of student and to the statistical significance has been declared to the doorstep of P <0, 05.

III. RESULTS

III.1 Raw and Middle DATA

I. picture raw and middle Values of the carbamazepine and the acidic valproïque gotten at the epileptics.

N°	Aged	Sex	Carbamazepine 8.00-12.00 mg/l	N°	Aged	Sex	Acidic valproïque 50.00-100.0 mg/l
01	16	M	1,29	01	47	F	105,40
02	20	F	2,94	02	31	M	31,29
03	30	F	0,48	03	13	M	105,00
04	49	F	1,91	04	46	F	91,92
05	29	M	3,84	05	15	F	25,02
06	28	M	0,70	06	9	M	70,62
07	16	M	2,91	07	37	M	66,16
08	22	F	1,95	08	16	F	146,00
09	22	M	1,56	09	59	M	84,01
10	18	M	1,70	10	22	M	98,06
11	16	M	3,82	11	15	F	103
12	19	F	2,7	12	51	M	65,20
13	22	M	0,82	13	10	M	71,27
14	26	F	0,74	14	40	M	107,00
15	60	M	0,26	15	36	M	80,01

16	50	F	0,38	16	20	F	91,11
17	25	M	0,36	17	26	F	111,02
18	34	M	1,86	18	60	M	40,12
19	13	F	0,98	19	31	M	76,13
20	22	F	0,95	20	18	F	44,70
Average	**26,85**		**1,60**		**30,1**		**80,70**

III.2. Analyse of the data Statistical

Our data have been analyzed statistically with the help of the t test of student and our results will be compared with those found by our predecessors.

A. Tegrétol (Carbamazépine)

N = 20

$Tc = \bar{X} \pm T\alpha \frac{S}{\sqrt{n}}$

S = 0,99

$T\alpha =$ degree of liberty in the table of student

$\bar{X} = 1,60$

$Tc = 1,60 \pm 2,09 \frac{0,99}{\sqrt{20}}$

$= 1,60 \pm 0,462$

$1,138 \leq \mu \leq 2,062$

Here the lower value (1,138) and the superior value (2,062) are below normal limits that are from 8,00 to 12,00 mg/l.

B. Dépakine (acide valproïque)

N = 20

S =7,056

$\bar{X} = 80,70$

$Tc = 80,70 \pm 2,09 \frac{7,056}{\sqrt{20}}$

$= 80,70 \pm 3,297$

$77,403 \leq \mu \leq 83,997$

Here the lower value (77,40) and the superior value (83,99) are in the normal limits that are from 50,00 to 100,00 mg/l.

DISCUSSION

Our results gotten after the dosages plasmatics of carbamazepine among subjects under treatment of tegrétol and valproïque acidic and among subjects under treatment of dépakine it agrees to point out that the middle concentration of the carbamazepine and valproïque acidic have been respectively of 1,60 mg/l and 80,70 mg/l concerning carbamazepine, our result are in agreement with those found by lancelin and coll (2003) in their structural article carrying the influence of carbamazepine -10,11 epoxyde in the dosage of the carbamazepine <<Flex dimension carbamazepine>> in this survey, the concentrations of carbamazepine and carbamazepine -10,11 epoxyde have been determined to the state of balance and the residual rates to 72 patients treated by carbamazepine (tegrétol) alone or associated to another anti comitial. The three methods compared two to two were carrelated very well between them. The derivative carbamazepine -10, 11 epoxyde were on average. Of 1, 33 ± 1, 1 mg/l of the whole population studied the report carbamazepine 10, 11 epoxyde/ carbamazepine was 17% among patients treated by tegrétol only and 30% to the association of tegrétol to the valproïque acidic in the population of patients studied.

Authors noticed that the metabolite carbamazepine plasmatics -10,11 epoxyde, in weak proportion doesn't influence meaning fully the dosage of carbamazepine plasmatics by flex carbamazepine technical. The zone of the therapeutic concentrations of carbamazepine proposed was from 4 to 2 mg/l adapted to dosage by the flex carbamazepine technical. The zone of the therapeutic concentrations of carbamazepine proposed was from 4 to 12 mg/l adapted to dosage by the Flex carbamazepine Kit.

For the dépakine our results contrast with. Those found by benjalloun and coll (2013) in their structural article on the treatment of a resistant depression by substitution of the depamide by the dépakine to patients with resection of pockmarked Valpromide .of patients presenting a resection of the pockmarked, have been hospitalized for resistant depression on the occation of bipolar trouble have been treated by valpromide since a year. The dosage of depakimemy had shown a low middle value of 27 mg/l (normal fork between 50 and 100 mg/l) in spite of the daily posology important of 1200 mg/day a deepen survey of the pharmacokinetics of depamide had allowed authors to highlight the fact that the transformation of the valpromide (De pamide) in valproïque acidic (dépakine) that usually make itself level of the intestine was probably very ducreased among these patients because of the spread intestinal resection that they had undergone and the diarrheas that they presented this trouble of the absorption of depamine explains the low rate of dépakine recovered in blood and the fast fluctuation of the mood because of the inefficiency of the thymoregulator. The relay of dopamine by dépakine permitted to bring back the dosage of depakinemy In the therapeutic fork and an improvement of the fluctuation of the mood.

