

Abstracts de trabajos presentados en Congresos Internacionales 2017

DEPARTAMENTO DE MEDICINA

ONCOLOGÍA

ESMO WORLD CONGRESS ON GASTROINTESTINAL CANCER 2017 – BARCELONA, ESPAÑA

PROGNOSIS FACTORS OF SURVIVAL OF GALLBLADDER CANCER (GC) IN CHILE. A RETROSPECTIVE ANALYSIS OF PATIENTS ASSISTED IN HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE

Luis Villanueva Olivares, Silvia Catalán Elgueta, Monica Ahumada Olea, Olga Barajas Barajas, Rodrigo Vasquez Morales

Introduction: The GC is an aggressive neoplasm with a short survival. The high lethality is associated with diagnosis in advanced stages due to the anatomical position and the mild and unspecific symptoms. Chile is the country with highest incidence and mortality rates of the GC in the world. The objective of the study was to determine the prognosis factors associated with the overall survival (OS) in patients with the diagnosis of GC. Methods: Retrospective study that includes patients with diagnosis of GC confirmed by biopsy, stratified according to images or surgical procedures. They were presented to the oncological committee joint during the period between January, 2010 to December, 2015. They were analyzed by demographic, clinical and pathological variables and related to the chemotherapeutic treatment received. Results: There were 61 patients, 42 women (68%) and 19 men (32%). The mean age was 61 years (35-83 years). Median albumin 3.5g/dl (1.2-4.6g/dl). Median hemoglobin: 12.0g/dl (7.1-16.5g/dl). The histopathological diagnosis was adenocarcinoma NOS in 75% of the cases. 64% of the patients debuted in IV stage. The liver was the most frequent metastasis localisation in 32% of cases. Twentyone patients (34%) received first line of chemotherapy. 90% of patients received gemcitabine with cisplatin, mean cycles was 5.5 cycles (1-19 cycles). The median OS was 10.9 months for the total group. The OS of patients that received first line of chemotherapy was 13.6 months (0.63-4.6 months). The OS was 2.8 months in patients stage IV not treated with chemotherapy. In the multivariate analysis the factors that determined a better OS were ECOG: 0-1 versus ECOG \geq 2 with OS 14.9 versus 2 months (HR 0.25, 95% CI 0,09-0,63; p 0,0001). Albumin \geq 3,5 vs < 3,5g/dl with OS 11,8 vs 3,4 months respectively (HR 0,44, 95% CI 0,19-0,99; p=0,0185). In the group of patients treated with chemotherapy, the women reached a median OS 23,5 versus 13,5 months of men (HR 0,27, 95% CI 0,060-1,24; p=0,0239). There were non-statistically differences in the OS according to sex in the patients no treated with chemotherapy and according to IMC, hemoglobin, nor age in the global group. Conclusion: The GC is one of the most aggressive cancer with a short survival rate. In our analysis, the patients with an ECOG 0-1 and levels of albumin \geq 3,5g/dl demonstrated a better OS due to the best nutritional and functional status of the patients. The women who received chemotherapy were also associated to a better prognosis. Probably this finding is related to an early consultation which would favor an earlier treatment.

GASTROENTEROLOGÍA

CONGRESS OF EUROPEAN SOCIETY OF NEUROGASTROENTEROLOGY AND MOTILITY - CORK, IRLANDA

PROSPECTIVE RANDOMIZED CLINICAL TRIAL WITH THREE ANTIBIOTICS THERAPIES IN TREATMENT OF SMALL INTESTINAL BACTERIAL OVERGROWTH

D. Vera; E. Pérez de Arce; C. Defilippi; G. Landskron; A. M.

Background: There is evidence of the importance of treatment for small intestinal bacterial overgrowth (SIBO) in patients with functional gastrointestinal disorder (FGD). AIM: to evaluate efficacy, safety and tolerability of three antibiotic treatments for SIBO and the presence of pain and bloating in patients with FGD. Methods: 97 patients with FGD and diagnoses of SIBO according lactulose breath test (LBT) were included in this prospective, double-blind, longitudinal, randomized study with three antibiotics therapies during 10 days. Group A: 32 patients, rifaximin 400 mg twice daily; Group B: 32 patients, ciprofloxacin 500 mg twice daily; Group C, metronidazole, 500 mg three times daily. 15 days after the treatment LBT was performed in order to analyse intensity of symptoms (visual scale from 0 to 10), compliance with therapy and side effects. Statistical analysis with Fisher's test. Results: 81 patients completed the study (27, 29 and 25 per group, respectively) (Figure 1), 90% women. SBI improvement was observed in 81% with metronidazole, 62% with rifaximin and 43% ciprofloxacin ($P=.016$). There was improvement of symptoms: pain and boating in three groups ($P=.021$). 28 patients presented side effects: 50% with metronidazole, 39% with ciprofloxacin and 11% rifaximin ($P=.001$). Conclusion: Metronidazole and Rifaximin showed significant improvement in SIBO compared to ciprofloxacin. Moreover, there was improvement of symptoms with three therapies independent of SIBO. Metronidazole had a high incidence of side effects. Our results confirm that Rifaximin is effective for the treatment of SIBO with less adverse effects.

PRESENCE OF NON- INCLUDED DIGESTIVE SYMPTOMS IN ROME III CRITERIA FOR DIAGNOSIS OF IRRITABLE INTESTINAL SYNDROME IN SYMPTOMATIC PATIENTS

D. Vera; N. Hernández; E. Pérez de Arce; A. M. Madrid

Background: The diagnosis of Irritable Bowel Syndrome (IBS) is established according to Rome III criteria. These criteria consider abdominal pain or discomfort as the main symptom. There are symptoms not included as painful defecation, compromise of daily life activities, mucus in feces, feeling of incomplete evacuation and bloating. AIM: to evaluate the presence of non-included digestive symptoms in Rome III criteria in patients with IBS and patients with abdominal discomfort, or abdominal pain without IBS by Rome III (No-IBS). In addition, to determine the proportion of IBS patients who meet Rome IV criteria. Methods: Rome III for IBS were completed by 963 symptomatic patients, 76% female sex. The frequency and intensity (analogous visual scale from 0 to 10) of non-included symptoms in Rome III criteria were considered. The Rome IV criteria only considers abdominal pain but not discomfort. Statistical analysis with Mann-Whitney test and Chi-square. Results: 816 symptomatic patients (85%) presented IIB according to Rome III criteria, 78% female sex. Pain interferes with daily activities 56% of patients with IBS and 29% of No-IBS ($P=.0004$). In IBS patients, 45% reported incomplete evacuation feeling, 95% reported bloating and 35% mucus in feces vs 10%, 80% and 21% respectively in No-IBS patients ($P<.005$). The intensity of non-included symptoms in IBS patients revealed a score of: 4.4 ± 2.6 in pain during defecation, 5.7 ± 2.6 in feeling of incomplete evacuation and 7.5 ± 2.3 in bloating vs 3.3 ± 2.4 ; 3.7 ± 3.0 and 6.5 ± 2.3 , respectively, in No-IBS ($P<.005$). No differences were found in the intensity of difficulty in defecating. 35% of IBS patients met criteria according to Rome IV, 82% female. Conclusion: The non-included digestive symptoms in Rome III criteria for the diagnosis of IBS are highly frequently in symptomatic patients. These symptoms affect significantly the daily activities. The Rome IV criteria indicate a decrease in the number of patients meeting criteria for IBS, although it maintains a higher proportion of women.

