

## THESES

BEHAVIORAL-PHARMACOLOGICAL STUDY OF A POSSIBLE ANALGESIC EFFECT OF VIGABATRIN (gamma-vinil-GABA) IN EXPERIMENTAL CHRONIC NEUROPATHIC PAIN (Abstract)\*. **THESIS. FORTALEZA, 1997.**

*NILZA DUTRA ALVES\*\**

Pain is responsible for most of patients complaints. The mechanisms involved in chronic pain are still unknown and they are object of intensive studies. Recently, important steps in this area have been done thanks to the use of new animal models of chronic pain, this way bringing further contribution for therapeutical approaches.

Among pain modalities, the neuropathic pain is not yet well known. Anticonvulsants have been used in its treatment with partial success.

With the aim of contributing for the understanding and alleviation of the human neuropathic pain syndromes we have tried to study the effect of vigabatrin, a new gabaergic anticonvulsant, in an animal model of chronic neuropathic pain, described by Bennet and Xie (1988) and modified by Seltzer (1990).

For this, 36 Wistar rats divided in 2 experimental groups (n=20), and 2 control groups (normal rats, n=8; and sham-operated rats, n=8) were used. As pain parameters, we have used the spontaneous scratching behavior, suggestive of chronic pain, and the latency of hindlimbs withdrawal and struggle reaction to nocive thermal stimuli (46°C).

The behavioral results showed a chronic significant ( $p<0.05$ ) increase of the scratching behavior and the presence of allodynia as shown by the thermal test in the experimental animals. Vigabatrin was effective in diminishing significantly ( $p<0.05$ ) the scratching behavior in a dose-dependent way as well as in reverting significantly ( $p<0.05$ ) the allodynia in those animals. This vigabatrin effect was not, however, reverted by naloxone, excluding this way an opioid participation in it. Moreover, the valproate acid, as a gabaergic, and other classical anticonvulsants with analgesic properties in neuropathic pain (carbamazepine and phenitoin) have corroborated the analgesic effect of vigabatrin.

This study leads to the conclusion that vigabatrin may possibly exert an analgesic effect on chronic neuropathic pain. Further studies are however needed to confirm these preliminary results.

**KEY WORDS: pain, neuropathic chronic pain, experimental, vigabatrin.**

\*Estudo comportamental-farmacológico do possível efeito analgésico da vigabatrina (gama-vinil-GABA) em dor neuropática crônica experimental (Resumo). Tese de Mestrado, Universidade Federal do Ceará (Área: Farmacologia). Orientador: Carlos Maurício de Castro Costa.

\*\*Address: Rua Jornalista Nerton Macedo 69, 60190-730 Fortaleza CE, Brasil.

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TEMPORAL LOBE EPILEPTIC SEIZURES: CLINICAL AND ELECTROENCEPHALOGRAPHIC ASPECTS (Abstract)\*. **DISSERTATION. SÃO PAULO, 1997.**

*FÁBIO GALVÃO DANTAS \*\**

Temporal lobe seizures often consist of a sequence of clinical features which includes aura, motionless stare, simple automatisms, contralateral motor activity, complex automatisms and secondary generalization. The analysis of clinical features suggests the localization and the lateralization of the epileptogenic lobe. Besides, the study of critical EEG specially when synchronized with clinical observation during video-EEG may improve the localization and the lateralization of ictal onset.

We analyzed clinical and EEG features of 50 temporal lobe seizures which were separated in group 1 (related to mesial temporal sclerosis) and group 2 (related to other neocortical temporal lesions).

Among the auras, the epigastric type was the most frequent and predominated in group 1.

There were differences between the two groups, considering dystonic and tonic posturing and versive head and eye movements. Dystonic posturing was more precocious and presented longer duration in group 2 seizures, while unilateral tonic posturing occurred mainly in group 1; versive head and eye movements were seen exclusively in group 1 seizures.

Dystonic posturing was always contralateral to the ictal onset in both groups and was considered the most useful lateralizing clinical feature. Ictal speech occurred in right temporal seizures. Spit automatism was seen in a patient with right temporal epilepsy.

Among the postictal features, disorientation only for place was found exclusively in right temporal seizures, while aphasia was observed in left temporal epilepsy.

EEG was important for lateralizing the epileptogenic lobe, specially considering rhythmic ictal activity and postictal findings.

**KEY WORDS: epilepsy, temporal lobe epilepsy, complex partial epilepsy, electroencephalography.**

\*Crises epilépticas do lobo temporal: aspectos clínicos e eletrencefalográficos (Resumo). Dissertação de Mestrado, Faculdade de Medicina da Universidade de São Paulo (Área: Neurologia). Orientadora: Elza Márcia Targas Yacubian.

\*\*Address: Rua São Sebastião 80 / 48, 04144-060 São Paulo SP, Brasil.

