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Abstracts de trabajos presentados en congresos internacionales 2013

DEPARTAMENTO DE OTORRINOLARINGOLOGÍA

ASSOCIATION FOR RESEARCH IN OTOLARYNGOLOGY (ARO) 36TH MIDWINTER MEETING – BALTIMORE, EEUU

CYTOARCHITECTURE AND PARVALBUMIN IMMUNOREACTIVITY OF THE AUDITORY CORTEX IN THE CHINCHILLA

Natalia Jara, Romina Falcon, Constantino Dragicevic, Jose Luis Valdes, Paul H. Delano

Background: Although chinchillas (Chinchilla laniger) have been widely used as a model to study middle ear and cochlear anatomy, there are relatively few studies focused on auditory cortex morphology. The bifurcation of the middle temporal artery has been proposed as a vascular landmark to identify primary auditory cortex in chinchillas. In addition neuronal responses to brief tones with a latency <15 ms, have been postulated to be generated in the primary auditory cortex of chinchillas. Here, we measured auditory cortex evoked potentials and correlate these findings with cytoarchitecture (Nissl) and parvalbumin immunoreactivity of the auditory cortex. Methods: Ten adult chinchillas were anesthetized and placed in a stereotaxic frame inside a sound attenuated room. Macroscopic vascular landmarks were measured from bregma. An electrophysiological characterization of the auditory cortex was performed using tones at different frequencies (1-8 kHz) and intensity levels (20-80 dB SPL). An electrolytic cortical lesion was made by a current pulse (1 mA for 15 s) throughout the recording electrode and the cytoarchitecture (Nissl) and immunohistochemistry with Parvalbumin were evaluated. Results: The bifurcation of the middle temporal artery was found in 8 animals, located in average at: 2.6 ± 0.9 mm (X axis), 10.0 ± 1.9 mm (Y axis), and 3.9 ± 1.3 mm (Z axis) as measured from bregma. The response latency of this brain position was shorter than 15 ms only in three animals. The average cortical thickness of sites with latencies < 15 ms was 2070±119µm, while that of sites with latencies between 15-20 ms was 2230±279µm ($p>0.05$). Both auditory cortices were thicker than parietal sensory cortex (1395±187µm; $p<0.001$). These thickness differences were mainly due to thicker layers V and VI in both auditory fields ($p <0.01$). The density of parvalbumin (+) neurons was similar in parietal and auditory cortex exhibiting higher counts in layers IV and V. Conclusion. The primary auditory cortex of the chinchilla was located in the bifurcation of the middle temporal artery in 30% of the experiments. A noticeable featur e of the chinchilla auditory cortex was its thickness around 2 mm, which depends mainly on thick layers V and VI. Parvalbumin (+) immunoreactivity was found mostly in layers IV and V. To guarantee the exact location of the primary auditory cortex in chinchillas, electrophysiological confirmation is needed in every experiment.

CORTICOFUGAL SLOW EFFECTS OF AUDITORY CORTEX ELECTRICAL MICROSTIMULATION ON COCHLEAR RESPONSES IN THE CHINCHILLA

Constantino Dragicevic, Natalia Jara, Gonzalo Terreros, Paul H Delano

Background: The auditory efferent system comprises descending pathways from the auditory cort ex to the cochlea, including the cortico-collicular and the olivocochlear system. The electrical stimulation of the medial olivocochlear fibers produces two types of effects with different time scales: (i) fast (tens of milliseconds) and (ii) slow effects (tens of seconds). Whether these two types of effects could also be obtained by electrical stimulatio n of the auditory cortex is unknown. Here, we recorded cochlear

microphonics (CM) and auditory-nerve compound action potentials (CAP) previous, during and after auditory cortex microstimulation and found slow but not fast corticofugal modulations. Methods: CAP and CM responses were recorded using a right round-window electrode. Cortical evoked potentials were obtained from a Nichrome® electrode positioned in the left auditory cortex of nine anesthetized chinchillas (ketamine/xylazine). Trains of four electrical pulses (0.25 ms each, separated by 2.2 ms) were delivered to the auditory cortex at different rates (1-33 Hz) and current intensities (1-100 μA), during one to five minutes, using an isolated pulse generator (2100, AM-Systems®). Tone bursts were presented at different frequencies (0.5-8 kHz) and intensities (20-90 dB SPL) using a Tucker-Davis-Technologies® system III hardware and ER-2 (Etymotic Research®). Data was acquired using a National Instruments® Board (NI-6071E). Results: Auditory-cortex microstimulation produced significant changes in the amplitude of CAP and CM in fiveexperiments. Of these, three (two) showed decrements(increments) of both potentials, 2.3 (2.7) and 2.6 (0.9) dBon average for CM and CAP, respectively. Only one showed modulations going in opposite directions, 1.5 and - 8.6 dB for CM and CAP, respectively. These corticofugalmodulations appeared only after three to five minutes of electrical stimulation. In addition, these effects wereobtained only using microstimulation rates higher than 30Hz. Conclusion: Different to olivocochlear electrical stimulation, auditory-cortex electrical microstimula tion in the chinchilla produced only a slow modulation of cochlear responses that builds up after three to five minutes. These results suggest that fast olivocochlear modulations are restricted to brainstem circuits, while slow efferent modulations are present from the auditory cortex to the cochlea.

2ND MEETING OF EUROPEAN ACADEMY OF ORL – NIZA, FRANCIA

SINONASAL FOREIGN BODY: PRESENTATION OF THREE CASES.
Rodolfo Nazar, Alfredo Naser, Natalia Cabrera, Cecilia Machiavello

Sinonasal foreign bodies are rare clinical entities, requiring a high index of suspicion for diagnosis. The diagnosis is based on the radiological findings and the clinical context of a unilateral rhinosinusitis in adults. Its etiology is divided into two groups, odontogenic and non-odontogenic, so with the advent of implantology the odontogenic cases have progressively increased. Their presence in the sinuses can cause several complications, so its removal is always indicated. We present three clinical cases with different sinonasal foreign bodies. First case, a 67-year-old man presented with bilateral maxillary pain, nasal obstruction and intermittent purulent rhinorrhea for the last three years. He had undergone several surgeries for dental implants. On computed tomography (CT), three dental implants were identified in both maxillary sinuses. Second case, a 60-year-old man presented with recurrent rhinosinusitis for several years. He had undergone nasal surgery due to ozena. On CT, the calcificated plastic grafts for ozena surgery were identified. Third case, a 35-year-old man consulted by the finding of a nail in paranasal sinus radiograph associated with purulent rhinorrhea. The three patients were successfully treated with transnasal endoscopic surgery for removal of foreign bodies, in the Clinical Hospital of Universidad de Chile.

DEPARTAMENTO DE CIRUGÍA

INTERNATIONAL SURGICAL WEEK - HELSINKI, FINLANDIA

TECHNIQUE FOR LAPAROSCOPIC TOTAL GASTRECTOMY FOR MULTIFOCAL CARCINOID TUMOR
M. Musleh, I. Braghetto, E. Lanzarini, C. Domínguez

Introduction: Total gastrectomy is a procedure performed by open surgery, for bening and malignant disease, with good results in specialized centers. In recent years, laparoscopic techniques have been in creasingly incorporated formore complex procedures. Material and Methods: This video shows the technique of laparoscopic total gastrectomy for gastric carcinoid tumor. Case: Malepatient 47, with pernicious anemia diagnosed 15 years ago and recently a multifocal gastric carcinoid, was found during endoscopy, confirmed with biopsy. PET-CT without pathological over expression of somatostatin receptors. For this reason it was decided to perform laparoscopic total gastrectomy. Results: Technique: pneumoperitoneum is performed with veress needle as usually, five trocars are introduced (5, 11,12mm), it begins with the dissection, starting with skeletonization of the great ercurvature from thepylorus to theangle of Hiss, right gastric artery division and transection of the duodenum with stapler, disecction of smaller curvature, up to fully release the abdominal esophagus; stapler is fired above the gastroesophageal junction. Reconstruction is performed with Roux–en-Y gastrojejunostomy using Brazilian technique, first performing a manually end-side esophago-jejunostomy with resorbable mono filament suture. Subsequently side to side jejuno-jejunostomy is performed using stapler device, resulting

a alimentary limb of approximately 1 mt. Methylene blue test to assess hermeticity of both anastomosis was performed, then a stapler transection between both anastomosis, forming the Roux in Y. In this surgery omentectomy, and lymphadenectomy was not performed. There were no incidents during the procedure, the operating time was 3,5hrs. The postoperatuve evolution was uneventfully, control anastomosis is performe don the 5th day, no evidence of leakage, with good barium transitto the distal jejunum. Therefore was discharged on day 7 postoperatively. No morbidity was detectedatlate controls. Conclusions: This technique could be an option for total gastrectomy.

HIATAL HERNIA: WHICH IS THE BEST MOMENT FOR SURGICAL TREATMENT?

I.F. Braghetto, O. Korn, H. Valladares, M. Musleh, A. Saure

Introduction: The literature shows the controversy between the expectant medical treatment versus surgical treatment, as to which is the best option depending on the presence or absence of symptoms.Material and Methods: This prospective study presents the results obtained by our group considering the time of disease evolution and postoperative results including 121 patients divided by age, duration of symptoms and type and size of hiatal hernia and postoperative outcomes after laparoscopic hiatal hernioplasty. Patients were followed up at least for 5 years. Results: In this serie, 32% of patients younger than 70 years and 68% of older patients more than 71 years had symptoms of long time, more than 11 years. ($p<0.05$). Type IV hernias (complex) and larger than 16cm. in diameter were observed in the group with a longer time of symptoms and age. Complications were observed more frequently the older age group, patients with more prolongued duration of symptoms or in patients with type IV complex hernias. There was no postoperative mortality and only 1 patient (0.8%) with type III hernia and severe oesophagitis should be re-operated. Conclusions: Patients with hiatal hernia should be operated at the time of diagnosis in order to avoid complications. Older patients should not be excluded from surgical indication but should be evaluated in full multidisciplinary way in order to avoid complications and postoperative mortality.

TIPS FOR THORACOSCOPIC ESOPHAGECTOMY FOR ESOPHAGEAL CARCINOMA

I. Braghetto, G. Cardemil, M. Musleh, E. Lanzarini, H.L. Valladares, G. Fernández

Introduction: Esophageal resection for esophageal cancer has allowed thoracoscopic anatomical dissection, with minimal bleeding, very accurately lymph nodal dissection, less respiratory complicationscompared to open transthoracic or transhiatal approach. However there are critical points during the procedure which are important in order to avoid complications Material and Methods: This video shows the dissection of the esophagus by thoracoscopy and critical points that must be carefully respected Results: The surgical steps are: 1.- Inferior pulmonary vein dissection. 2.- Separation of aorto-esophageal plane 3.- Lymphadenectomy 4.- Dissection of azygos vein. 5.- Separation of the upper thoracic esophagus from the trachea. Conclusions: Proper patient selection, according to the staging of the disease and observation of these critical points can prevent serious complications during the performance of the technique.