BCL-3 UPREGULATION BY MAST CELLS IN IRRITABLE BOWEL SYNDROME (IBS) PATIENTS

C. Beltran; V. Torres; H. Portillo; D. Vera; E. Pérez de Arce; A. M. Madrid; E. M. Quigley; J. F. Cryan; M. Vicario

Objective: Irritable Bowel Syndrome (IBS) is characterised by mucosal mast cell activation in association with increased epithelial permeability. The B-cell leukemia/lymphoma-3 (Bcl-3), a co-transcriptional regulator of the NF- κ B target gene, modulates inflammatory responses and has been associated with increased intestinal epithelial permeability in an experimental model of infection. Mast cell modulation of Bcl-3 expression in epithelial cells has not been addressed. Our aim was to assess the regulation of epithelial Bcl3 expression by mast cells in IBS and to underlying mechanisms. Methods: Colonic and ileal mucosal biopsies from IBS (IBS-D n=9; IBS-C n=6; IBS-M n=4; IBS-U n=1) patients (n=20) and healthy controls (HC n=19) were evaluated for Bcl-3 expression and mast cell number by immunoblot and immunofluorescence microscopy, respectively. Mast cell activity was assessed by measuring intestinal tryptase content (immunoblot and ELISA), and by analysing mast cell degranulation by transmission electron microscopy. In Caco-2 cells, Bcl-3 expression by tryptase was evaluated by immunoblot. Results: The epithelium of IBS patients showed increased expression of Bcl-3 in both the ileum (IBS: 2.154 ± 1.159 ; HC: 1.000 ± 0.6844 , $P=.0147$) and the colon (IBS: 2.221 ± 1.687 , HC: 1.000 ± 0.7248 , $P=.0094$) as compared to HC. The number of mast cells in the ileal (IBS: 26.00 ± 14.82 ; HC: 14.64 ± 8.10 , mast cell/hpf $P=.0050$) and the colonic mucosa

(IBS: 17.40 ± 10.39 ; HC: 11.94 ± 6.54 mast cell/hpf, $P = .0474$) was increased in IBS patients compared to HC. Morphological evidence of increased degranulation in the ileum of the IBS group was also observed (IBS: 78.2 ± 9.07 ; HC: $60.7 \pm 6.98\%$, $P = .0190$). Moreover, Bcl-3 expression was induced by tryptase in Caco-2 cells; an effect that was inhibited by FSLLRY-NH2, a selective PAR2 peptide antagonist ($P = .0245$). Conclusion: Our findings suggest that intestinal epithelial Bcl-3 expression is induced by mast cells, a mechanism that may modulate epithelial integrity and mucosal inflammation in IBS.

COLONIC FLORA AND SMALL INTESTINE BACTERIAL OVERGROWTH IN PATIENTS WITH INTESTINAL BOWEL SYNDROME (IBS) BY ROME III CRITERIA

Daniela Vera, Gonzalo Araneda, Mónica Villanueva, Edith Pérez de Arce, Ana María Madrid.

Background: Lactulose hydrogen breath test (LHBT) determines the presence of small intestinal bacterial overgrowth (SIBO) and allows the characterization of colonic flora, according to production of hydrogen (H_2) and methane (CH_4). It has been reported that the type of microbiota and the presence of SIBO could be involved in the patho-physiology of Irritable Bowel Syndrome (IBS). Aim: To characterize colonic flora according to production of H_2 and CH_4 in IBS- patients and evaluate SIBO. METHODS: 900 patients with IBS were evaluated by Rome III Criteria and LHBT standardized technique, 78% female sex, between 18 and 88 years. According to Rome III, 37% IBS-diarrhea (IBS-D), 27% IBS-constipation (IBS-C), 18% IBS-mixed (IBS-M) and 18% IBS-undetermined (IBS-U). It was characterized as H_2 -producing flora the presence of concentrations of H_2 more than 20 ppm sustained after of 60 minutes and CH_4 less than 12 ppm during study time (180 minutes); CH_4 -producing flora in concentrations of H_2 less than 20 ppm and CH_4 more than 12 ppm after 60 minutes and mixed flora concentrations of H_2 greater than 20 ppm and CH_4 greater than 12 ppm during study time. SIBO was diagnosed when elevation curve of H_2 more than 20 ppm above baseline and elevation of curve CH_4 over 12 ppm of baseline, in more than two consecutive measurements in the first 60 minutes. Statistical analysis Mann-Whitney and Chi-square. Results: 54% presented mixed flora, 41% H_2 -producing flora and 5% CH_4 producing flora. 34% of patients with mixed flora have IBS-D and 30% IBS-C. 42% of patients with H_2 -producing flora have IBS-D. 32% of patients with CH_4 -producing flora have IBS-C, without differences with other phenotypes. 43% of patients with IBS have SIBO; of these 68% have mixed flora. SIBO was more frequent between 27 and 43 years. Conclusion: Unlike other studies, the CH_4 -producing flora was not predominant in patients with IBS-C. Mixed flora is the most frequent in Chilean IBS-patients. It is confirmed that SIBO is common in IBS.

12TH CONGRESS OF ECCO CCIB - BARCELONA, ESPAÑA

LONG-TERM OUTCOMES OF ANTI-TNF THERAPY DISCONTINUATION IN PATIENTS WITH PENETRATING CROHN'S DISEASE

Gompertz M., Ricart E., Ordás I., Alfaro I., López A., Gallego M., Barastegui R., Giner A., Vara A., Masamunt M., Panés J.

Background. Discontinuation of anti-TNF maintenance therapy in patients with Crohn's disease (CD) in remission should be considered in order to reduce the potential long term side effects and costs. Several studies have evaluated relapse rate after discontinuation treatment, but data in penetrating CD are scarce. Methods. Retrospective observational study including patients with penetrating CD in clinical and endoscopic remission who underwent discontinuation of anti-TNF therapy. Clinical, biological and therapeutic variables were analyzed. Clinical relapse was defined as the presence of symptoms and/or fistule activity with the need of retreatment with anti-TNF. Results. Twenty-six patients were included: 54% men; median age 39 years (IQR 15–71); 18/26 (69.2%) had perianal disease, 4/26 (15.4%) internal penetrating and 4/26 (15.4%) internal penetrating and perianal disease; 54% treated with Adalimumab, 46% Infliximab. Median time with anti-TNF treatment before discontinuation was 61 months (IQR 6–146). All patients were in clinical remission at the time of anti-TNF discontinuation: in 62% of cases treatment was stopped because of sustained remission, in 16% due to adverse effects and in 12% by patient request. Median time of follow-up was 38 months (IQR 4–95). During follow-up 7/26 patients (27%) had a clinical relapse, with a median time until relapse of 14 months (IQR 3–29); all these patients regained clinical response after reintroducing anti-TNF treatment. Patients who continued maintenance immunosuppressive therapy after stopping anti-TNF treatment had numerically lower relapse rate [2/15 (13%) vs 5/11 (46%), $p = 0.081$]. Time to relapse was significantly prolonged in patients under immunosuppressive therapy (40.9 ± 12.3 vs. 82.2 ± 8.4 months, $p = 0.04$). Conclusion. A high proportion of patients with penetrating CD in clinical and endoscopic remission, have prolonged remission after discontinuation of anti-TNF therapy. Treatment with immunosuppressant prolongs the duration of remission after anti-TNF discontinuation.