CEREBROSPINAL FLUID IN ACQUIRED IMMUNODEFICIENCY SYNDROME (Abstract)\*.  
**THESIS. SÃO PAULO, 1997.**

*HELIO RODRIGUES GOMES\*\**

Central nervous system (CNS) involvement occurs early in the course of human immunodeficiency virus (HIV) infection. The main objective of this study is the interpretation of cerebrospinal fluid (CSF) findings in acquired immunodeficiency syndrome (AIDS). 2,327 CSF samples presenting anti-HIV antibodies, from 1,404 patients, were analysed.

Opening pressure, cytomorphological patterns, total proteins concentration, glucose rate, gamma globulin content, enzymatic activity of lactic dehydrogenase (LDH), glutamic-oxalacetic transaminase (GOT) and adenosine-deaminase (ADA) were studied. 2,219 samples (95.3%) presented abnormalities and 108 (4.7%) were normal.

Opening pressure was measured in 2,201 samples, and it was increased in 501 (22.7%). From all samples, 1,094 (47.0%) presented cell number above reference limit, proteins concentration was increased in 1,657 (72.0%) and glucose rate was decreased in 93 (4.0%). Gamma globulin increase was observed in 1,596 samples (73.9%) from 2,157 in which it was studied. Enzymatic activities of GOT and LDH were assessed in 1,172 samples. GOT activity was increased in 305 (26.0%) and LDH activity in 832 (71.0%). ADA enzymatic activity was determined in 1,210 samples being increased in 823 (68.0%). Oligoclonal bands were detected in 417 samples (19.3%).

A unique associated pathology was observed in 1,027 samples (44.2%); the association of more than one pathology was observed in 477 samples (20.4%). In 715 samples (30.7%) there was no evidence of opportunistic infection and/or neoplastic complication.

Observed in 513 samples (22.0%), cryptococcosis was the most frequent pathology, followed by toxoplasmosis in 419 samples (18.0%), cytomegalovirus infection in 246 (10.6%), syphilis in 117 (5.0%), lymphoma in 83 (3.6%), tuberculosis in 47 (1.9%) and herpes virus infection in 38 (1.6%).

Thereafter, the samples were divided into three different groups: the first group formed by samples in which the pathologic agent was identified (tuberculosis and cryptococcosis); the second group formed by those samples in which IgG antibodies were detected (toxoplasmosis, cytomegalovirus infection, syphilis and herpes virus infection); and the third group formed by samples in which cells with neoplastic features (lymphoma) were observed. The pathologies were analysed in isolated and in associated ways. The univariate analysis displayed that number of cells and protein concentration were statistically higher in every pathology except syphilis; variable neutrophils was higher in tuberculosis and in herpes virus infection; tuberculosis, cryptococcosis and lymphoma presented glucose rate statistically decreased; LDH activity was higher in cytomegalovirus infection, lymphoma and tuberculosis. Oligoclonal bands frequency was statistically higher in syphilis and cytomegalovirus infection (univariate analysis) and herpes

virus infection (multivariate analysis). By multivariate analysis, hypercytosis presents significance level in: tuberculosis, cytomegalovirus infection and lymphoma; neutrophils participation is significative in tuberculosis and cytomegalovirus infection. Enzymatic activity of GOT is frequently increased in lymphoma. Interferences among pathologies are analysed as well as risk probabilities related to the variables.

**KEY WORDS: cerebrospinal fluid, nervous system, human immunodeficiency virus (HIV), acquired immunodeficiency syndrome (AIDS), opportunistic infections, lymphoma.**

\* O líquido cefalorraqueano na síndrome da imunodeficiência adquirida (Resumo). Tese de Doutorado, Faculdade de Medicina da Universidade de São Paulo (Área: Neurologia). Orientador: José Luiz Dias Gherpelli.

\*\*Address: Praça Amadeu Amaral 47 / 33, 01327-010 São Paulo SP, Brasil.

EVALUATION OF THE BLOOD-BRAIN BARRIER IN THE CHRONIC GRAFT VERSUS HOST DISEASE (Abstract)\*. **THESIS. SÃO PAULO, 1997.**

*SÉRGIO MONTEIRO DE ALMEIDA\*\**

The central nervous system (CNS) involvement in chronic graft versus host disease (GVHD) has been suggested. Chronic GVHD resembles auto immune connective tissue disorders, which contributes to the hypothesis that immune mediated complications can occur in CNS during chronic GVHD. The blood-brain barrier (BBB) contributes to the CNS immunological isolation. The BBB integrity may contribute to the low frequency of direct involvement of the CNS in GVHD. However, in auto immune connective diseases there is both disruption of BBB and immunoglobulin synthesis in the CNS. The BBB has never been evaluated in patients submitted to bone marrow transplantation (BMT).

This study was done to evaluate BBB integrity and intra BBB immunoglobulin synthesis through the analysis of cerebrospinal fluid (CSF) proteins. Also, the general CSF features were studied. Thirty three CSF and matched serum samples, from chronic myelocytic leukemia (CML) patients who underwent allogeneic BMT from HLA identical related donors, were collected pre BMT, post BMT and during GVHD.

Total CSF cells were increased in cases with chronic GVHD (41.8%), which were not found in non chronic GVHD patients. These cells were mainly lymphocytes, and were not related to infection or relapse of CML.