UNIDAD DE TRASPLANTE

19TH ANUAL INTERNATIONAL LIVER TRANSPLANT SOCIETY – SYDNEY, AUSTRALIA

GRAFT SURVIVAL IN PATIENTS UNDERGOING ORTHOTOPIC LIVER TRANSPLANTATION AT THE HOSPITAL CLINICO UNIVERSIDAD DE CHILE.

Juan Pablo Miranda, Danny Oksenberg, Jaime Poniachik, Jose Ibarra, Angelica Borquez, Jaime Castillo, Gonzalo Cardemil, Juan Carlos Diaz.

Introduction: Orthotopic liver transplantation (OLT) has become an effective procedure for patients with advanced liver disease, reporting a survival rate between 70% - 80% at 36 months. In our country there are few publications in relation to graft survival in OLT. Aim: To evaluate the survival post OLT at the Hospital Clinic, University of Chile. Material and Methods: A retrospective study of demographic and clinical variables of patients undergoing OLT at the Hospital Clinico Universidad de Chile, by creating a standardized database and subsequent application of survival analysis and a model Cox proportional hazards Results: We evaluated 195 OLT performed during the period 2002-2012, there was a 56.4% male patients, mean age was 53.5±10.8 (21-68) years old, median graft survival time was 72.9 months. The use of cyclosporine compared to tacrolimus as primary immunosuppressant was associated with an increased prevalence of infections (24.5% v/s 8.7%) and moderate and severe graft rejections (17.4% v/s 9.2%),

p <0.0002. It adjusted a risk function that showed the higher risk profile for graft failure corresponds to patients with a pre-OLT MELD score ≥ 28 points, HR 5.2 (2.5 – 15.3). Conclusions: Immunosuppression based in Tacrolimus is the better treatment than cyclosporine and the main risk factor for graft loss are patients with a score pre-OLT MELD more than 28 points.

IMMUNOSSUPRESSION AND MORTALITY RISK FACTORS ASSOCIATED IN LIVER TRANSPLANTATION CHILEAN PATIENTS.

Juan Pablo Miranda, Jaime Poniachik, Danny Oksenberg, Jose Ibarra, Angelica Borquez, Jaime Castillo, Gonzalo Cardemil, Juan Carlos Diaz.

Introduction: Orthotopic liver transplantation (OLT) has become an effective procedure for patients with advanced liver disease, In our country there are not publications in relation the risk factors involved in graft survival in OLT. Aim: To evaluate the immunosuppression risk factor involved in graft survival in OLT at the Hospital Clinic, University of Chile. Methods: From 2002 to 2012, 195 liver transplantation from cadaveric donors were performed at the Hospital Clínico Universidad de Chile. 172 (88.2%) received CsA-me or generic tacrolimus (T-Inmun®) as primary immunosuppression. We evaluated clinical variables, risk factors and the survival of these patients. Results: 42.6% (83) received CsA-me and 45.6% (89) received Tac. Median age was 53.5±10.8 (21-68) years old, not differences for sex. Causes for transplantation in CsA-me group was HCV 37.5%; NASH 15.7%; alcoholic cirrhosis 14.5%; cryptogenic cirrhosis 10.8%; other 25.3% and in the Tac group: NASH 29.2%; alcoholic cirrhosis 14.6%; autoimmune hepatitis 14.6%, cryptogenic cirrhosis 13.5%; and other 28.1% (p=ns). Graft Survival analysis of group CsA-me were 83%,68% and 55% at 1,3 and 5 year, respectively, on group Tac were 89%, 70% and 56% respectively (log rank p<0.0001). The risk factor associated to mortality was hematocrit and hemoglobin difference between the time of registration on the waiting list and OLT of 2 % points and 0.7 g/dl, HR 2.9 (1.3 - 4.5) and 2.6 (1.1 - 3.8) respectively. The infections (24.5% v/s 8.7%) and moderate and severe graft rejections (17.4% v/s 9.2%), were more frequent at CsA-me group (p<0.0002). No Differences in acute kidney failure and de-novo insulin-requiring diabetes mellitus were seen. Conclusion: The hematocrit and hemoglobin difference between the time of registration on the waiting list and OLT was a risk factor associated to mortality. Tac has superior to CsA-me in improving survival (patient and graft) and preventing acute rejection in OLT.

FIVE YEAR SURVIVAL ANALYSIS AFTER LIVER TRANSPLANTATION IN CHILEAN PATIENTS RECEIVING ORIGINAL CYCLOSPORINE OR GENERIC TACROLIMUS AS PRIMARY IMMUNOSUPPRESSION. PRELIMINARY ANALYSIS.

Sylvia Marquez, Juan Pablo Miranda, Camila Tagle.

Introduction: Cyclosporine or tacrolimus are widely used as primary immunosuppression to prevent rejection in liver transplant recipients. Both are calcineurin inhibitors but with different immunosuppression potency and some differences in their secondary effect profile. In Chilean liver transplantation patients, the implications of these differences are not assessed. Aim: We evaluated results and survival from a prospective trial that compared cyclosporine microemulsion (CsA-me) and Tacrolimus (Tac) for primary immunosuppresion. Methods: From 1995 to October 2012, 25 liver transplantation from cadaveric donors were treated in the Hospital Barros Luco. 24 (96.0%) received original CsA-me (Neoral®) or generic tacrolimus (T-Inmun®) as primary immunosuppression. We studied demographic and clinical variables. Results: 17 (70.8%) patients receiving CsA-me and 7 (29.2%) received Tac. Median age was 49.2±15.6 (15 - 67) years. Causes for transplantation in CsA-me group was: HCV 41.2%; cryptogenic cirrhosis 17.6%, alcoholic cirrhosis 11.8%; autoimmune hepatitis 11.8%, other 17.6% Tac group was: cryptogenic cirrhosis 28.6%, autoimmune hepatitis 28.6%; alcoholic cirrhosis 14.3%, NASH 14.3%; Other 14.3%. At survival analysis group CsA-me presented 1 and 5 year patient survival were respectively 94.1% and 87.8, on group Tac were 100% and 100% (log rank test p=0.04). The most frequent complications were infections (33%) and biliary stenosis (25%). Conclusion: In the Chilean population generic tacrolimus would not inferior to cyclosporine microemulsion at 5 year graft survival, further study is necessary to find definitive conclusions.

TACROLIMUS VERSUS CYCLOSPORINE IN ELDERLY LIVER TRANSPLANTATION CHILEAN PATIENTS.

Juan Pablo Miranda, Jaime Poniachik, Danny Oksenberg, Jose Ibarra, Angelica Borquez, Jaime Castillo, Gonzalo Cardemil, Juan Carlos Diaz.

Introduction Almost every liver transplant recipient takes either cyclosporin or tacrolimus to prevent rejection of the graft. There are no evaluated immunosuppression to prevent rejection in liver transplant recipients in elderly patients. Aim: To compare the survival from a prospective trial that compared Tacrolimus (Tac) and cyclosporine microemulsion (CsA-me) for primary immunosuppresion in elderly patients. Method: Descriptive study, from 2002-2012, in elderly patients. 195 liver transplantation from cadaveric donors were performed in the Hospital Clínico Universidad de Chile. 57 OLT patients were elderly (Age ≥ 60). 48 (84.2%) patients received

CsA-me or generic tacrolimus (T-Inmun®) as primary immunosuppression. We show a survival analysis of these patient. Results: Median age was 63.8±2.3 (60-68) years, 29 male (60.4%). Patients were analized into 2 groups: Cyclosporine (C) and Tacrolimus (T). Median age without differences. Transplant etiology: 31.3% NASH, 18.8% hepatic cirrhosis due to HCV, 18.8%alcoholic hepatic cirrhosis and 31.3% other. Group C received a cyclosporine dose of 15 mg/k/day, divided into two oral doses every 12 h, with dose adjustments based on C2 plasma levels between 800-1200 ng/ml at the early period (1-3 months). Group T received a Tacrolimus dose of 0,05 to 0,15 mg/kg/day, divided into two oral doses every 12 h, and adjusting doses in order to maintain T trough plasma levels between 10-15 ng/ml, at the early period (1-3 months). Each group also received steroids with or without mycophenolate mofetil. No differences were seen between the drugs with respect to acute cellular rejection and adverse events (renal failure, lymphoproliferative disorder, diabetes mellitus). The Survival of C were 90.9%, 59.1% and 31.8% at 1,3 and 5 year respectively, on T were 92.3%, 69.2% and 50.0% respectively ($p<0.0001$). Conclusions: After liver transplantation tacrolimus patients had longer survival than cyclosporine patients. Tacrolimus should be considered the treatment of choice in elderly liver transplantation. It's necessary continue this study for definitive conclusions.

DEPARTAMENTO DE NEUROLOGÍA Y NEUROCIRUGÍA

INTERNATIONAL STEREOTACTIC RADIOSURGERY SOCIETY (ISRS) - TORONTO, CANADA

FIRST RESULTS IN LINAC RADIOSURGERY WITH INTENSITY MODULATION IN THE NATIONAL CANCER INSTITUTE- CHILE.

Zomosa, Gustavo; Fariña, Ariel; Piriz, Gustavo; Banguero, Yolma

INTRODUCTION: In 2009, the INC purchased a VARIAN LINAC radiosurgical facility with a Fast Plan/Eclipse planification system and a OGP navigation system to monitorize inframilimetric movements during the therapy. PURPUSE: To relate our experience with Intensity modulated radiosurgery (IMSRS) ,some fractionated for selected benign and malignant tumors. MATERIAL AND METHODS : 11 patients were treated with IMSRS , 3 of them because of the relative big size for SRS and of their proximity to the organs at risk (OAR) were treated by frameless fraccionated IMSRS : ! skull base meningioma, other breast cancer brain metastasis and a pituitary GH tumor. All patients were followed 24 to 6 months for the last cases. RESULTS: During the therapy there were no severe complication only mild in two and in the later followup only mild ataxia an headache were noticed in skull base tumors. Control with MRI showd tumor control in all case and regression in metastatic tumors. DilSCUSSION & CONCLUSION: IMSRS is a good therapy in selected patients with irregular tumors and in particular when they are close to OAR and there are rather big for SRS to perform fractionated IMSRS but this need to have a navigation system like OGP and a very sofisticated calibration team.