The epilepsy is a chronic affection characterized by the repetition of paroxysms due to epileptic discharges, that is to say the sudden simultaneous activation and abnormally intense in a great number of cerebral neurons its treatment consist's of the complete disappearance of the crises or the liver is the biggest gland of the organism, it is essential to life because it fills a large range of biochemical and metabolic functions, including the metabolism of medicines and the detoxification.

There are two phases in the metabolism of medicines in the phase I, the main reaction is a hydroxylation, catalyzed mainly by the members of enzymes class called mono oxygenases or cytochromes P 450. The hydroxylation can disactivate a medicine, but it is still not a case besides the hydroxylation, these enzymes catalyze a big number of reactions as the desanimation, the deshalogenation… and à few other reactions that are not catalyzed by. The cytochromes P 450 and that can take place in phase I.

In the phase II the compounds hydroxyls or, other products the phase I are transformed by specific enzymes in various polar metabolites by conjugation or combination with gluconic acidic, the sulphate, glutathion by methylation. The final objective of these two phase is to increase the hydrosolubility of the therapeutic agents and to facilitate their excretion out of the body (GANONG and coll 2012 MURRAY and coll 2012) the carbamazepine is a inductive enzymatic (inhibitor of the tyrosine kinase) influencing many medicines effect and its own metabolisation (LOICHOT and GRIMA, 2004, ROYER-MARROT, 2005).

On basis of our results, we think that at the time of the metabolism, if a therapeutic agent is very hydrophobic, it stays nearly indefinitely in the fatty tissue, in some cases the metabolic reactions of phase I can convert this inactive therapeutic agent in active biologic compound; in the other case the supplelmentary reactions of the phase I transform active compounds in a shape less active or inactive before they are conjugated. The metabolites of some therapeutic agents can inhibit or can stimulate the enzymatic activities of the metabolism of the other therapeutic agents, Again it can modify the dose of some medicines to give to patients, various illnesses (for example of the cirrhosis of the liver) can influence the activity of the enzymes of the metabolism of the medicines, what sometimes requires the adjustment of the doses of these therapeutic agents that must itself by the dosage of theirs therapeutic minimal concentrations in plasma. Among patients reached by such illnesses.

The induction of the cytochromes P450 has the important chemical implications since it is about à biochemical mechanism of medicinal interaction.

The activity of the enzymes can meaning fully vary from an individual to another these differences sum controlled by genetic factors. The use of tegrétol the epileptics is metabolized differently from an organism to another and interacts with many medicines in polytherapy or in monotherapy by the no respect of the posology, what can make it inefficient or toxic in fact its minimal concentration therapeutic in plasma decreases or increase. Being a no borbituric, it must not be associated to the barbiturates.

In polythérapie, the carbamazepine leads a rick of reduction of the concentrations plasmatics of some medicines and their therapeutic efficiency by increasing of their hepatic metabolism by the carbamazepine on the other hand the association of the carbamazepine with other medicine (rifampicine) risk of decreasing the plasmatic concentrations and the efficiency of the carbamazepine by increasing its hepatic metabolism by these medicines the use of the dépakine at the epileptics, relieves the patients, bus its metabolite has a close spatial configuration to the one of the fatty acids with with which it enters in competition at the time of its transportation it metabolism intra-mitochondrial and its elimination. Its therapeutic inefficiency can also be due to a no respected posology; while its toxicity is in relation with an individual sensitivity. provoking deadly secondary effects but especially its interference with. The metabolism of the fatty acids (activation of the fatty acids) lead to an inhibition of the beta oxidization of these consistent reduction of the circulante by default of carnitine, the transportation of the valproïque acidic is not assured anymore, in the mitochondrial, it under goes an omega-oxidization microsomal leading to the derivatives hepatotoxic.

The clinical surpervision of dosage and the posological adaptation during the treatment by the carbamazepine and dépakine after its stopping are very crucial.

CONCLUSION

Our survey had the main objective to make the Therapeutic consistent of the dépakine and tegrétol to the epileptics by the dosage of the valproïque acidic and the carbamazepine the middle concentrations of the carbamazepine and valproïque acidic to the epileptics under treatment, were respectively to 1,60 /l and 80, 70 mg/l.

After statistical analyse by the T Test of student, the middle concentration of valproïque acidic is in the normal limits while.

These of the carbamazepine are lower to the normal limits. The use of tegrétol the epileptics is metabolized differently organism to another and it interacts with from many medicines in polytherapy or in monotherapy by the no respect of posology, what can make it inefficient or toxic in fact, its therapeutic minimal concentration in plasma decreases or increases.

These use of the dépakine to the epileptics relieves the patients but its metabolite has a close spatial configuration to the fatty acids with which it enters in competition at the time of its transportation, it intra-mitochondrial metabolism and its elimination.

The addition of the carnitine to the epileptic treatment by the dépakine is a necessity to take in account, the dosage of the valproïque acidic and the carbamazepine to the

epileptic under treatment of tegrétol and dépakine is part of the treatment.

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