INFLIXIMAB BIOSIMILAR CT-P13 IN INFLAMMATORY BOWEL DISEASE PATIENTS THAT REQUIRE INTENSIFICATION TREATMENT

Gompertz M., Alfaro I., Ricart E., López A., Panés J., Gallego M., Barastegui R., Giner A., Vara A., Masamunt M., Ordás I.

Background. CT-P13 was the first Infliximab biosimilar approved in Europe. Several studies confirmed the efficacy, safety, and interchangeability of CT-P13 in patients with immune mediated inflammatory disorders, but there are limited reports on clinical outcomes in patients with inflammatory bowel disease (IBD) requiring dose escalation. Methods. IBD patients that required dose escalation during treatment with Remicade, or were previously under escalated dosing, were switched to biosimilar CT-P13. Escalation was defined as increased dose ≥ 7.5 mg/kg/8 weeks and/or a shortening of the interval ≤ 6 weeks. Disease activity was evaluated with the Crohn's

Disease Activity Index (CDAI) for Crohn's Disease (CD) and full Mayo Score (including endoscopy) for Ulcerative Colitis (UC). Clinical and biological variables were analyzed before the first infusion of CT-P13 and after 24 weeks of treatment. Results. Thirty patients received escalated CT-P13 dose (18 CD and 12 UC), 53% men, median age 42 years (IQR 22–71). 9/30 patients (30%) were previously intensified with Remicade and switched to CT-P13 maintaining the same dose and 21/30 patients (70%) were switched at the time of dose escalation. Median time with Remicade treatment before switching to CT-P13 was 44 months (IQR 4–110). At 24 weeks of follow-up 80% were in clinical remission: 15/18 (83%) of CD patients had CDAI<150 and 9/12 (75%) of UC patients had Mayo score \leq 2 points. No adverse events were observed in this group of patients treated with CT-P13. 26/30 patients (87%) had Infliximab serum levels <3.0 before intensification and 5/30 (17%) after intensification. No patient developed antibodies against Infliximab, during CT-P13 treatment. No significant changes were observed in clinical and biological parameters after switching to CT-P13 in patients previously intensified with Remicade in whom the dose of Infliximab was maintained stable. Conclusion. This study provides evidence of the efficacy and safety of CT-P13 in IBD patients that require intensification of anti-TNF treatment, and would incur in the highest cost.

2017 ACR/ARHP ANNUAL MEETING - SAN DIEGO, CALIFORNIA

PERFORMANCE OF 2017 ACR/EULAR PROVISIONAL CLASSIFICATION CRITERIA FOR GRANULOMATOSIS WITH POLYANGIITIS IN CHILEAN POPULATION

SF Elgueta, L Ricci Larrea, D Vargas, P Wurmman, I Goecke.

Background Anca Associated Vasculitis (AAV), are a group of necrotizing primary vasculitis, with multisystemic manifestation, of unknown etiology. The variants are: Microscopic Polyangiitis (MPA), Granulomatosis with polyangiitis (GPA), Granulomatosis with Polyangiitis and Eosinophilia (GPE) and AAV limited to one organ. Until now, there are no diagnostic criteria for AAV. Therefore definitions, as Chapel Hill consensus Conference Nomenclature, classification criteria and the physician judgement are used for diagnosis. Currently the DCVAS (Diagnosis and Classification Criteria in Vasculitis) project is developing diagnostic criteria for AAV, using data-driven methods. The preliminary DCVAS classification criteria for granulomatosis with polyangiitis has been recently released. Objectives To evaluate and compare the accuracy of ACR/EULAR 2017 provisional Classification Criteria for GPA with the ACR 1990 Classification Criteria in Chilean patients with AAV. Methods All adult patients (>18 yo) with diagnoses of AAV according to their rheumatologist judgment, from 2000–2016 at the University of Chile, Clinical Hospital (UCCH), were included. Clinical variables of interest were extracted from medical chart and AAV database, which is kept for these patients at the Rheumatology Section of UCCH. Based on that data, the Classification criteria ACR 1990 and 2017 preliminary ACR/EULAR (DCVAS) classification criteria for GPA were applied to each individual. Sensibility, specificity, Likelihood ratio (LR +/-), predictive values (PPV/NPV) and accuracy were calculated for both sets of Criteria as compared to Clinical diagnosis. Results 93 patients were included in the study. 59 patients with GPA, 33 with MPA and 1 with GPE (Patients characteristics are described in Table 1). From the 59 patients with GPA according to clinical judgment, 34 fulfilled the ACR 1990 criteria (57,63%) whereas 51 (86,44%) fulfilled the ACR/EULAR 2007 criteria. From the 33 patients diagnosed as having MPA 9 (27,27%) and 3 (9,09%) fulfilled classification criteria for GPA according to ACR 1990 criteria and 2017 ACR/EULAR preliminary criteria, respectively. The patient with GPE did not classify as GPA by either set of criteria. The values for Sensibility, Specificity, LR+ LR-, PPV and NPV in our population for both Criteria sets, are described in table 2. Conclusions In our population, provisional 2017 ACR/EULAR criteria for classification of GPA have better accuracy than ACR 1990 classification criteria.

DEPARTAMENTO DE PSIQUIATRÍA Y SALUD MENTAL

25TH EUROPEAN CONGRESS OF PSYCHIATRY – FLORENCIA, ITALIA

RELATIONS BETWEEN MINKOWSKI AND LEVINAS, A LOOK BEYOND THE PHENOMENOLOGY IN THE CONSTRUCTION OF THE PSYCHE J. Veliz Uribe, M. Ugalde, P. Catrifi.