THE INCREASED SUSCEPTIBILITY TO OXIDATIVE DEATH OF LYMPHOCYTES FROM PEOPLE WITH ALZHEIMER'S DISEASE CORRELATES WITH THE SEVERITY OF DEMENTIA AND IS SPECIFIC FOR OXIDATIVE DAMAGE

Daniela P Ponce, Felipe Salech, Monica Silva, Chengjie Xiong, Catherine Roe, Mauricio Henriquez, Nicole Rogers, Andrew Quest, Maria Behrens

Background: We have previously reported an increased susceptibility to cell death of lymphocytes obtained from patients with Alzheimer's disease (AD) when exposed to oxidative stress induced by hydrogen peroxide (H2O2). Herewe investigated whether the susceptibility to H 2 O 2 –induced death was related to the degree of dementia severity. Methods: Lymphocytes were extracted from peripheral blood from 25 AD patients (9 mildmoderate, CDR 1-2; 6 severe, CDR 3) and 10 healthy controls (all 60 years old) and exposed to H 2 O 2 for 20hrs - in the presence or absence of 5 mM 3-aminobenzamide (3-ABA), a PARP-1 inhibitor- or to staurosporine, an apoptosis inducer. Cell death was evaluated by flow cytometry and propidium iodide (PI) staining, whereby viable (PI-negative), apoptotic (PI-positive, hypodiploid) and necrotic (PI-positive diploid) cells were distinguished. Results: The dose response curve of lymphocyte viability in the presence of H2O2 was shifted to the left in AD patients compared to healthy controls, with severe dementia showing the highest vulnerability to H 2 O 2 and those with mild to moderate dementia showing intermediate values; i.e. treatment with 50 m M H 2 O 2 (around LD50) for 20 hrs induced death of 68.1% of lymphocytes from patients with severe dementia, 51.1% of those with mild to moderate dementia, and 34.6% of healthy control lymphocytes. The greater susceptibility to death was due to an increase mostly of apoptosis. Staurosporine, an apoptosis inducer, at concentrations between 0.6 -6mM provoked death to a similar extent in the three groups of patients. As previously shown, H 2 O 2 -induced death

was significantly reduced by PARP inhibition, whereby the extent of protection was less significant in lymphocytes from patients with severe dementia. Conclusions: We confirm our previous results showing that lymphocytes from AD patients are more susceptible to H2O2-induced death, whereby extent of death observed correlated with dementia severity. Moreover, increased susceptibility to death observed for AD lymphocytes was specific for oxidative damage, since no differences between groups were detectable with staurosporine, a kinase inhibitor. These results suggest that measurement of lymphocyte death induced by H 2 O 2 might be exploited to serve as a non-invasive biological marker of the severity of Alzheimer's disease.

TEST YOUR MEMORY SPANISH VERSION (TYM-S): VALIDATION OF A SELF ADMINISTERED COGNITIVE SCREENING TEST
Andrea Slachevsky, Carlos Munoz, Fernando Henrıquez, Carolina Delgado

Background: The TYM (Test Your Memory) is a self administered cognitive screening test which was developed to meet three critical requirements for widespread use by a non-specialist: take minimal operator time to administer, test a reasonable range of cognitive functions, and be sensitive to mild Alzheimer's disease. The aim of this study was to validate the TYM Spanish Version (TYM-S) in a Chilean elderly sample. Methods: After translating into Spanish and adapting to Chilean population, the TYM-S was developed and administered to 30 dementia patients, 14 mild cognitive impairment (MCI) subjects and 30 controls in addition to MMSE and ACE-R-Ch for assessing global cognitive efficiency. Caregivers of dementia patients and collateral sources of MCI and control subjects were interviewed with measures of dementia severity, functional status in activities of daily living and cognitive changes. Convergent validity, internal consistency reliability, cut-off points, sensitivity and specificity for the TYM-S were estimated. Results: Table 1 summarizes the demographic characteristics and clinical profiles of the sample. Regarding convergent validity, the TYM-S showed significant correlations ($p<0.001$) with other cognitive measures (r¼0.902 with MMSE; r¼0.922 with ACE-R-Ch; r¼0.923 with MoCA and r¼0.862 with FAB), a rating for dementia severity (r¼-0.757 with CDR), functional capacity assessments (r¼-0.864 with T-ADLQ; r¼-0.748 with PFAQ and r¼0.769 with IADL Scale) and a measure of cognitive changes (r¼-0.700 with AD8). In terms of reliability, a Cronbach alpha coefficient of 0.776 was obtained. The best cut-off point to distinguish cases of dementia and MCI from control subjects was reached at 40 with a sensitivity of 0.860 and a specificity of 0.862 (Figure 1). Conclusions: The TYM-S showed acceptable psychometric properties, becoming a valid and reliable instrument to assess cognitive impairment. Its diagnostic utility to detect dementia and MCI patients also works very well.

WORLD MUSCLE SOCIETY CONGRESS 2013 – MONTEREY, CALIFORNIA, EEUU

A NOVEL DE NOVO MUTATION IN ACTA1 CAUSES A CONGENITAL MYOPATHY WITH MISLEADING TYPE 1 FIBER PREDOMINANCE AND A PECULIAR MRI.
Castiglioni, C.; Cassandrini, D.; Fattori, F.; Bellacchio, E.; Alvarez, K.; D'Amico, A.; Gejman, R.; Díaz, J.; Santorelli, F.M.; Bevilacqua, J.A.

Nemaline myopathy is a genetically heterogeneous disease showing wide clinical variability. Disease severity and prognosis range from neonatal death to almost normal motor function. We report on a 19-year-old boy with reportedly absence of fetal movements. He was severely hypotonic at birth with dolichocephaly, weak facial movements, bilateral clubfoot and feeding difficulties, requiring nasogastric tube feeding; gastrostomy was applied at age 3months and removed at 12. Motor milestones were delayed: walking at 24months, with marked foot drop. He has always been unable to eat solid foods because of impaired chewing. Since the age of 8 he is on nocturnal BiPAP. A first muscle biopsy of the quadriceps at age 8months, and a second biopsy of vastus lateralis performed at age 10years, both showed variability in fiber diameter, marked type 1 fiber predominance (90%), with neither evidence of endomysial fibrosis nor nemaline bodies. A third biopsy of the right deltoid muscle at age 19 showed marked fibrosis and dystrophic features with proliferation of nemaline bodies. Current neurological examination showed a young intelligent man with nasal voice, generalized weakness, ptosis, and no limitation of ocular movements. The MRI showed marked involvement of glutei muscles, together with involvement of sartorius, tibialis anterior and peroneus longus. Sequencing of ACTA1 in blood DNA detected a novel heterozygous de novo variant. The new mutation affects a highly preserved Threonine. No mutations were detected in SEPN1 and TPM3. We report on a long follow-up in a patient with a congenital myopathy related to a de novo mutation in ACTA1. Of the 3 muscle biopsies performed, the first 2 were not contributory for diagnosis and the clinical presentation did not offer additional clinical clues. The last muscle biopsy performed in adulthood revealed nemaline rods prompting specific molecular investigations and ultimately allowing a genetic diagnosis.

NEUROSCIENCE 2013 – SAN DIEGO, EEUU

SMALL SACCADES AND IMAGE COMPLEXITY DURING FREE VIEWING OF NATURAL IMAGES IN SCHIZOPHRENIA

R. Mayol, J. Egaña, C. Devia, J. Parrini, A. Ruiz, P. Maldonado

Abnormalities in persons affected with schizophrenia encompass a variety of brain cognitive processes, including eye movement's control, which require extensive resources from the brain. Patients display dysfunctions during the execution of simple visual tasks such as anti-saccade or smooth pursuit. In more ecological scenarios, such as free viewing of natural images, patients appear to make fewer and longer visual fixations and display shorter scanpaths. It is not clear whether these measurements reflect alterations in their proficiency to perform basic eye movements such as saccades and fixations or are related to higher-order brain mechanisms, such as visual exploration or attention. We utilized free exploration of natural images of different complexity as a model of an ecological context where normally operative mechanisms of visual control can be accurately measured. We quantified visual exploration, scanpaths, saccades and visual fixation, using the standard SR-Research eye tracker algorithm (SR) and compared this result with a computation that include saccades and microsaccades (EM). We evaluate 8 schizophrenia patients and corresponding healthy controls and tested whether the decrement in the number of saccades and fixations, as well as their increment in duration reported previously in schizophrenia patients, resulted from the increasing occurrence of undetected small saccades. We found that when utilizing the standard SR algorithm, patients display shorter scanpaths as well as fewer and shorter saccades and fixations, showing significant difference with the control group. When we employed the EM algorithm, difference in these parameters between patients and healthy controls were no longer significant. On the other hand, we found that content of images plays an important role in exploratory behaviors. These results contribute to elucidate the mechanisms of visual motor control that are affected in schizophrenia and contribute to the finding of adequate markers for diagnosis and treatment for this condition.

CLINICAL AND GENETIC CHARACTERIZATION OF A COHORT OF 30 CHILEAN PATIENTS WITH DYSFERLINOPATHY

P. A. Caviedes, C. Castiglioni, G. A. Di Capua, L. Woudt, J. Díaz, M. Campero, R. Hughes, P. González-Hormazábal, R. Godoy-Herrera, N. Levy, M. Krahn, L. Jara, J. A. Bevilacqua

Mutations in the dysferlin gene lead to LGMD2B and Miyoshi myopathy among other phenotypes. We describe a cohort of 31 patients, from 25 non-related Chilean families, harbouring point mutations in the DYSF gene. Diagnosis was based on clinical findings or absence of dysferlin in muscle biopsies. Assessment workup consisted of clinical evaluation, Motor Function Measure (MFM) scale, CK level, electrodiagnostic testing, whole body MRI, echocardiogram, spirometry and DYSF gene direct sequencing. Eight mutations were consistently found in the cohort, four of which (c.5979dupA; c.2858dupT; c.2779delG and c.4390G>T) accounted for 82% of the mutations found. In four patients only one mutation was found after complete DYSF gene sequencing. The age at symptom onset ranged from 10 to 33 years (mean 20.8), symptoms manifesting invariably as weakness in the legs, distally (21/31) or proximally (10/31), progressing later to the upper limbs. Mean serum CK level was increased 57(±35) times above normal values. Electrodiagnostic assessment showed normal NCV and repetitive stimulation testing, with distinct degrees and distribution of myopathic changes on needle EMG. Single fibre EMG was normal in six confirmed dysferlinopathy patients. Muscle MRI done in 28/31 patients showed impairment with a similar distribution in all patients despite clinical phenotype. Spirometry showed a mild restrictive defect in 3/18 patients at late stages of disease. Echocardiogram performed in 23/31 patients was within normal range. The clinical spectrum of dysferlinopathy in the series is in agreement with similar cohorts reported. The relative high frequency of some mutations suggests a founder effect for such mutations in the Chilean population. We therefore propose to evaluate the effect these recurrent mutations in vesicle trafficking and cell membrane fusion events, using in vitro cell models such as the RCMH human muscle cell line, muscle primary cultures and myogenic cell lines from patients. We will pay special consideration to prevalent Chilean mutations. Regarding the association of dysferlin with the dihydropyridine receptor and proteins such as annexins and AHNAK that are involved in actin organization, we will also evaluate the role of dysferlin in calcium signals and cortical actin organization.

