

THESES

TRANSCRIPTION ANALYSIS OF TIMP-1 AND NM23 GENES IN GLIOMA CELL INVASION (ABSTRACT)*. **THESIS. SÃO PAULO, 2005.**

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Purpose: To evaluate using transcription analysis the presence and importance of two genes: NM23-H1 and TIMP-1 on control of tumor cell invasion in diffuse astrocytomas (WHO II) and glioblastoma multiforme (WHO IV).

Method: Northern Blot analysis of NM23-H1 and TIMP-1 was performed. Eight diffuse astrocytomas and nineteen glioblastomas (WHO IV) were analyzed to determine if TIMP-1 and NM23-H1 were candidates to inhibition of tumor cell invasion quantitated RNA levels. The samples were collected directly from operating room. Total cellular RNA was extracted from frozen tissue samples using guanidinium-isothiocyanate and cesium chloride gradients. Total RNA (10 μ l per sample) from tumor tissue were size fractionated through 1% agarose-formaldehyde gels and transferred to nylon filters and then hybridized to ³²P-labeled DNA probes

and placed for autoradiography. Levels of specific RNAs were determined by computer-assisted laser densitometry. Blot filters were sequentially hybridized to nm23 and TIMP-1 probes in addition to GAPDH, as a control. Statistical analyses were carried out according to t-test for equality of means.

Results: NM23-H1 was detected in each sample, however it was not correlate malignancy and invasiveness with NM23-H1 expression. On the other side TIMP-1 gene expression showed a clear correlation between low expression and invasiveness.

Conclusion: The data suggest that TIMP-1 is an inhibitor of high grade gliomas invasion. NM23-H1 was present in the entire gliomas sample, but it did not vary in diffuse astrocytomas and glioblastomas.

KEY WORDS: tumor cell invasion, TIMP-1, NM23, RNA levels, gliomas.

*Análise transcricional dos genes TIMP-1 e NM23 na invasão celular em astrocitoma difuso e glioblastoma multiforme (Resumo). Tese de Doutorado. Universidade Federal de São Paulo, EPM/UNIFESP (Área: Ciências, Neurocirurgia). Orientador: Fernando Patriani Ferraz.

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CLINICAL AND GENETIC EVALUATION OF EIGHT BRAZILIAN FAMILIES WITH SPINOCEREBELLAR ATAXIA TYPE 10 (ABSTRACT)*. **THESIS. CURITIBA, 2004.**

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Spinocerebellar ataxia type 10 (SCA10) is an autosomal dominant ataxia caused by an expansion of a pentanucleotide (ATTCT) repeat in an intron of the SCA10 gene on chromosome 22. SCA10 has been previously reported only in Mexican families, in which the disease presented with a unique combination of pure cerebellar ataxia and epilepsy. So far, SCA 10 has not been reported in a non-Mexican population. Thus, this may very well be the first description of SCA 10 series outside Mexico.

We report on 47 patients with the SCA10 mutation on 8 new Brazilian families. All patients showed pure cerebellar ataxia without epilepsy, suggesting a different phenotype of the SCA 10 mutation in Brazilian families, when compared to their Mexican counterparts.

Cerebellar ataxia (gait ataxia, dysarthria and nystagmus) was seen in all Brazilian patients, whereas sac-

cadic eye movement dysmetria was present in 76.6% of this population. Brisk deep tendon reflexes and lower limbs spasticity were observed in 10.63% and 6.38%, respectively. Peripheral neuropathy was not diagnosed in the Brazilian series.

Patients became symptomatic at the mean age of 35 years old and their illness last an average of 13.59 years.

Neuroimaging studies displayed signs of cerebellar atrophy in all cases. Molecular genetic studies showed an expansion repeat (ATTCT) on gene SCA 10, between 1350 and 2370, with an average of 1820. A correlation between age of clinical onset and type of expansion could be clearly established, as follows: the earlier the clinical onset, the longer the expansion ($r=0,44$, $t=2,5$). There is a difference between the average size of expansions in Brazilian (1820) and Mexican (2838) families.