Introduction Both Minkowski and Levinas introduced in France phenomenological thinking, psychopathology and metaphysics, respectively. Objectives It is in this context that interested raise the similarities and differences in relation to the study of time these authors in their link to the construction of the self (soi-même). Aims both authors take up the relevance of temporality in the Construction of the psychic, overtaking Husserl's phenomenology, the distinction between thinking and intuition discursive and theoretical thinking and sensitivity. Methods Comparative analysis of the problem of time and its relation to the psyche, Le temps vécu of Minkowski, Autrement qu'être of Levinas. Results you can set a break with Husserl's phenomenology, inspired by the philosophy of Bergson, based on the living back in the studio. At the same time, among the authors reviewed, there is an irreconcilable discrepancy in the notions of activity and passivity in relation to the construction of the self (soi-même). Conclusions Phenomenology applied to the psychic needs to return to its original inspiration to go beyond a methodological rigid reading, which ends up betraying its spirit, which leads her to forget the living world in its complexity. Disclosure of interest the authors have not supplied their declaration of competing interest.

THREE FORMS OF INTUITION IN EUGÈNE MINKOWSKI

J. Veliz Uribe, M. Ugalde, C. Pastén

Introduction Eugène Minkowski is one of the great authors of structural phenomenological psychiatry. However, it has stressed only its influence on the study of schizophrenia, however, the scope of its investigations is much coarser, while addresses issues that attempt to illuminate the way they are set life and humans. Objectives It is interesting to pose as the author emphasizes the importance of intuition, on more than one level, giving an epistemologically worthy rank in the constitution of the self (soi-même), in psychopathology and even in the ontology. Aims It is shown that in Minkowski research on intuition it appears as a study of a symptom called autism, as a psychopathological diagnostic method called empathy, and even as an ontological understanding that purpose of the study time. Methods Reconstruction of the uses of the notion of intuition in the work of Minkowski. Results three ways clearly appear in different planes but complementary, pointing not only to a clinical trial, but take a glimpse metaphysical aspects. Conclusions. The conclusions aimed are highlighting how Minkowski think intuition not only as a dignified way to understand the suffering, or establish a knowledge, but necessary for a clinic and even an approximation of what we are. Disclosure of interest the authors have not supplied their declaration of competing interest.

DEPARTAMENTO DE NEUROLOGÍA Y NEUROCIROLOGÍA

THE 3TH INTERNATIONAL CONFERENCE ON ALZHEIMER'S & PARKINSON DISEASES – VIENA, AUSTRIA

VITAMIN D SUPPLEMENTATION INCREASE PLASMA A β 40 LEVELS AND DECREASE SUSCEPTIBILITY TO OXIDATIVE DEATH OF LYMPHOCYTES FROM MCI PATIENT

C.D. Sanmartin, D.P. Ponce, F. Salech, C. Chacon, M.I. Behrens

Aims. Deficiency of vitamins D (VitD) is a risk factor for the development of mild cognitive impairment (MCI). Low plasma A β levels have been associated to increased AD risk in humans, while VitD supplementation increases A β clearance in an AD transgenic model. We have previously reported that lymphocytes from AD patients have increased susceptibility to oxidative death by H₂O₂ exposure. We evaluated the effect of VitD supplementation on the susceptibility to oxidative death of lymphocytes, A β 40 plasmatic levels and cognitive status in patients MCI of the amnesic (aMCI) and non-amnesic (naMCI) type. Method. Participants were classified in 3 groups: 9 aMCI, 7 naMCI (Clinical Dementia Rating CDR=0.5, Montreal Cognitive Assessment (MoCA) \leq 22), and 16 controls (CDR=0, MoCA \geq 23). Plasma A β 40, cell death and cognitive status were evaluated before and after 6 month supplementation with 50.000 IU VitD per week for 6 weeks. Cell death of lymphocytes was determined by flow cytometry after 20 h treatment with H₂O₂. Plasma A β 40 was detected by ELISA. Results. Lymphocytes from naMCI patients displayed a higher susceptibility to oxidative death than controls and aMCI, but less than AD patients. After VitD supplementation, the susceptibility to death decreased and plasma A β 40 levels increased in controls and naMCI patients. Conclusion. Adjusting the plasma levels of VitD improved the susceptibility to oxidative death of lymphocytes and increased the clearance of A β 40 which might represent a cost-effective and safe way of reducing the incidence of MCI in the growing elderly population.

FIXATION-RELATED POTENTIALS AND VISUAL EXPLORATION DURING A VIRTUAL WATER MAZE TASK IN AGING AND EARLY ALZHEIMER'S DISEASE

A. Paula-Lima, R. Hafelin, S. Madariaga, J.L. Valdes, M.I. Behrens, C. Hidalgo, P. Maldonado, E. Brunetti

Aims. Alzheimer's disease (AD) is the leading cause of dementia worldwide. Studies of large populations promote understanding of the mechanisms involved in memory loss and the search for markers to facilitate early diagnosis. In the present investigation, we combined electroencephalography (EEG) and eye movement records during the performance of a virtual navigation task, in which subjects with very early AD and healthy controls had to learn a trajectory in space, based on visual cues. Method. We compared human EEG records, registered under baseline conditions or when performing a virtual space navigation task (virtual Morris Water Maze), in subjects diagnosed with very early or incipient AD, in aged subjects with no cognitive impairment, and in young subjects. We analyzed navigation strategy, visual exploration, eye-fixation related potentials and performance in the MoCA test for each group. Results. The results show that subjects with initial EA: 1) do not exhibit spatial learning along the task, unlike control subjects; 2) the electrical activity associated with visual information extraction is significantly lower in these subjects than in the control group; 3) visual information does not spread from occipital regions to parietal regions; 4) Visual exploration is impaired and 5) the level of activity in each subject correlated with the score on the MoCA test. Conclusion. These results represent a significant advance in the understanding of the mechanisms involved in the loss of spatial encoding in AD, and might be used as an early test for these patients. This work was supported by FONDECYT (1150736, 1140545), BNI P-09-015F, CENEM-ICM-P10-001-F.

ALZHEIMER ASSOCIATION INTERNATIONAL CONFERENCE – LONDRES, REINO UNIDO

AMPLITUDE AND LATENCY OF AUDITORY BRAINSTEM RESPONSES CORRELATE WITH IMPAIRMENT IN ACTIVITIES OF DAILY LIVING IN HEALTHY ELDERLS

Carolina Delgado, Alexis Leiva, Melissa Martinez., Kattalin Elespuru, Ambar Soto., Paul H. Delano.