XXI WORLD CONGRESS OF NEUROLOGY – VIENA, AUSTRIA

SURVIVAL OF INTRACEREBRAL HEMORRHAGE IN CHILE. A POPULATION BASED REGISTER

V. Diaz, I. Delgado, S. Illanes, J. Antinao, V. Olavarria, D. Carcamo, P. Lavados

Background: The average incidence of intracerebral hemorrhage (ICH) is 25 per 100,000 inhabitants in the world; in Chile is 20 per 100,000. The mortality of hemorrhagic stroke is between 30 and 45%. Objective: To stud intrahospitalary mortality and survival of ICH through the country. Method: Is a descriptive and ecological study of national discharge database from 2003 to 2007 from

ICD-10 category I 61.0 (0 to 9) and I 62.9 of the National Health Ministry (MINSAL) and National Socioeconomic Survey (CASEN). A survival analysis estimated long term survival. Kaplan – Meier survival curves and Cox proportional hazard models were used to demonstrate predictors. Result: 13,256 registered and 10,267 persons were identifi ed, 93.6% had only one event. 37% died during the hospitalization, 44% the first day and 70% before five days. The survival is higher in female tan in male (p = 0.02). The higher case-fatality rates are in IV, VI, VIII and Metropolitan regions (≥ 40 per 100,000). The lethality has been decreasing from 42.6% to 36.4%. The correlation of lethality rates was only with poverty (r = 41%, p = 0.0001). Conclusions: The lethality was decreasing during the study period. Most of the patients died during the first five days, survival is higher in women.

DEPARTAMENTO DE PSIQUIATRÍA Y SALUD MENTAL

68TH ANNUAL SCIENTIFIC CONVENTION AND MEETING OF SOCIETY OF BIOLOGICAL PSYCHIATRY – NUEVA YORK, EEUU

BDNF PLASMA LEVELS OF SCHIZOPHRENIC PATIENTS CLASSIFIED ACCORDING TO THEIR COGNITIVE FUNCTION IN COMPARISON TO HEALTHY SUBJECTS

Rodrigo Nieto, Hernan Silva, Manuel Kukuljan, Cecilia Rojas, Alejandra Armijo, Ruben Nachar, Alfonso Gonzalez, Carmen Paz Castaneda, Cristian Montes, Cristian Aguirre, Daniel Castillo, Andrea Silva

Background: Schizophrenia is characterized by positive, negative, cognitive and affective Symptoms. Cognitive symptoms are important because they are significantly related to quality of life. Despite the relevance of cognitive symptoms, the study of the biological basis of this deficit is still insufficient. Several studies have linked BDNF not only to the pathogenesis of schizophrenia, but also to neuronal plasticity, learning, and memory. Methods: We measured BDNF plasma levels with ELISA in 20 subjects, 14 schizophrenia patients and 6 control group subjects, and we evaluated cognitive functioning with the Montreal Cognitive Assessment (MOCA). Results: We found significantly lower BDNF plasma levels in schizophrenia patients (2.1 ng/ml) in comparison to control subjects (3.2 ng/ml) (p = 0.03). We classified schizophrenia patients into two subgroups according to their performance in MOCA, and found that patients with a normal cognitive evaluation had significantly lower BDNF plasma levels (1.6 ng/ml) than control subjects (p = 0.02), but patients with cognitive deficit had no significant differences in BDNF levels (2.6 ng/ml) in comparison to controls (p = 0.27). Conclusions: Consistent with prior reports, BDNF plasma levels were lower in schizophrenic patients than in healthy subjects. However, the finding of lower BDNF levels in the subgroup of patients with a normal cognitive evaluation, instead of as expect in the subgroup with cognitive deficit, has not been previously reported and may add new information on the role of BDNF in schizophrenia.

WPA INTERNATIONAL CONGRESS 2013 – VIENA, AUSTRIA

SMALL SACCADES AND IMAGE COMPLEXITY DURING FREE VIEWING OF NATURAL IMAGES IN SCHIZOPHRENIA – PRELIMINARY RESULTS

Egaña J, Devia C, Mayol R, Parrini J, Orellana G, Ruiz A, Durán E, Maldonado P.

In schizophrenia, dysfunctions have been reported during visual tasks. In more ecological scenarios patients appear to make fewer and longer visual fixations and display shorter scanpaths. It is not clear whether these measurements reflect alterations in their proficiency to perform basic eye movements or relate to high-level mechanisms. We utilized free exploration of natural images as a model of an ecological context. We quantified visual exploration, scanpaths, saccades and visual fixation, using the SR-Research eye tracker algorithm (SR) and compared this result with a computation that include small (micro) saccades (EM). Initially, we evaluated 8 patients and 8 healthy controls (HC) and tested whether the decrement in the number of saccades and fixations, as well their increment in duration resulted from the increase occurrence of undetected small saccades. We found that when utilizing SR algorithm, patients display shorter scanpaths as well as fewer and shorter saccades and fixations. When we employed the EM algorithm, difference in these parameters between patients and HC were no longer significant. We found that image complexity plays an important role in exploratory behaviors, demonstrating that this factor explain most of differences between eyemovement behaviors in schizophrenics. These results contribute to find biological markers in schizophrenia.

RELATIONSHIP BETWEEN IMPULSIVITY AND ATTENTION IN BORDERLINE PERSONALITY DISORDER

Silva H, Villarroel J, Jerez S, Montes C, Montenegro M, Bustamante M.

Introduction: Although impulsivity and attention have been studied extensively in various mental disorders, is not yet well established the relationship between these functions in subjects with borderline personality disorder. Objective: The main objective of this study

is to assess whether there is a correlation between impulsivity and attention in subjects diagnosed with borderline personality disorder, compared with healthy volunteers. Methods: We performed a case-control study, enrolling 14 subjects with borderline personality disorder diagnosed by SCID II, without current Axis I pathology, excluded with SCID I. The control group was confirmed by 16 healthy volunteers of similar demographic characteristics, mental disorders was ruled out with SCID I and SCID II. Were excluded subjects with medical conditions or who were taking medications at the time of the evaluation. We applied Barratt Impulsiveness Scale (BIS-11) and a computerized continuous performance test (CPT). It was performed parametric and nonparametric test and multiple regression analysis. Results: We found higher impulsivity and lower performance on attention in borderline personality disorder subjects, noting that in this group show marked deficits in performing CPT even those subjects wi.

WORLD MENTAL HEALTH CONGRESS 2013 – BUENOS AIRES, ARGENTINA

INTERVIEW WITH RESPECT TO TRATORNOS PERSONALITY: PROPOSITION OF A MATRIX

M. Angelica Montenegro Medina, Claudia Ornstein Letelier, Patricia Tapia Ilabaca

The large spectrum of psychopathology is Personality Disorders, which makes it difficult to gather reliable information that accounts of what happens to the patient. Jaspers points out that self-observation is an excellent source of knowledge to explore the psychic life. Because patients with personality disorders especially borderline spectrum have low capacity for introspection by the powers deposited in the environment, the process of defining symptoms is difficult. Hence there is a need to collate information, validating it with third parties regarding the member closest index.

THE TASK AND ITS MEANING FROM THE MODEL OF HUMAN OCCUPATION

M. Angelica Montenegro Medina, Claudia Ornstein Letelier, Patricia Tapia Ilabaca

Occupational Therapy (OT), discipline supported by the humanistic model, must put human beings first and foremost integrating skills, weaknesses, interests. Key TO occupational balance is treated as harmonic distribution of time as to the discharge of a person. Find that subjects perform satisfactorily in meaningful tasks. Each person will be a potential agent to choose and engage in an occupation protagonist feeling. Based on this model, we invited 44 patients to complete admission trasvasijar from the work performed, meaning that they represented what they were doing.

DEPARTAMENTO DE DERMATOLOGÍA

8TH WORLD CONGRESS OF MELANOMA, EUROPEAN ASSOCIATION OF DERMATOLOGY (EADO) – HAMBURGO, ALEMANIA

BASAL CELL CARCINOMA OF THE FACE AND SCALP: ANALYSIS OF THE LOCATION, GENDER AND HISTOLOGICAL TYPE OF PUBLIC HOSPITALS CONSULTING POPULATION IN CHILE

Zemelman V., Yagnam M., Valenzuela C.

Question: Which is the anatomical distribution of basal cell carcinoma according to sex and histological aggressiveness in public hospitals consulting population in Chile? Methods: A total of 1732 (958 females, 774 males), basal cell carcinoma from 4 state hospitals from Santiago, Chile (2005–2009) was studied. The analyzed subsides were: scalp, forehead, eyelid, eye zone, ears, left cheek, right cheek, middle face and chin. Micronodular, Morpheiform and Metatipical histological subtypes were classified as aggressive and Superficial, Keratotic, Adenoid, Nodular were classified as non-aggressive histological subtypes. The statistical analysis was performed by the Chi square test. Results: We observed a highest frequency of basal cell carcinoma in middle face (42.8%) followed by forehead (11.3%), eyelid (10%), ears (7.5%) scalp (4.21%) and chin (1.85%). Conclusion: Results are mainly in agreement with those obtained in other populations reported in the international literature; the basal cell carcinoma distribution in the head is related to ultraviolet radiation exposure of each anatomical site. Regarding the gender, the frequency of basal cell carcinoma was higher in females than in males in all anatomical locations within the face. In the scalp, males showed a higher proportion of basal cell carcinoma. Regarding the aggresitivity of the tumours, no differences within the locations were observed. Also, non-aggressive histological tumors were higher in frequency in all locations within the head. This investigation helps to identify the possible risk zones of basal cell carcinoma within the face and scalp in the Chilean population.

MALIGNANT MELANOMA IN CHILE. DIFFERENT SITE DISTRIBUTION BETWEEN PRIVATE AND STATE PATIENTS

Zemelman V., Yagnam M., Valenzuela C., Sazunic I., Brant M., Araya I.

Question: How is the site distribution of malignant melanoma in private and state patients in Chile? Methods: Records of 1148 cases of malignant melanoma, 575 cases from state hospitals (Low Socioeconomic Strata) and 573 cases from private clinics (High Socioeconomic Strata) were analysed by body site. Results: Comparing both strata, females from low socioeconomic strata showed a higher number of malignant melanoma in soles, cheeks, and in eye area. Furthermore, females from the high socioeconomic strata showed a higher number of malignant melanoma in dorsal foot and dorsal hand. Comparing males from both strata, males from low socioeconomic strata showed a higher number of malignant melanoma in soles, eye area, and cheeks. However, males from high socioeconomic strata showed a higher number of malignant melanoma in trunk and in arms. Conclusion: Chilean populations from the high and low socioeconomic strata showed differences in the distribution of malignant melanoma by site. Furthermore, gender differences in the proportion of malignant melanoma analysed by anatomical site is different in both strata. Genetics factors, sun exposure, or other environmental or cultural factors of both populations may explain these differences. These results are important since the clinical behavior and etio-pathogenesis of MM are related to anatomical sites.