Comparison between SCA 10, SCA 3 and other SCA

patients revealed distinguished clinical features. In SCA 10 cases the phenotype is rather peculiar, including pure cerebellar ataxia and saccadic eye movement dysmetria. SCA 3 patients, on their turn, show cerebellar ataxia, oph-

thalmoplegia, diplopia, eyelid retraction, facial fasciculation, pyramidal signs and peripheral neuropathy.

KEY WORDS: spinocerebellar ataxia type 10, autosomal dominant cerebellar ataxia, pure cerebellar ataxia.

* Avaliação clínica e genética de oito famílias brasileiras com ataxia espinocerebelar tipo 10 (Resumo). Tese de Doutorado. Universidade Federal do Paraná (Área: Medicina Interna). Orientador: Lineu César Werneck.

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GROUP PHYSIOTHERAPY IMPACT OF QUALITY OF LIFE IN HEMIPARETIC PATIENTS WITH STROKE.(ABSTRACT)*. **THESIS. SÃO PAULO, 2004.**

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Background and Purpose. Stroke is the disease that disables the most people in the world, influencing in a very unfavorable way the quality of life of the patients and their relatives. Therefore, physiotherapy must be part of their recovering process, and can be in a group.

Objective. To verify and compare the effects of the group physiotherapy on a health-related quality of life and on the activities of daily living (ADL) of hemiparetic patients with ischemic stroke in the acute phase of the disease to the effects on patients who received an individualized physiotherapy.

Method. The clinical trial study with randomized allocation was the method used. We included patients treated at the Physiotherapy Service of the outpatient Department of Neurology of the São Paulo Federal University – Paulista Medicine School, from January 2001 to December 2003, aged over 21 years, with hemiparesis caused by ischemic stroke in the territory of middle cerebral artery, after hospital discharge, within 30 days of the stroke, and that could count on a relative or a helper to participate in the physiotherapy sessions, agreeing to and signing a document of free and explained consent to participate in the study. The patients were sequentially allocated in study groups of 2 patients (to receive group physiotherapy) or 1 patient in the control groups (to receive individualized physiotherapy) respectively. Then they were paired according to the initial Barthel Index Score below 85 points to enable comparative analysis between the groups. The evaluation instruments employed included the Barthel Index (BI) and the Stroke Impact Scale (SIS), and were applied before and after the physiotherapy. The therapy was similar to both study group and control group, was ministered by the same physiotherapeutic in 24 weekly sessions (in consecutive weeks), of 60-minute duration each, and uti-

lized the functional kinesiotherapy based on the American Physical Therapy Association guide.

Results. A total of 157 patients participated in the study, with a drop out of 8% loss, including 145 patients (88 from the study group and 57 from the control group) who improved significantly in all evaluation variables of the BI and the SIS. We paired a total of 56 patients (16 from the study group and 40 from the control group) and the comparative results didn't show a significant difference in the improvement in the BI and SIS between the groups, except for the dimension mobility of SIS, in which we detected better improvement in the control group patients.

Conclusion. Group physiotherapy for hemiparetic patients from ischemic stroke during the acute phase of the disease, improved the health-related quality of life, evaluated with the Stroke Impact Scale (strength, mobility, hand function, activities of daily living and instrumental activities of daily living, memory, communication, emotion, handicap and stroke recovery), perceived by the patient himself, and improved the ADL, evaluated with Barthel Index under the physiotherapeutic evaluation. The impact of group physiotherapy on stroke patients in the acute phase was similar to the individual physiotherapy, except for the mobility, which according to the patient's perspective was better developed during the individualized physiotherapy. Group physiotherapy can be considered a valuable therapeutic strategy for physiotherapy services with a huge demand and/or physiotherapy programs which want to address aspects connected to the quality of life of stroke patients, beyond the physical ones.

KEY WORDS: group physiotherapy, stroke, quality of life, rehabilitation, clinical trial.

* Impacto da fisioterapia em grupo na qualidade de vida de pacientes por acidente vascular cerebral isquêmico. (Resumo). Tese de Doutorado. Universidade Federal de São Paulo – Escola Paulista de Medicina (Área: Neurologia). Orientador: Alberto Alain Gabbai. Co-orientador: José Osmar Cardeal

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