Background. There is increasing epidemiological evidence showing an association between presbycusis or age-related hearing loss and cognitive decline in elderly people. The Health ABC Study has shown that presbycusis subjects with audiometric hearing thresholds (PTA) worse than 40 dB are more likely to develop cognitive decline. Before the development of audiometric hearing loss, aged subjects could have communication problems, a clinical entity known as hidden hearing loss (HHL). The amplitudes and latencies of auditory brainstem responses (ABR) at supra-thresholds levels have been used as objective measures to detect HHL. Objective: To study whether supra-thresholds ABR responses are associated with impairment in activities of daily living (ADL) in healthy elders. Methods. 52 Persons from the ANDES study ≥ 65 years without dementia (MMSE >24) with normal hearing thresholds (PTA <20 dB, n=13), with mild (PTA 20-39dB, n=29) or moderate presbycusis (PTA ≥ 40 dB, n=10), were evaluated with a comprehensive neuropsychological assessment, questionnaires of ADL and with auditory measurements including: PTA, and amplitudes and latencies of ABR waves I and V obtained at supra-thresholds levels. Neuropsychological and ADL data were compared between groups of hearing impairment, and lineal regressions between these data and different auditory assessment were performed. Results. Those with moderate presbycusis (n=10) had more perseverative errors in the Wisconsin card sorting task (ANOVA, F(2)=3.4, p=0.04) than the other groups, without any other differences in the neuropsychological or ADL assessment (Table 1). Instrumental ADL impairments were correlated with latencies of bilateral ABR waves V: shopping (right: r=0.44, p=0.001; left: r=0.63, p<0.001), work (right: r=0.33, p=0.02; left: r=0.3, p<0.03) and house hold (right: r=0.29, p=0.04; left: r=0.39, p<0.006). Once excluding those with moderate presbycusis, we found significant correlations in the latencies of left wave V for house hold (r=0.38, p=0.013) and for communication (r=0.36, p=0.019). In addition, the amplitudes of wave I from the left ear were correlated with impairment in traveling (r=-0.40, p=0.013) and technology (r=-0.45, p=0.005). Conclusions. Supra-thresholds ABRs are good predictors of ADL impairments in elderlies without evident cognitive or hearing impairment. These results reinforce the study of other risk factors for cognitive decline in the elderly.

ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY - MADRID, ESPAÑA

MITOCHONDRIAL DYSFUNCTION IN IDIOPATHIC INFLAMMATORY MYOPATHY DERIVED MYOBLASTS

C Basualto-Alarcon, MF Bozán, J Bevilacqua, F Urra, D González, H Gatica, A Göecke, P Wurmman, MF Sabugo, S Saavedra, C Cárdenas

Background Idiopathic inflammatory myopathies (IIM) are acquired skeletal muscle diseases, characterized by proximal muscle weakness. This syndrome includes five different (1) diseases, nevertheless, in this work, we included dermatomyositis (DM) and polymyositis (PM) patients. Has been reported that despite treating inflammation, muscle atrophy and weakness persist in some patients, suggesting an inherent muscle cause (2,3). In addition, histological studies show some mitochondrial abnormalities. Our aim was to evaluate a possible role for mitochondrial dysfunction in the pathophysiology of this diseases. Objectives To compare the mitochondrial status of myoblast obtained from myositis patients -and healthy control- biopsies. Methods Primary cultured myoblasts extracted from the deltoid of IIM patients were used and compared with myoblasts obtained from normal patients subjected to shoulder surgery. Also, a human skeletal muscle cell line (RCMH) was used as control. The bioenergetic profile was analyzed with an Extracellular flux analyzer96 (Seahorse Biosciences). Also, biopsy tissue was used for Western blot (WB) and immunofluorescence experiments. Results Basal oxygen consumption rate, ATP-linked oxygen consumption, maximal oxygen consumption and spare respiratory capacity were lower in IIM myoblasts when compared to RCMH myoblasts, however, when compare to control primary cultured myoblasts we only find differences in ATP-linked oxygen consumption. Expression levels of mitochondrial complexes (I, III, IV and V) were analyzed by WB in tissue samples. No differences were observed between control and IIM patients. Mitochondrial area was estimated by immunofluorescence of the voltage dependent anion channel (VDAC), which show no differences between control and patients. Conclusions IIM derived myoblasts present a compromised mitochondrial function, compared to control myoblasts. Specially, oxygen consumption associated with ATP synthesis show decreased levels in patients. Although, expression levels of the mitochondrial complexes as well as mitochondrial area were not different between control and patients. Future experiments should address if IIM mitochondria are consuming less oxygen because of a lower ATP demand or because a primary mitochondrial damage.

22ND INTERNATIONAL CONGRESS OF THE WORLD MUSCLE SOCIETY – ST. MALO, FRANCIA

CONNEXIN-BASED HEMICHANNELS ARE KEY FACTORS IN THE PATHOLOGICAL MECHANISM UNDERLYING DYSFERLINOPATHY

G. Fernández, J. Bevilacqua, A Cardenas, J Sáez, P Caviedes, L Cea

Dysferlinopathy onsets during the second and third decades of life, usually as progressive lower-limb weakness that later involves trunk and upper-limbs. Dysferlin is localized mainly in the sarcolemma and participates in membrane repair. However, in dysferlin-deficient (DD)

mice the recovery of the membrane resealing function by expression of a mini-dysferlin does not arrest progressive muscular damage. The latter suggests the presence of dysferlin-dependent pathogenic mechanisms still unknown. In this regard, we have demonstrated a persistent de novo expression of functional connexin-based hemichannels (Cx HCs) in pathological conditions that affect skeletal muscles. Such membrane channels are permeable to Ca²⁺ and contribute critically to muscular damage. Connexins 40.1, 43 and 45 were localized in the sarcolemma of myofibers of human muscle biopsies from 5 unrelated dysferlinopathy patients. DD mice myofibers also exhibited positive immunostaining for Cxs 39, 43 and 45. In addition, an elevated Cx HCs activity, concomitant with elevated resting intracellular free Ca²⁺ levels, was observed in myofibers obtained from DD mice, compared to control myofibers. Further, we detected a lower performance of DD mice in rota-rod motor testing compared to control mice. Moreover, all these changes were prevented in triple knockout mice deficient in Cx 43 Cx 45, and dysferlin, suggesting that Cxs are relevant in the pathogenic mechanism of dysferlinopathy. Therefore, Cx HCs could be a most suitable candidate for pharmacological therapy.

FURTHER INSIGHTS IN NEMALINE MYOPATHY (NM) WITH HYALINE MASSES

J. Bevilacqua, Malfatti, C.Labasse, G.Brochier, A.Madelaine, E. Lacene, J. Rendu, B. Doray, J. de Monredon, P. Laforêt, B. Eymard, M. Fardeau, N. Romero

Nemaline myopathies (NM) comprehend a heterogeneous group of rare congenital muscle conditions characterised by hypotonia, muscle weakness, skeletal deformities with nemaline bodies (rods) in muscle biopsy. Here we describe four NM patients with distinctive hyaline masses in the muscle biopsy in addition to the typical NM histological features. Age at onset varied from early childhood, presenting with myopathy, skeletal deformities and retard on developmental motor milestones, to late-onset-myopathy beginning in the third decade as progressive generalized amyotrophy and muscle weakness. All patients presented with a moderate restrictive respiratory impairment, but no cardiac involvement was observed. Muscle biopsy analyses revealed in all samples round-shaped centrally located protein aggregates corresponding to hyaline masses, clusters nemaline bodies and type 1 fibre predominance or uniformity. Electron microscopy confirmed that hyaline masses consisted of centrally located protein aggregates originating from the z-line extending longitudinally through several sarcomeres. Typical rods were found separated from the protein aggregates, often localized in the subsarcolemmal areas. Genetic screening revealed two pathogenic mutation in nebulin (NEB) gene (P14, Malfatti et al. 2014) and one single exon 151 NEB gene deletion in another. Molecular screening is ongoing for the other two patients. Similar histopathological findings were previously reported by Selcen et al. in 2002 in two patients with cardiopathy and no genetic characterization. In conclusion we further characterized nemaline rods myopathy with hyaline masses and we enlarge the histopathological spectrum of NEB-related nemaline myopathies.