SCALP ECCRINE POROCARCINOMA ARISING IN NEVUS SEBACEOUS OF JADASSOHN

F Mardones

Nevus sebaceous of Jadassohn (NSJ) is a cutaneous hamartoma usually located in the scalp and may contain epidermal, follicular, sebaceous, apocrine and eccrine elements. Up to 15 percent of them may develop benign or malignant tumors, most commonly syringocystoadenoma papilliferum, trichoblastoma and basal cell carcinoma. Although surgical removal is indicated, the timing of excision is controversial, since malignant degeneration is rare before puberty. Localized enlargement and ulceration suggest malignant transformation in a preexisting NSJ. In this case report, an unusual porocarcinoma (PC) developed within a long standing scalp NSJ. A 35 year old healthy man consulted for a rapidly growing tumor in his scalp. He had this lesion since childhood, but in the last 4 months, a nodule had grown in one of its margins. Physical examination showed a 1.5 by 1.1 cm. yellowish - orange irregular alopecic plaque in the left parietal area. Complete surgical excision was performed and histopathology informed marked epithelial hyperplasia, prominent sebaceous glands together with small and rudimentary hair follicles, suggestive of the NSJ. In the same sample, multiple intraepidermal nests of poroid cells were observed, with atypia, pleomorphism, necrosis that also extended into the dermal stroma. These findings indicated a PC. Eccrine PC is uncommon and develops from intraepithelial or upper dermal acrosyringium of eccrine sweat glands. It may develop as a primary tumor or from malignant transformation of eccrine poroma. Less than 5% of them are reported in the scalp and it has the potential to disseminate locally and systemically. The treatment of choice is surgical excision with broad margins. This case emphasizes the importance of prophylactic removal or close clinical follow up of NSJ in an adult.

7TH WORLD CONGRESS FOR HAIR RESEARCH – GLASGOW, ESCOCIA

ANALYSIS OF ANDROGENETIC ALOPECIA IN AMERINDIAN PEOPLE (MAPUCHE) FROM SOUTHERN CHILE

FA Mardones, Y Valenzuela V Zemelman

Background: Androgenetic alopecia (AGA) is a common cause of hair loss in men and women. Studies in Caucasian and Asian populations have established racial differences in prevalence and clinical types of AGA. Investigators have suggested that native American (Amerindian) populations would have a lower prevalence and less severe type of AGA. Objective: To determine the prevalence and clinical patterns of AGA in adult males and females in an Amerindian (mapuche) population of Chile. Methods: Sample size was calculated using an estimated population proportion. Individuals included adults with two or more surnames of mapuche origin who attended outpatient clinics for general morbidity. Participants were excluded if they had scarring or other causes of non-scarring alopecia or known triggering factors of effluvium. The Norwood-Hamilton and Ludwig classifications were used for clinical pattern evaluation. Results: 231 patients (88 males and 143 females) were evaluated, men averaging 46.2 years and women 40.7 years. The prevalence of men with AGA was 32.9% and that of women 8.29%. The percentage of AGA increased with age: in the 20–29-year group, 6% affected males and none in females; in the 30–39-year group, 10.5% affected males and 5% in females; in the 40–49-year group, 20% affected males and 7% in females; in the 50–59-year group, 21.4% affected males and 6% in females. In the sixth decade, 46.6% of men and 27% of women were affected. In subjects older than 70 years, all of the men and 42.8% of the women had AGA. Regarding the clinical pattern of AGA in men, 27.6% (8/29) had a female pattern, 20.7% (6/29) had type IV, 17.2% (5/29) were types III vertex or VI, 10.3% (3/29) had type V, and 6.9% (2/29) had type VII. All of the women with

AGA showed a female pattern classified as type I. Conclusions: Chilean mapuche men and women showed a lower prevalence of AGA compared to Caucasians, but higher than reported in Asian populations. Likewise, the prevalence of AGA in our Amerindian population increased with age. Unlike Caucasian men, the female pattern was the most common clinical pattern in mapuche men. As in Asian reports, Ludwig type I was the most common pattern in mapuche women. The similarities of AGA prevalence and clinical pattern of our study group with Asian studies may support the genetic and anthropologist evidence of a common genetic link.

CLINICAL AND EPIDEMIOLOGICAL STUDY OF CHILDHOOD ALOPECIA IN TWO PEDIATRIC HOSPITALS IN SANTIAGO, CHILE
FA Mardones A Cortes

Background: Scalp hair loss in children is a relatively rare event with a negative impact on the child's psychosocial wellbeing. International studies of alopecia in the pediatric population have reported multiple causes, usually acquired and non-scarring forms. Also, there may be etiologic differences according to age groups. No clinical or epidemiological surveys have been done in the pediatric population of Chile. Objective: To describe the clinical and epidemiologic profile of alopecia in children from two Chilean pediatric hospitals. Methods: Retrospective and prospective analysis of clinical records from Roberto del Rio and Luis Calvo Mackenna Children's Hospitals between January 2007 and June 2010. Patients under 15 years of age with diagnosis of scarring and non-scarring alopecia were included. Clinical and epidemiologic characteristics were recorded. Statistical analysis was performed using the SPSS 11.5 program. Results: 345 clinical records were analyzed, 179 male (51.9%) and 166 female (48.1%). The median age of patients was 72 months. Overall, most of the cases were acquired forms of alopecia, 97.4% were non-scarring. The most common diagnoses were: alopecia areata (36.8%), tinea capitis (21%), nevus sebaceous (13.2%), telogen effluvium (8.7%), and trichotillomania (5.2%). Only telogen effluvium and loose anagen syndrome were statistically higher in girls. According to age groups the principal causes were aplasia cutis and nevus sebaceous in newborns; nevus sebaceous, alopecia areata, tinea capitis, and telogen effluvium in toddlers and preschoolers; alopecia areata, tinea capitis, tellogen effluvium, and trichotillomania in school years; and nevus sebaceous, alopecia areata, tellogen effluvium, and trichotillomania in adolescents. Conclusions: This is the first study of alopecia in the Chilean pediatric population. As in international reports, most of the cases were acquired and non-scarring forms of hair loss. The most prevalent causes were alopecia areata, tinea capitis, nevus sebaceous, telogen effluvium, and trichotillomania. However, this may vary according to the age group analyzed.

INTERNATIONAL INVESTIGATIVE DERMATOLOGY – EDIMBURGO, ESCOCIA

TOFACITINIB HAS NO CLINICALLY SIGNIFICANT EFFECTS IN CELLS CONTROLLING CHRONIC VIRAL INFECTION AND REACTIVATION
F. Valenzuela, K. A. Papp, D. Pariser, S. Tyring, R. Wolk, M. Buonanno, H. Valdez

Systemic psoriasis therapies have been associated with viral reactivation (eg CMV, zoster, PML). To evaluate the effects of tofacitinib on lymphocyte subpopulations, and CMV and EBV viral loads (VL), T cell subpopulations and VL were prospectively examined in a Phase 2b, 12-week, study. In a double-blind randomized controlled trial, the effects of tofacitinib 2, 5, and 15 mg BID on T helper (CD4+), T cytotoxic (CD8+), B (CD19+), and NK (CD16/56+) lymphocyte counts and serial CMV and EBV VL, were compared with placebo in patients with moderate to severe chronic plaque psoriasis. 197 patients participated (49 in each tofacitinib arm; 50 in the placebo arm). Most patients were male (63%), mean age 44 years and mean baseline PASI score was 21. After 12 weeks of treatment, 32, 51, 67, and 3% of patients in the 2, 5, 15 mg BID and placebo arm, respectively, achieved a PASI75 response. At Week 12 there was a dose-dependent decrease in median NK cells in the tofacitinib arms (-27, -24, and -52 cells/mm3) and an increase in median number of B cells (+51, +65, +89 cells/mm3). There was no change in CD8+ T cells. An initial increase at Week 4 in CD4+ T cells in the tofacitinib arms (+36, +86, +129 cells/mm3) returned towards baseline at Week 12. Median (Q25, Q75) CMV VL was 0 (0,0) at baseline with no change observed through Week 12 in any group. Baseline EBV VL was 0 (0, 0.95), 0 (0, 1), 0 (0, 0.85), 0 (0, 1.3) in the 2, 5, 15 mg BID and placebo arm. Median changes through Week 12 were 0 (0, 1.25), 0 (0, 0.6), 0.7 (0, 0.9), and 0 (-1.1, 0). For CMV, 11, 7, 34, and 4% of patients with an undetectable VL at baseline had a detectable VL on follow-up. For EBV, these values were 44, 20, 48, and 23% in the tofacitinib 2, 5, 15 mg BID and placebo arm. Tofacitinib was associated with dose-dependent decreases in NK cells and increases in B cells. No meaningful change occurred in T lymphocytes (CD4+ or CD8+) and EBV or CMV VL.

OFICINA APOYO INVESTIGACIÓN CLÍNICA

EUROPEAN CONGRESS OF IMMUNOLOGY - GLASGOW, ESCOCIA

BLOCKING OF PD-L1 ON THERAPEUTIC DENDRITIC CELLS MODULATE IN VITRO T CELLS PROLIFERATION AND DIFFERENTIATION TO TH1 AND TH17 SUBPOPULATIONS (P4230)

Mercedes Lopez, Carolina Behrens, Cristian Falcon-Beas, Fabian Tempio, Flavio Salazar-Onfray

DCs constitute a promising treatment against melanoma. Recently, we showed the effectiveness of an allogeneic melanoma lysate DC-based immunotherapy for improving long-term survival in melanoma patients. Moreover, an elevated proportion of regulatory T lymphocytes (Tregs) was observed in non-responder patients. PD-L1 is an important co-inhibitory molecule expressed on DCs binding to PD-1 on T cells. This interaction promotes the induction, conversion and maintenance of Tregs, suggesting a role in immunosuppression. Here, we studied if the blockade of PD-1-PD-L1 interaction reverses Tregs differentiation and increases T helper populations. Monocyte-DCs were generated in the presence of pro and anti-inflammatory factors, and the PD-L1/PD-1 signaling was blocked by anti PD-L1 mAbs. Allo-stimulatory capacity of DCs was impaired, and inversely correlated with PD-L1/CD86 ratio. However, blocking PD-L1 on DCs increased of Th1 and Th17 proliferation, concomitant with a Tregs reduction, independently of the DCs phenotype and functional characteristics. We demonstrated that the PD-L1/CD86 ratio play a key role in the functional capability of DCs. Therefore, blocking this molecule on DCs becomes an attractive strategy to improve the efficacy of DCs-based vaccines in melanoma patients.