There were no evidences of BBB disruption or intra BBB immunoglobulin synthesis, and no oligoclonal band were found among patients studied.

**KEY WORDS: blood-brain barrier, cerebrospinal fluid, immunoglobulin synthesis, chronic myelocytic leukemia, bone marrow transplantation, chronic graft versus host disease.**

\*Avaliação da barreira hemato-encefálica na doença do enxerto contra o hospedeiro crônica (Resumo). Tese de Doutorado, Universidade Federal de São Paulo – Escola Paulista de Medicina (Área: Imunologia). Orientador: Eurípedes Ferreira; co-orientador: José Antonio Livramento.

\*\*Address: Especialidade Neurologia, Hospital de Clínicas de Curitiba, Universidade Federal do Paraná – Rua General Carneiro 181 – 80060-900 Curitiba PR – Brasil.

NEUROCYSTICERCOSIS: CLINICAL, EPIDEMIOLOGICAL AND DIAGNOSTIC ASPECTS. A PROSPECTIVE STUDY OF 157 PATIENTS IN THE NORTHEASTERN REGION – BAHIA STATE, BRAZIL (Abstract)\*. **THESIS. NITEROI, 1997.**

*ANTONIO DE SOUZA ANDRADE FILHO\*\**

Neurocysticercosis (NC) is a parasitic disease, common in our environment, displaying different neurological manifestations. It has been known since ancient times, and described around 380 to 375 b.C. in one of Aristophanes' comedies. It has been reported for the first time in Brazil by Magalhães, in Bahia State, in 1881. It is a typical parasitosis in developing areas, significantly associated to poor hygiene and basic sanitation conditions, mainly in areas where extensive swine breeding has taken place. The disease is endemic in Mexico, Central and South America, Indonesia and East Europe, being often found in Portugal, Spain and Poland, but also reported in other countries.

The life cycle of the parasite presents important characteristics, with phases at which it is found in different stages. It is important to understand its morphological structures and the contribution of these stages to perpetuate infestation. Man, inside life cycle, can take part as a definitive host, being bearer of the adult worm form (*Taenia solium* – teniasis), or as an intermediary host, displaying the larva form (*Cysticercus cellulosae* – cysticercosis) inside tissues, mainly in the central nervous system (75%), which has been the subject of the present study; it can also reach the retina, the heart, the (striated) muscles, and the subcutaneous tissue, among others.

In NC, the cysts can be located at the parenchyma (gray matter or periventricular tissue), at the ventricular system or at the subarachnoid space, bringing up several clinical pictures. The NC diagnosis is based mainly on the patient's epidemiological history, clinical symptoms, cerebrospinal fluid (CSF) study and neuroimage exams.

The purpose of this study is, besides reviewing world literature about NC, to carry out a prospective analysis of 157 patients followed up during a minimal period of six months, from March 1988 to December 1995: at the Neurology Service of University Hospital Professor Edgard Santos, attached to the Medicine Faculty of Bahia Federal University; at the Santa Isabel Hospital, attached to Bahia School of Medicine and Public Health; and at the Neurology and Neurosurgery Foundation, Brain Institute.

The average age was  $29.2 \pm 13.1$ , with a proportion of 58.6% males and 41.4% females. Several other demographic features – such as color, schooling, occupation and origin, among others – were studied as to determine these patient's epidemiological aspects. The disease has clinically appeared as pure convulsion in 80.3% of cases, intracranial hypertension syndrome (ICHS) in 9.6%, psychic form in 5.1%, convulsive form plus ICHS in 3.8%, and as convulsive form plus psychic form in 1.3% of cases. In this series, none of the 157 patients displayed spinal cord damage. The physical exam was normal in majority of patients (83.4%); 8.3% of cases had hemiparesis, 2.5% had hemiplegia; in some cases occurred dysarthria, cerebellar syndrome, alterations of cranial nerves, and associated forms. It was performed the analysis of the evolution of image, CSF and electroencephalographic exams in three distinct periods: starting or diagnostic period, post-intervention period (30 days after treatment), and control period (six months after treatment).

With this study, bearing a pioneer character in Bahia State – Northeastern Region, it was possible to emphasize the clinical, epidemiological and diagnostic aspects which are relevant to characterize NC, and are useful for better understanding this affection in our environment.

**KEY WORDS: cysticercosis, central nervous system, clinical aspects, diagnosis, epidemiology, biostatistics.**

\*Neurocisticercose: aspectos clínicos, epidemiológicos e diagnósticos. Estudo prospectivo de 157 pacientes na região nordeste – Estado da Bahia (Resumo). Tese de Doutorado, Universidade Federal Fluminense (Área: Neurologia). Orientador: Marcos Raimundo Gomes de Freitas.

\*\* Address: Departamento de Neuro-Psiquiatria, Faculdade de Medicina, Universidade Federal da Bahia – Av. Reitor Miguel Calmon s/n – 40110-100 Salvador BA – Brasil.

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