DEPARTAMENTO DE CIRUGÍA

ANNUAL MEETING AMERICAN SOCIETY OF COLON RECTAL SURGEONS – WASHINGTON, EEUU

TRANSANAL TOTAL MESORECTAL EXCISION (TaTME): LONG-TERM ONCOLOGICAL AND FUNCTIONAL OUTCOMES.

M. Abedrabo, K. Carrillo, A. Sanguinetti, S. Lopez, R. Azolas, M. Diaz, J. Llanos, G. Botic

Purpose/Background: Since transanal approach gives better vision for surgical planes, in theory, better mesorectal quality and nerve preservation could be achieved. If this leads to better oncological and functional outcomes has not been established. We present our case series at a University Hospital. Methods/Interventions: TaTME was introduced in 2012 at our institution. Since then, patients were prospectively enrolled in a database. We included patients with rectal at < 10 cm from anal verge, eligibility criteria for TaTME was at least one of the following: narrow pelvis, obese patients, and intraoperative decision. Preoperative study included colonoscopy, rigid rectoscopy, pelvic MRI and Chest/Abdomen/Pelvis CT in all patients. When considered necessary, abdomen MRI, endorectal/endoanal ultrasound, or PET-CT were performed for selected cases. Patients with cT3-4 or cN+ received neoadjuvant chemoradiation. Demographic and clinical data was obtained. TaTME was performed as part of a hybrid procedure, with an abdominal and transanal approach. Surgical and histopathological data was collected. Standard oncological follow-up for all patients was done. Functional outcome was evaluated with Low Anterior Resection Syndrome (LARS) score survey, we only included patients with >12 months after ileostomy closure. Results/Outcome(s): A total of 37 patients were prospectively included for this study. Male to female ratio was 4.3:1 and mean age was 56,9 ± 13,3 years old. Mean distance from anal verge was 4.6 cm (range 1-10 cm). All patients, except one, received neoadjuvant therapy. Intersphincteric resection with coloanal anastomosis was performed in 15 patients (40.5%), none received partial external sphincter resection. Ultralow anterior resection was performed in the remaining 22 patients. Median lymph node harvest was 12 (range 1 to 38). Only 1 patients had positive circumferential margin. Distal margin was <1 cm in 10 patients (33.3%). Seven patients had complete pathological response. Anatomopathological staging was 18.9%, 29.7%, 18.9%, 21.6% and 10.8% for Stage 0, I, II, III and IV, respectively. Four year overall survival (OS) was 81.2%. Recurrence was found in 4 patients (10.8%), but only 1 local recurrence (in the rectovaginal septum). Of 19 eligible patients, 14 (73.7%) answered the

LARS score questionnaire. Mean follow-up was 18.6 ± 8.9 months. Only 1 patient had no LARS, 2 had minor LARS, and 11 (57.9%) had major LARS. Mean LARS score was 32.6 ± 6.6 pts. Conclusions/Discussion: We find adequate oncological outcomes in our series. Functional outcomes after surgery in low rectal cancer are usually unsatisfactory. High prevalence of low anterior resection syndrome was found in our series, most of them with severe LARS.

TRANSANAL TOTAL MESORECTAL EXCISION (TATME): SHORT-TERM SURGICAL OUTCOMES.

M. Abedrapo, K. Carrillo, S. Lopez, A. Sanguinetti, J. Llanos, M. Diaz, R. Azolas, G. Bocić

Purpose/Background: One of the pillars of surgical treatment is total mesorectal excision (TME). Classical abdominal TME has been recently challenged by new approaches. Transanal approach has theoretical benefits, 199 however we still lack strong evidence. We present our case series at a University Hospital. Methods/Interventions: TaTME was introduced in 2012 at our institution. Since then, patients were prospectively enrolled in a database. We included patients with rectal cancer at < 10 cm from anal verge, eligibility criteria for TaTME was at least one of the following: narrow pelvis, obese patients, and intraoperative decision. Preoperative study included colonoscopy, rigid rectoscopy, pelvic MRI and Chest/Abdomen/Pelvis CT in all patients. Abdomen MRI, endorectal/endoanal ultrasound or PET-CT were performed for selected cases. Patients with cT3-4 or cN+ received neoadjuvant chemoradiation. Demographic and clinical data was obtained. TaTME was performed as part of an hybrid procedure, abdominal and transanal approach. Gelpoint® Path (Applied Medical Resources Corporation, CA) was used. After marking by electric diathermy at least 1 cm distal to the tumor, a 2-0 Prolene purse-string suture was placed. A pneumorectum/perirectum was created using a standard laparoscopic CO2 insufflator at a pressure of 12-15 mmHg. A 10-mm camera and conventional laparoscopic instruments were used. Surgical and postoperative data was collected. Postoperative complications were organized according to Clavien-Dindo classification. Results/Outcome(s): A total of 37 patients were prospectively included for this study. Male to female ratio was 4.3:1 and mean age was $56.9 \pm 13,3$ years old. Twenty four (64.8%) patients were overweight/obese. Mean distance from anal verge was 4.6 cm (range 1-10 cm). All patients, except one, received neoadjuvant therapy. Intersphincteric resection was performed in 15 patients (40.5%). Ultralow anterior resection was performed in the remaining 22 patients. Laparoscopic abdominal approach was performed in 34 patients (91.9%), conversion rate of 11.8%, and open abdominal approach in 3 patients. Two significant intraoperative events were reported: prostatic bleeding, and urethral injury. All patients had diverting loop ileostomy. Median operative time was 270 minutes. Mayor complications defined as Clavien Dindo III-IV were found in 9 patients (24.3%). Five reoperations for: 2 anastomotic dehiscence, 2 partial necrosis of descended colon, 1 late anastomotic stricture. We had no mortality in this group. Median hospital stay was 6 days. To date, 75.7% underwent reversal of their loop ileostomy. Conclusions/Discussion: Transanal approach gives better vision of surgical planes. However, in our series it has not proven better surgical outcomes than conventional abdominal approach. Nonetheless, most morbidity cannot be entirely attributed to the TaTME, only urethral injury seems specific for TaTME.