DEXAMETHASONE INHIBITS TUMOR CELL LYSATE INDUCTION OF A PRO-INFLAMMATORY DENDRITIC CELL PHENOTYPE AND FUNCTION MODULATING T CELL CYTOKINE PROFILES (P4246)

Cristian Falcon, Fabian Tempio, Claudio Perez, Carolina Behrens, Ana-Adelia Riberos, Felipe Falcon, Flavio Salazar-Onfray, Mercedes Lopez

Recently, we showed the effectiveness of a DCs-based immunotherapy for improving long-term survival in patients with melanoma using an allogeneic melanoma cell lysate. Glucocorticoids are used in cancer patients being implicated in immune suppression. Here, we aim to study the effect of dexamethasone on the inhibition of the pro-inflammatory phenotype and immunogenicity capacity of melanoma cell lysate-loaded DCs. Monocytes were differentiated to DCs as previously described. Dexamethasone was given at day 1 and 2 to obtain tolerogenic DCs. DCs maturation markers and TH1, TH17 phenotype were determined by flow cytometry. T cell cytokines were measured by ELISA and proliferation evaluated by CFSE dilution assay. We show that dexametasone stimulus elicits a semi-mature DC phenotype (low MHC II, CD83, CD80 and CD86) sharing mature and immature DCs characteristics, secreting low levels of IL1β, IL-6 and IL-12 and high levels of IL-10, but not affecting DC phagocytosis capacity. TolDCs inhibited T cell proliferation and IFN{gamma}, IL-17 and TNF-α release by T helper cells. At contrary, an augment of Treg cells could be observed. The used glucocorticoids affects the maturation of newly differentiated monocytes-derived DCs in presence of immunogenic tumor cells, affecting the activation of a correct adaptive anti tumor immunity.

DEPARTAMENTO DE MEDICINA

SERVICIO DE NEUMOLOGÍA

CONGRESS OF AMERICAN THORACK SOCIETY (ATS) – PENSILVANIA, EEUU

EFFECT OF A PROGRAM OF PHYSICAL ACTIVITY ENHANCEMENT USING PEDOMETERS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

L. Mendoza, M. Aguilera, Balmaceda, Student, J. Espinoza, P. Horta, A. Castro, O. Diaz, N. Hopkinson

Introduction: The level of physical activity is reduced in COPD and has a negative effect on the morbidity and mortality of this condition. The advice is not good enough to reverse the sedentary condition. Pedometers are broadly used but their effects in COPD are unknown. Aim: To determine the effect of pedometers in the physical activity level of COPD patients. Method: 55 COPD patients were randomly assigned to a 3 months individual pedometer-based program promoting daily physical activity enhancement (experimental group) or usual care (control group). At the beginning and at the end of the intervention period we estimated the average one-week daily steps, the exercise capacity using the six-minute walking test (6MWT), the MMRC scale of dyspnoea, the Saint George Respiratory Questionnaire (SGRQ) and the COPD assessment Test (CAT) to estimate quality of life, additionally we

documented the incidence of acute exacerbations of COPD (AECOPD) during the follow-up. The study was approved by the local ethics committe. Results: 69% of the subjects were male, mean age 68 years, mean FEV1/FVC 55%, mean FEV1 63% of predicted value. Experimental (n= 29) and control group (n = 26) have comparable basal characteristics. There is a significant difference in the average of increase of steps/day in the experimental group in comparison with the control group (2906 versus 310, p = 0.016). Also, a significant difference is observed in the symptoms subscale score of the SGRQ (reduction of 9.65 versus 0.05 points, experimental versus control group, p = 0.048). The incidence of AECOPD was significantly lower in the experimental group (0.1 versus 0.6 per patient, experimental and control group respectively, p = 0.002). Conclusions: A program of physical activity enhancement using pedometers is useful to increase the average of steps walked daily and apparently h

SERVICIO DE GASTROENTEROLOGÍA

EASL 48TH ANNUAL MEETING EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER - AMSTERDAM, HOLANDA

THE SPANISH-LATIN AMERICAN DILI NETWORK: PRELIMINARY RESULTS FROM A COLLABORATIVE STRATEGIC INITIATIVE

F. Bessone, N. Hernandez, A. Sanchez, M. di Pace, M. Arrese, J.R. Brahm, A. Ruiz, J. Arancibia, D. Kershenobich, A. Loaeza del Castillo, M. Girala, R. Paraná, M.I. Schinoni, N. Mendez-Sanchez, I. Medina-Cáliz, A. González-Jiménez, C. Stephens, M. Robles-Díaz, M.I. Lucena, R.J. Andrade.

Background and aims: Idiosyncratic hepatotoxicity induced by drugs or herbal remedies (DILI) is an important health problem. DILI is expected to differ across geographical areas due to differential drug polices, prescription habits, drug consumption and genetic factors. In 2011 the Spanish DILI Registry contacted leading Latin American hepatologists in order to establish a Latin American DILI Registry. The objectives of this initiative were to stimulate detection and collection of well phenotyped cases to provide information on the Latin American DILI profile and corresponding risk factors. Methods: Reference hepatologists were identified in Argentina, Uruguay, Chile, Brazil, Mexico, Peru, Venezuela and Bolivia, who in turn were commissioned to establish national specialist networks contributing to the project. Data would be obtained using the methodology in place at the Spanish DILI Registry. Identified cases would be remitted to the coordinating centre in Málaga for causality assessment and information storage. Results: Seventy-three DILI cases have been analyzed up to November 2012, having a mean age of 52 years (range 15-86) and female predominance (60%). The therapeutic groups most frequently implicated were NSAIDs (22%) including nimesulide (5 cases) and diclofenac (4 cases); antiinfectives (19%) including nitrofurantoin (3 cases), herbal remedies (12%) including Morinda citrifolia, Peumus boldus and Monascus purpureus; hormonal therapy (12%) including cyproterone acetate (4 cases); and central nervous system drugs (11%). Hepatocellular injury (50%) was the most common type of liver damage. Jaundice was seen in 71% of cases, 53% required hospitalization and 38% fulfilled Hy's Law criteria (66% of hormonal therapy cases, 44% of herbal cases). Positive autoantibody titers were present in 29% of cases, mainly antinuclear. Six cases were autoimmune hepatitis DILI (8%) and five cases had experienced a second DILI episode (7%). Conclusions: This initial analysis demonstrates similar phenotypic characteristics as observed in registers outside Latin America with respect to type of injury and severity. However, female cases seem to predominate in Latin America. With regards to causative agents, elevated representation of NSAIDs, hormonal treatments and herbal remedies were evidenced.

EASL 48TH ANNUAL MEETING – AMSTERDAM, DINAMARCA

CORRELATION OF IL28B POLYMORPHISM WITH DEGREE OF FIBROSIS: ANALYSIS OF TREATMENT-NAÏVE AND TREATMENT-EXPERIENCED CAUCASIAN PATIENTS INFECTED WITH HCV GENOTYPE 1 IN THE GEN-C STUDY

Mangia, V. de Ledinghen, J. Keiss, J. Valantinas, J. Brahm, N. Rasmann, D. Messinger, F. Tatsch

Introduction: The recently described single nucleotide polymorphism (SNP rs12979860) 3 kb upstream of the host IL28B gene is the strongest baseline factor associated with treatment response in G1 patients chronically infected with HCV. The association between this SNP and fibrosis progression has been the subject of debate. The current analysis evaluates the correlation of IL28B polymorphism with a diagnosis of cirrhosis or transition to cirrhosis among chronic hepatitis C (CHC) Caucasian patients infected with HCV G1 from the Gen-C study.

SERVICIO DE GENÉTICA

EUROPEAN HUMAN GENETICS CONFERENCE 2013 - PARÍS, FRANCIA

OSTEOMALACIA AS A KEY FEATURE OF RAINE SYNDROME: CHANGING THE PARADIGM.

V. Faundes, P. Gonzalez-Hormazabal, S. Castillo Taucher, A. Crosby, A. Maturana

INTRODUCTION: Raine syndrome is a skeletal dysplasia characterised mainly by osteosclerosis of bones, facial dysmorphism, and a course frequently lethal. However, we present the first alive case molecularly confirmed whose radiographs showed osteomalacia. CASE REPORT: The patient was born at 26 weeks of gestation to non-consanguineous and healthy parents, due to intrauterine growth retardation and worsening of Doppler examination. His birth parameters were all p<2, and albeit delivery and Apgar scores were normal, he subsequently suffered from different premature birth complications. Furthermore, at 70 days old bilateral forearm spontaneous fractures were suspected and confirmed, whereas follow-up radiographs revealed broad epiphyses and thin diaphyses of long bones, accompanied of generalised osteomalacia. At physical examination, the patient had some dysmorphic characteristics which suggest Raine syndrome such as ocular proptosis, hypertelorism, slightly downslanted palpebral fissures, broad nasal bridge, midface hypoplasia, micrognathia and short limbs and fingers. Karyotype was normal, and although his cerebral ultrasounds were normal, renal echography revealed nephrocalcinosis. One year later, his health status has improved substantially, specially his osteomalacia and nephrocalcinosis. Parallelly, FAM20C sequencing analysis was performed, which demonstrated the heterozygous duplication g.286470_286503dup34 and heterozygous SNP rs192542992, which is present just in 0.7% of the population. In silico analysis of these findings showed rupture of splicing site of exon 4, and the creation of a new splicing regulatory element, respectively. CONCLUSION: Although these results should be confirmed experimentally, it seems that osteomalacia is also a key feature of Raine syndrome, in concordance with the recently published murine model.

SERVICIO DE REUMATOLOGÍA

EULAR 2013 - MADRID ESPAÑA

A RANDOMISED, DOUBLE-BLIND, PARALLEL-GROUP, PHASE 1 STUDY COMPARING THE PHARMACOKINETICS, SAFETY AND EFFICACY OF CT-P13 AND INFLIXIMAB IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: 54 WEEK RESULTS FROM THE PLANETAS STUDY

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Background: CT-P13 is a biosimilar product of infliximab (INX). Data up to week 30 has been reported at EULAR 2012.1 Objectives: To assess the PK, efficacy and safety of CT-P13 in patients with active AS up to week 54 and to compare this with INX, also in relation to the formation of anti-drug antibodies (ADAs). Methods: Patients with active AS (1984 modified NY criteria) were randomised (1:1) to receive either CT-P13 (5mg/kg) or INX (5mg/kg) at weeks 0, 2, 6 and then every 8 weeks up to week 54. Results: Of 250 patients randomised at baseline, 213 patients were treated up to week 54. Cmax of CT-P13 and INX were shown to be equivalent, since 90% CIs for the ratio of geometric means were within 80–125% at all doses (CT-P13, 128.1µg/mLβ172.2µg/mL; INX, 123.0µg/mL–176.7µg/mL). At week 54, the proportion of patients testing positive for ADAs was comparable between CT-P13 and INX (22.9% [25/109] vs 26.7% [28/105]). ADAs had similar effects on PKs in both groups. Patients with negative ADA results had higher Cmax values (CT-P13, 134.5µg/mL–177.2µg/mL; INX, 131.9µg/mL–177.4µg/mL) compared with patients with positive results (CT-P13, 101.8µg/mL–160.4µg/mL; INX, 104.0µg/mL–175.2µg/mL). At week 54, ASAS40 and ASAS partial remission were comparable between groups (CT-P13, 54.7% and 19.8%; INX, 49.1% and 17.6%, respectively). More patients with negative ADA results achieved ASAS40 responses (CT-P13, 61.0%; IFX, 54.7%) compared with patients with positive results (CT-P13, 37.9%; IFX, 36.4%). The safety profiles of CT-P13 and INX were also comparable (table). Active tuberculosis (TB) was reported in 3 patients (CT-P13, 2; INX, 1) and there were no malignancies. Conclusions: CT-P13 has similar PK values and a clinical efficacy comparable to INX up to week 54. CT-P13 was well tolerated with a safety profile comparable to that of INX up to 54 weeks. ADAs seem to diminish the clinical response to both agents in some patients.

A PHASE 3 RANDOMISED CONTROLLED TRIAL TO COMPARE CT-P13 WITH INFLIXIMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: 54 WEEK RESULTS FROM THE PLANETRA STUDY

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Background: CT-P13 is a biosimilar product of infliximab (INX). Data up to week 30 has been reported at EULAR 2012.1 Objectives: To compare the efficacy and safety of CT-P13 and INX in active rheumatoid arthritis (RA) patients up to week 54. Methods: Patients with active RA (1987 ACR criteria) and inadequate response to methotrexate (MTX) were randomised (1:1) to receive either CT-P13 (3mg/kg) or INX (3mg/kg) at weeks 0, 2, 6 and then every 8 weeks up to week 54 in combination with MTX (12.5-25mg/week). Results: Of 606 patients randomised at baseline, 457 patients were treated up to week 54. At week 54, ACR20 was highly similar between groups (CT-P13, 57.0% [172/302]; INX, 52.0% [158/304]; 95% CI: -0.03-0.13). ACR50 and ACR70 scores were also comparable between groups (CT-P13, 33.1% and 16.2%; INX, 31.6% and 15.1%, respectively). In the CT-P13 and INX groups respectively, 26.4% and 27.8% of patients reached remission with DAS28-CRP; additionally, 14.3% and 14.8% reached low disease activity compared to approximately 80% high disease activity in both groups at baseline. The proportion of patients testing positive for anti-drug antibodies (ADAs) was comparable between CT-P13 (52.3%) and INX (49.5%). More patients with negative ADA results achieved ACR20 responses (CT-P13, 73.9%; INX, 67.2%) compared with patients with positive results (CT-P13, 53.2%; INX, 48.1%). Total Sharp scores at baseline and week 54 were comparable (CT-P13, 104.6 and 70.4; INX, 103.6 and 73.0). Cmax of CT-P13 or INX at all doses ranged from 66.1µg/mL–112.2µg/mL and 60.3µg/mL–104.5µg/mL, respectively. The safety profiles of CT-P13 and INX were also comparable (table). Conclusions: CT-P13 showed comparable efficacy and PKs to those of INX up to week 54. CT-P13 was well tolerated with a safety profile comparable to that of INX up to week 54.

INTERNATIONAL CONFERENCE INTEGRATED MEDICAL IMAGING IN CARDIOVASCULAR DISEASES (IMIC) 2013 – VIENA, AUSTRIA

^{99}MTC-SESTAMIBI EXERCISE SPECT AND FOLLOW-UP IN PATIENTS ABLE TO REACH 10 METABOLIC EQUIVALENTS OF TASK (METS)

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Good exercise performance during a stress test gives important clinical information. Being able to achieve 10 Metabolic Equivalents of Task (METs) appears to have a good negative predictive value for cardiac events in coronary artery disease (CAD), independent of the cardiac condition. Aim: to know the prevalence of isotopic ischemia with myocardial SPECT and the outcome in patients who obtained ≥10METs in their treadmill test. Methods: We reviewed 2.571 consecutive stress myocardial 99mTc-sestamibi SPECT, 780 of them performed exercise stress test (EST); 152 were able to reach at least 10 METs and ≥85% maximal predicted heart rate (MP HR); 82% males; group age was 56±9 years (range: 26-77 and 5% <40 years). All performed Bruce protocol and were studied with 99mTc-sestamibi SPECT gated in both phases. Record of major or minor cardiac events was performed through phone contact, reviewingclinical files or inquiring in the civil registration office. Results: SPECT was required due to CAD screening in 75% of the group and to risk stratification in 25% (including myocardial infarction and/or revascularization); 99% was in NYHA functional class I. The electrocardiogram at rest was normal in 41%; with Q wave in 6% and with other conduction abnormalities in 12% (no left bundle branch block included). Main EST parameters were: test duration 9±1 min; MPHR 94±6%; METs 11.5±1.7; 48% suspended for fat igue; 47% reached MPHR and the rest for dyspnea, hypertensive response or angina. EST was positive for ischemia in 16%, negative in 64% and non-conclusive in 20%. SPECT myocardial perfusion was normal in 72%; all had adequate normal size left ventricle fun ction but 10 dilated and 4 with diminished function. There were reversible perfusion defects in 25% of cases (10% with some fixed component) and only 4% with purefixed defects (the more extended: 45% of the LV). Ischemia was moderate or severe in 47% of the reversible cases: mean SDS 8.3; ischemia extension 23%; TPD at stress 20. There was 75% of concordance between reported ischemia with EST and reversibility with SPECT (Cohen kappa: 0.31). We were able to follow-up 84% of the cases [mean: 30 m ±15; median: 25 m; range: 10-82 m]. There were no cardiac deaths, myocardial infarctions or strokes. There were 8 patients with coronary revascularization procedures, 7 of them performed within 1 year post SPECT; 69 6 out of 8 of them had significant ischemia of diverse extension. Another patient without ischemia was submitted to coronary an giography without intervention. Conclusion: A quarter of the patients with good exercise capacity submitted to myocardials estamibi SPECT had reversible perfusion defects. There were no major cardiac events; only 16% of the patients with SPECT ischemia were submitted to revascularization. In good functional capacity patients, this findings support the idea to select with appropriate criteria non-invasive strategies to evaluate CAD, in spite of their relative high prognostic value.

IMPORTANCE OF ADEQUATE QUALITY CONTROL OF LEFT VENTRICULAR BOUNDARIES WITH COMMERCIAL SOFTWARE IN GATED MYOCARDIAL PERFUSION SPECT: ANALYSIS OF PATIENTS WITH VENTRICULAR DILATION AND MYOCARDIAL INFARCTION

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Background: Gated myocardial SPECT allows to know important additional left ventricular (LV) functional parameters such as dilation, decreased ejection fraction (EF) or their changes due to myocardial infarction (MI), ischemia or even stunning. However, automatic methods could conduce to wrong values and incorrect boundary estimations caused by diminished perfusion and or extra cardiac activity that need semiautomatic or manual processing. Goal: to compare the influence of diverse extension MI and dilation using automatic and manual methods in gated myocardial SPECT. Methods: We studied 132 patients with gated SPECT using 99mTc sestamibi referred to evaluate coronary artery disease, 80% males, mean age 63.7 years. The stress was Dipyridamole in 104 and exercise or Dobutamine in 27 cases. We measured end diastolic volume (EDV), end systolic volume (ESV) and LVEF at stress and rest with QGS® program with automatic and manual methods. We included 109 patients with MI, all with Q wave and/or fixed perfusion defects plus any abnormal regional wall motion: 48 non dilated (EDV<120 ml at rest) and 61 dilated; other 23 patients with dilated LV and no IM, corresponding mostly to ischemic cardiomyopathy were added. We employed paired student t test and Spearman correlation to analyze according to the data normalcy.Results: Ten percent of our gated studies did not require modification of fully automatic method in stress and rest processing. MI rest defect extension ranged from 0-55% of LV and total perfusion defect (TPD) from 2 to 55. Correlations between automatic and manual methods for EDV and ESV (stress and rest together) in Group A were r=0.6728 and 0.6461; in Group B r=0.8879 and 0.8938; in Group C r=0.8801 and 0.8590, respectively; all cases p<0.0001. Regarding LVEF, correlation in Group A was r=0.6831, in Group B 0.8961 and in Group C 0.8002; there was more dispersion observed with higher LVEF values. Means ± SD values for volumes and LVEF are displayed in Table 1: globally, a) for volumes, automatic method presented large r values than manual in almost all dilated ventricles, and b) in all cases, automatic method presented larger LVEF. We also analyzed the correlation between both methods for rest EDV according to defect extension also at rest; more dispersion was obtained in non dilated hearts with smaller lesions (<20% defect extension) compared with a subgroup of larger MI and LV (>35% defect extension) with r=0.773 (mean EDV=108 ml) versus r=0.948 mean EDV=171 ml), respectively. Conclusion: Quality control of automatic technique is necessary in all gated myocardial SPECT in order to report precisely functional parameters. In patients with abnormal LV perfusion, independent of dilation and MI size, the difference after manual intervention is considerable. Non dilated MI cases presented the worse adjustment between both approaches.