DEPARTAMENTO DE OTORRINOLARINGOLOGÍA

ENT WORLD CONGRESS – PARIS, FRANCIA

ADAPTIVE GAP IN NOISE TEST PERFORMANCE IN NORMAL HEARING ADULTS ACROSS LIFESPAN

M. Torrente, D. Retuert, C. Martinez

Purpose. Asses the variation of an adaptive test of gap in noise detection (GIN) in different age groups. Hypothesis: the GIN threshold will increase in older subjects. Material and method. Subjects included were volunteers of three age groups: 20 to 39, 40 to 59, and over 60 years of age. Exclusion criteria: cognitive impairment (assessed with Mini Mental test), history of otic diseases, average pure tone threshold (PTA) for 0.5, 1, and 2 KHz greater than 30 dBHL, no consent. For the evaluation of GIN we used the Beta Adult version of the Adaptive Tests of Temporal Resolution© (ATTR). Presentation of the stimulus was within channel, that is narrow band noise centered on 2KHz before and after a silence with adaptive duration; and across channel, narrow band noise centered on 2KHz before the silence and centered on 1KHz after the gap. In both situations the duration of the burst prior to gap is 300 ms and posterior to the gap varies between 250 and 350 ms. Data analyzed with program Stata 13.0. The study was approved by the local ethics committee. Results. A total of 53 subjects were recruited, age between 23 and 77 years. For the young group, the median within channel (WC) detection gap was 4.33 ± 1.8 s; for the middle age group 4.58 ± 2.63 s and for the older patients 6.75 ± 5.75 s. The across channel (AC) detection gap median thresholds were 57.13 ± 20.8 s; 77.46 ± 36.79 s; and 71.92 ± 62.21 s respectively for each group. A significant correlation with age was identified for both modalities of GIN tested, $p=.004$ and $p=.03$ respectively. No difference between sexes. Conclusions. This paper provides reference data of GIN detection threshold for an adaptive test, with stimulus within and across channel, for different age groups. We identified a significant correlation between gap detection and age.

QUALITY INDICATORS OF THE NEWBORN HEARING SCREENING PROGRAM IN A HOSPITAL FROM SOUTH AMERICA.

M.Torrente, R.Bravo, M.Kreff, M.Garci, F.Gomez, P.Sandoval

Purpose. Assess the accomplishment of quality indicators of the newborn hearing screening program in Hospital Padre Hurtado, Chile, as proposed by the Joint Committee on Infant Hearing Loss. Methods. Two stage screening protocol: otoacoustic emissions for babies in the well-infant nursery (WIN) and automated auditory brainstem responses for those in the intensive care unit (NICU) or with risk factors. If they fail one or both ears they proceed to a comprehensive audiological assessment. Results. 12.309 live births between 01/01/2014 and 108/31/16, 12.103 were screened before discharge (98.5%). 79 cases proceeded to diagnostic assessment, referral rate 0.6%. 95% infants completed audiological evaluation before three months, seven cases were diagnosed with permanent sensorineural hearing loss. Amplification was provided before 6 months of age in 57% of deaf children. Four patients attend follow up, three of them had the first developmental assessment with standardized protocols before 12 months of age (43%). Conclusions Quality indicators of the JCIH are met by our newborn hearing program regarding screening and diagnosis. Timing for amplification and follow up of children with hearing loss is adequate in less than 60% of the cases.

REFERENCE VALUES OF THE SPANISH VERSION OF THE STAGGERED SPONDAIC WORD TEST IN ELDERLY PATIENTS.

M. Torrente, O. Cañete, V. Almasio, S. Purdy

Purpose. Assess the performance of the Spanish version of the Staggered Spondaic Word Test (S-SSW) in a group of elderly patients. Hypothesis: the total number of errors increases with age. Material and method. Patients attending the Otorhinolaryngology clinic of Hospital Padre Hurtado, Chile, were recruited. Inclusion criteria: older than 60 years of age, without cognition impairment evaluated by the Mini Mental test. Exclusion criteria: cognition impairment, previous otological disease, previous use of hearing aid. All cases underwent a tonal audiometry, speech recognition with monosyllables and the S-SSW test. The study was approved by the local ethics committee. Correlations were assessed with Spearman test and group differences with Mann Whitney test. A p value < .05 was significant. Results. 70 patients were included. The median age was 73 years old, with a range between 60 and 89. Pure tone threshold average (PTA) for frequencies 0.5 to 2 KHz was $40 \pm 13,9$ dBHL. The median corrected number of errors (cS-SSW) for all patients was $7,69 \pm 14,21$. When grouped by decades, the median cS-SSW for 60's was $2,32 \pm 14,42$, for 70's $15,32 \pm 13,33$, and 80's $9,75 \pm 13,76$. There was a significant correlation between cS-SSW and age, $r=.85$, $p<.001$. The median number of errors was significantly lower for the 60's versus 70's patients, $p=.03$. There was no significant difference between 70's and 80's, $p=.6$. In the SSWgram, the left competing situation performed worst than right competing across all age groups. Discussion. This is the first report of the S-SSW in elderly patients to our knowledge. The number of errors increased with age, independent of hearing loss, with a turning point at 70 years old. The left competing situation always perform worst, independent of age.

DEPARTAMENTO DE UROLOGÍA

CONGRESO 47TH ANNUAL MEETING OF THE INTERNATIONAL CONTINENCE SOCIETY – FLORENCIA, ITALIA

FACTORS RELATED TO THE VOIDING PATTERN IN WOMEN WITHOUT VOIDING SYMPTOMS

Valdevenito J P, Mercado A, Hernandez-Matas R M, Alvarez D, Kobus C, Bull L

Hypothesis / aims of study: Most of our knowledge of voiding function in women has been extrapolated from studies of patients with lower urinary tract dysfunction. Few studies have described the voiding patterns of "healthy, continent and/or asymptomatic" women. All women included in these reports voided with a measurable detrusor contraction and variable participation of abdominal muscles, which might be considered the normal voiding pattern. Definitions of what is considered detrusor contraction and abdominal contraction during voiding vary between these studies. It has been declared that only patients with low urethral closure pressure void with negligible or no detrusor contraction, which leads to question if these types of voiding are indeed normal. The aim of this study was to describe the voiding pattern in women without voiding symptoms and compare clinical and urodynamic characteristics between women who urinate using detrusor contraction (with or without participation of abdominal muscles) and women who do not use detrusor contraction. To our knowledge this is the first study to investigate this. Study design, materials and methods In a three year period, 580 consecutive women underwent conventional cystometry following "good urodynamic practices". At the time of examination and in a standardized manner, symptoms were obtained by a directed anamnesis as being either present or absent without any stratification for severity. We included patients without voiding symptoms (slow stream, straining to void and intermittent stream) and excluded those with: a) previous lower urinary tract surgery, b) pelvic organ prolapse > stage II, c) pelvic radiotherapy, d) medications active on the lower urinary tract, e) bladder pain syndrome/interstitial cystitis, f) insulin-dependent diabetes mellitus and g) neurological diseases. In the pressure-flow study, detrusor contraction (Det-cont) was defined as an increase of detrusor pressure at maximum flow rate ≥ 10 cm H₂O over baseline and abdominal contraction (Abd-cont) as an increase of abdominal pressure at maximum flow rate ≥ 10 cm H₂O over baseline. Four voiding patterns were determined: a) voiding using Det-cont, b) voiding using Det-cont and Abd-cont, c) voiding using Abd-cont and d) voiding without Det-cont or