ASSESSMENT OF PERIPHERAL NEUROPATHY AND MICROALBUMINURIA IN CORONARY ASYMPTOMATIC PATIENTS WITH DIABETES MELLITUS TYPE 2 RELATED WITH MYOCARDIAL STRESS PERFUSION ABNORMALITIES

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Background: Diabetes mellitus type 2 (DM2) may affect diverse systems even in early stages and asymptomatic patients. Autonomic peripheral neuropathy (PN) is a serious complication observed usually in delayed stages and suboptimal metabolic control cases. Microalbuminuria (MA) is a good marker of renal damage also related to increased cardiovascular risk. Silent myocardial ischemia may present initially with systolic dysfunction or even fatal infarction. Objective: To study an association between NP and MA in asymptomatic DM2 patient without known coronary artery disease, with the presence of myocardial perfusión abnormalities using stress test. Methods: Population: As a part of An IAEA multicentric project we evaluated 32 DM2 patients with >5 years of disease (average 12 years); they were 61±7 years old; 59% men, body mass index 29±4 kg/m 2; coronary asymptomatic, without electrocardiographic Q wave and all with at least another cardiovascular risk factor. Technique: All patients were studied with 99m Tc Sestamibi SPE CT using Bruce exercise initially ad after 3 years as well as serum profile and HbA1C. Ultrasensitive Reactive C Protein (usRCP), MA and a Michigan Test (MT) for PN detection were also performed at 3 years [Abnormal MT were: >2/10 points or according to physical auto evaluation score]. Analysis : Student t, Pearson r and Cohen k were applied. Results: Main serum and urine mean and SD values at 3 years are shown in Table 1; 43% of the group had HbA1C<7,5%. They were treated medically with intensification of their lipid control. Basal SPECT was positive for silent ischemia in 34% initially and in 28% of the group at 3 years (p=ns) with transient perfusion defects (mild to moderate) but only 1 fixed defect corresponding to a myocardial infarction. At 3 years. 15 out of 32 patients had normal feet and 1 distal amputation; 10 had MT>2. MT correlated with physical exam with r=0.579 (p=0.0006) although both scores with time of DM had p=ns. MA was present in 10 cases (>30 mg/L) and usRCP elevated in only 4. The 75% of the patients with elevated usRCP also presented MA, PN and/or silent ischemia. The agreement between abnormal perfusion SPECT and NP presence was 59% (k=0.028); between abnormal perfusion and MA 62% (k=0.076) and between NP and MA 72% (k=0.36). Conclusion: Almost a third of our coronary asymptomatic DM2 patients, presented

persistent silent myocardial ischemia, NP or certain renal damage after 3 years of observation. There was agreement between those results, with greater strength between NP and MA association.

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INFLAMATORY AND REMODELING RESPONSE TO SURGICAL REPAIR FOR PELVIC ORGAN PROLAPSE

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OBJECTIVE The purpose of this study was to compare the inflamatory and tissue remodeling response to polypropylene mesh with site-specific repair in the treatment of anterior vaginal wall prolapse. BACKGROUND Tissue repair is a dynamic and variable process; first, there is an inflammation phase, followed by a fibrosis phase with subsequent remodeling and scarring. Different mechanisms, which are generated in different stages, stimulate the release of chemical signals. These modulate, in an orderly fashion, cell migration, proliferation and differentiation, as well as extracellular matrix (ECM) protein synthesis and degradation. Studies have shown changes in the ECM of the paraurethral connective tissue in patients with urinary incontinence1, and different collagen metabolism in women who suffer from genital prolapse2. Some evidence suggests that the degradation of both collagen and elastin by matrix metalloproteinase (MMP) can occur in these groups of patients as well3. We investigated the effect in the inflammatory and tissue remodeling response of surgical repair in the treatment of genital prolapse. METHODS This is a randomized prospective trial. Patients with symptomatic anterior vaginal wall prolapsed at stage II, III or IV were randomized to receive either a site-especific or polypropylene mesh (Prolift®, Johnson&Johnson) repair. In all subjects, we obtained a tissue specimen from the anterior vaginal wall for histochemical analysis prior and six month after the surgical procedure. The samples were obtained from a standarized location and had a minimal of 1 cm^2 in size, including vaginal mucosa, pubocervical fascia and mesh when required. All patients were given an explanation of the study and written informed consent was procured. Ethics approval was acquired from de local committee. All samples were splited in half. While one sample was sent for tissue morphology, inflamation and fibrosis assessment through inmunohistochemistry, the other was stored in liquid nitrogen for Western blot analysis, allowing the detection of collagen I and III, fibronectin and MMP-2 and MMP-9. Quantitative detection of MMP-2 y MMP-9 activity was also performed by zymography. Statistics were performed using Stata v12.0 (StataCorp LP, College Station, Texas, EEUU). A descriptive analysis of the variables was done. T student test and Wilcoxon signed-rank test was applied for non-parametric variables, which were normally distributed according to Shapiro-Wilks test. An alfa error of 5% will be considered. RESULTS Twenty-one patients were recruited from the Female Pelvic Floor Unit at our institution from may 2010 to march 2011. We randomized 10 and 11 patients to each group. The demographic and clinical data for both groups were similar. When we compared the histologic and inmunohistochemistry results there were no significant differences in vascular density, leucocyte migration, foreign-body gyant cells, birefracting material and granuloma formation. Likewise, we found no significant differences on the mean difference of collagen type I and III (p= 0.29; p = 0.16, respectively), fibronectin (p= 0.08), MMP-9 (p= 0.78), MMP-2a (p= 1.00) and MMP-9a (p= 0.33) between the both surgical procedures. The mean difference of MMP-2 was increased in mesh repair group (p= 0.01). CONCLUSIONS We found no differences in the amount of ECM proteins and fibronectin between both polipropilene mesh repair and site-specific repair prior and after surgical correction of anterior vaginal prolapse. It seems that polipropilene mesh does not generate more inflammatory changes on the vaginal wall than a traditional colporrhaphy. Therefore, the use of this kind of mesh would essentially play a functional support role for the treatment of pelvic organ prolapse without any additional structural tissue changes.

TRANSCUTANEAL TIBIAL NERVE STIMULATION VERSUS LONG RELEASE OXIBUTININ IN THE TRATMENT OF PATIENTS WITH OVERACTIVE BLADDER. A RANDOMIZE CONTROL TRIAL

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Objective: The purpose of this study was to prospectively and randomly compare transcutaneal tibial nerve stimulation with an antimuscarinic drug for the treatment of OAB in women. Background: Overactive bladder (OAB) has become a prevalent disease that affects a large number of women and men around the world, generating a detrimental effect on their quality of life. One option for the treatment of this condition is the use of antimuscarinic drugs. Although its efficacy is well known, the compliance with this treatment is low because of the adverse effects and the high cost involved. Transcutaneal tibial nerve stimulation seems to be a good alternative with similar efficacy, lower cost and better tolerance. For these reasons it may be a truly novel management for some patients. Methods: This is a prospective, randomized trial for the treatment of OAB patients

comparing long release oxibutinin 10 mg versus transcutaneal nerve stimulation for a 12 weeks period. To define OAB we used the definition of the International Continence Society published in 2002. Ethics approval was obtained from the local committee. The randomization was made by permutated blocks. All subjects were given an explanation of the study and written informed consent was obtained. All patients had a negative urine culture, completed a 3-day voiding diary and the oab-q questionnaire. If the patient had had a previous antimuscarinic treatment, she was asked a 2 weeks wash out period. Voiding diary and oab-q were also carried out after finishing the treatment. Transcutaneal neuromodulation was performed 2 times a week with at least 48 hours intervals for 12 weeks for patients allocated to this arm of the trial. Patients randomized to receive oxibutinin were asked to fill a daily diary for oral intake pill registration. They received the antimuscarinic drug each month in our unit after checking they have taken all the pills the previous month. We compared the efficacy of both treatments using the voiding diary and oab-q questionnaire. For the statistical analysis we used t-test for cuantitative variables and fisher test or chi-square for cualitative variables. Considering significant results with p value less that 0.05. This analysis was made using STATA V11.0. Results: Between January 2010 and July 2012 we randomized 56 patients to receive transcutaneal nerve stimulation or oral long release oxibutinin. Before treatment bothgroups were similar regarding age, BMI, smoke habit, menopause status, menopausal treatment, urinary frequency, urgency, urgeincontinence and oab-q parameters. When we compared the voiding diary and oab-q results after 12 weeks treatment there were no significant differences between groups, except for the use of daily pads. (Table 1). Conclusions: The analysis of our data shows a similar efficacy of the transcutaneal nerve stimulation versus long release oxibutinin in the control of OAB symptoms and in the improvement of their quality of life. Since this novel technique has limited side effects and a low cost, it should be considered in the algorithm for the treatment of overactive bladder.

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GLOBAL PERFUSION PARAMETERS AND POSTOPERATIVE DELIRIUM IN OLDER PATIENTS UNDERGOING TO OPEN COLON SURGERY

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Introduction: Postoperative delirium (POD) is a potential complication after colon surgery in older patients that affects between 5-15% of patients. POD is associated to worst outcomes including prolonged lenght of stay, and declination of cognitive and functional status at hospital discharge. Together with recognized predisposing factors, has been suggested that intraoperative events could be involved in POD. Of them, perioperative hemodynamic and cerebral perfusion have been proposed as relevant, but to this time there are not categorical data about this association. Our aim was to explore association between perioperative hemodynamics, brain oxigenation, and global perfusion parameters (ScvO2 and Lactate) with POD in older patients undergoing elective open colon surgery. Methods: We enrolled patients older than 60 years with elective indication of colon surgery excluding patients with neurologic disorders including dementia. Informed consent were obtained of patients and protocol was approved by IRB. Standard hemodynamic monitoring was started before anesthesic induction including invasive blood pressure, heart rate, central venous pressure, arterial oxygenation and diuresis monitoring. Additionally to this, we added monitoring with non invasive cerebral oxygenation (rSO2%, measured by near infrared spectroscopy, NIRS, INVOS 5100, Somanetics®), continuous central venous oxygen saturation (ScvO2, Presep catheter, Edwards®) and intermitent postoperative lactate measure. Hemodynamics parameters and perfusion was measured for 24 hours. All surgical and anesthetic procedures were standardized to minimize the presence of confounding factors. All patients were managed with balanced intravenous and inhalatory anesthesia guided to BIS 45-65. Postoperative pain was controlled with i.v. and peridural analgesia. Delirium was evaluated with CAM twice a day for five postoperative days. To explore association between baseline characteristics, intraoperative and postoperative data values with postoperative delirium, we used Fisher Exact Test, or U Mann Withney Test. All analysis were bilateral, with p value of 0,05. Results: We enrolled 22 patients, age 73 + 7 years, female 13 (59.1%). 18 patients underwent resection for cancer of the colon or rectum (81.8%). Albumin 3.4 + 0.7 g / dl, hematocrit 34 + 5%. The operative time was 153 + 47 minutes and anesthetic time 209 + 48 minutes. . Ten patients (45.5%) had lactate greater than 2.5 mEq / L, and 5 cases (22.7%) over 4 meq / lt. Regarding the ScvO2, 10 patients (45%) had values below 70% during intraoperative, and 16 patients (72.7%) had values below 70% in postoperative period. rSO2 was below 50% in 35% of patients, and this was <20% of rSO2 baseline un 38%. Two patients developed DPO (9.1%). The only variable associated with the presence of DPO were ScvO2 below 70% postoperatively (p = 0.046). No association between lactate values and rSO2 cerebral was founded. Conclusions: This preliminary observations suggest a role for postoperative ScvO2 as tool to predict POD. rSO2 in our data was not associated to POD, as well as values of hemodynamic parameters. If this data are confirmed with more patients and similar studies, could be a role of ScvO2 guided reanimation protocols to reduce POD in older surgical patients.