Abdcont. Patients were classified according to their: a) age (≤ 50 or > 50 years old), b) history of hysterectomy, c) symptoms of stress, urgency or mixed urinary incontinence, d) presence of detrusor overactivity and e) degree of sphincteric deficiency (abdominal leak point pressure < 100 or ≥ 100 cm H₂O). We compared these variables between women who voided using Det-cont (with or without Abd-cont) and those who do not (women that voided using Abd-cont and women that voided without Det-cont or Abdcont). Either Student's t test or Wilcoxon rank-sum test was used to compare the numerical variables. Either the chi-square test or Fisher's exact test was used to compare the categorical variables. The odds ratios were calculated. The multivariate analysis was performed with the logistical regression method. The information was processed with the Stata 12.1 program (StataCorp, 2012), and statistical significance was defined as $P < 0.05$. Results One hundred eighty six women age 58 ± 10.7 (range 24 – 83) years formed the study group. Table 1 shows some of their clinical and urodynamic characteristics. The vast majority of women voided using Det-cont with or without Abd-cont (77.4%). Women that voided using Det-cont with or without Abd-cont were significantly younger than the others (56.8 ± 10.8 versus 62.2 ± 9.6 years, $p=0.004$), had similar maximum flow rates (26 ± 8.8 versus 28 ± 11.5 mL/s, $p=0.513$) and had not significantly different post void residual volumes (9 ± 33 versus 17 ± 58 mL, $p=0.667$) than the others. Table 2 shows the univariate and multivariate analysis of the variables associated with voiding using Det-cont with or without Abd-cont. Interpretation of result. The classic description of voiding patterns in women did not provide information on symptoms of the women studied. This study included only women without voiding symptoms and excluded many factors that can alter lower urinary tract function. Although they are not completely healthy individuals (due to detrusor overactivity and urodynamic stress urinary incontinence during the filling phase), we think that these results give a good approximation to the voiding phase of normal women. Statistically significant association between age and degree of sphincteric deficiency with voiding using Det-cont (with or without Abd-cont) suggest that voiding pattern may vary with ageing and changes in the sphincteric deficiency status. These factors should be taken into consideration when analyzing the voiding phase in women. Further studies are required to define normal and abnormal voiding patterns in women. Concluding message: The vast majority of women without voiding symptoms voided using Det-cont with or without Abd-cont. Voiding pattern may vary with ageing and changes in the degree of sphincteric deficiency.

DEPARTAMENTO DE OBSTETRICIA Y GINECOLOGÍA

22ND WORD CONGRESS OF ADVANCES IN ONCOLOGY - ATENAS, GRECIA

METFORMIN PREVENTS NGF-DEPENDENT PROLIFERATIVE AND PRO-ANGIOGENIC EFFECTS IN EPITHELIAL OVARIAN CANCER AND ENDOTHELIAL CELLS

Maritza Garrido, Margarita Vega, Andrew Quest, Carmen Romero.

Epithelial ovarian cancer (EOC) is detected in advanced stages with poor prognosis and is characterized by high angiogenesis that promote tumor growth and metastasis and are regulated by pro-angiogenic as well as growth factors. Our group has reported that Nerve Growth Factor (NGF) is overexpressed in EOC, where it promotes proliferation and survival of ovarian cancer cells. Moreover, NGF stimulates directly and indirectly the production of pro-angiogenic factors in endothelial cells, thereby, contributing to tumor angiogenesis. Currently available therapies yield modest results in patients making it necessary to develop new alternative therapies. Metformin is of interest in this context, because it has been attributed anti-carcinogenic effects but the underlying mechanisms remain unknown. The aim of this study, was to determine the effects of the antidiabetic drug metformin on NGF-dependent proliferation in epithelial ovarian cancer cells and vasculogenic potential in endothelial cells. To this end, cell lines (epithelial ovarian cancer cell A2780, human ovarian surface epithelial HOSE and human endothelial cells EAhy926) were treated with NGF with or Without metformin. Cell viability was evaluated using the MTS assay, the cell proliferation was examined by immunodetection of ki-67 and cell cycle progression was evaluated by flow-cytometry in all cellular lines, while the vasculogenic potential of endothelial cells was evaluated using vasculogenesis assay in matrigel. Our results, showed that NGF increases cell viability, cell cycle progression and Ki-67 immunodetection in A2780, HOSE and EA.hy926 cells. In contrast, Metformin decreases cell viability cell cycle progression and Ki-67 immunodetection in A2780 and EA.hy926 cells, without significant changes in HOSE cells. Interestingly, the effect of NGF was prevented in the presence of Metformin. Additionally, in EA.hy926 cells metformin prevented the increased angiogenic score observed in response to NGF stimulation. Altogether, these results show that metformin prevents the pro-angiogenic and proliferative effects of NGF in endothelial and ovarian cancer cells. Given that, NGF plays a significant role in EOC progression and our findings here showing that metformin blocked NGF-induced effects, we anticipate that metformin holds considerable promise in the future for the treatment of ovarian cancer.

ROLE OF MICRORNA-23B IN EPITHELIAL OVARIAN CANCER AND ITS REGULATION BY NERVE GROWTH FACTOR

Carmen Romero, Andrea Hernandez, Paula Cuevas, Rocío Retamales, Carolina Vera, Margarita Vega

Epithelial ovarian cancer (EOC) represents 90% of ovarian cancer. Nerve growth factor (NGF) and its high affinity receptor TRKA levels are elevated in this pathology. NGF increases proliferation, migration and vasculogenesis through its TRKA receptor on endothelial cells, and by indirectly inducing vascular endothelial growth factor (VEGF) expression in epithelial ovarian cancer cells. It is known that microRNAs

(miRs) are the widest family of non-coding RNAs; they bind to 3'-UTR of mRNAs to inhibit their translation or to degrade them. Therefore, in cancer when some miRs increase, tumour suppressor proteins decrease and when some miRs decrease, oncogenic protein increase. In EOC, a deregulation of some miRs expression has been described, including alteration of miR-23b, among others. The relationship of NGF-miRs in EOC has not been well studied. The aim of this study was to evaluate miR-23b in EOC progression and the changes of this miR by NGF in ovarian cellular line. We found that miR-23b decrease with the EOC progression of TRKA receptor by NGF decreases miR-23b in human ovarian surface epithelial cell line (HOSE cells) and in epithelial ovarian cancer cell line (A2780). When antibody against NGF and a soecific inhibitor to TRKA receptor was used, the decrease of miR-23b by NGF action was inhibited. It has been reported that the transcription factor c-MYC changes miR-23b levels in multiple mveloma cells. Additionally, this factor is involved in cellular proliferation and VEGF expression by action of NGF in epithelial ovarian explants. These results suggest that some miRs can change their levels in EO by NGF action, increasing oncoproteins and decreasing tumors suppressors protein.