El material que se presenta a continuación proviene de los datos proporcionados por la OAIC (Oficina de Apoyo a la Investigación Clínica) de nuestro Hospital.

Abstracts de publicaciones internacionales ISI 2012

DEPARTAMENTO CARDIOVASCULAR

PREVIOUS ADMINISTRATION OF NALTREXONE DID NOT CHANGE SYNERGISM BETWEEN PARACETAMOL AND TRAMADOL IN MICE.

PHARMACOL BIOCHEM BEHAV. 2012 JUL;102(1):72-6.

Miranda HF, Noriega V, Prieto JC.

In the treatment of acute and chronic pain the most frequently used drugs are nonsteroidal anti-inflammatory drugs (NSAIDs), e.g., paracetamol; opioids, e.g., tramadol, and a group of drugs called coanalgesics or adjuvants (e.g., antidepressants, anticonvulsants). The aim of this work was to determine the nature of the interaction induced by intraperitoneal or intrathecal coadministration of paracetamol and tramadol. The type of interaction was evaluated by means of isobolographic analysis, using the acetic acid writhing test as an algesiometer in mice. In addition, the involvement of opioid receptors in the interaction was studied using naltrexone, a non-selective opioid receptor antagonist. The administration of paracetamol or tramadol induced a dose-dependent antinociceptive activity in the assay. The dose-response curves were characterized by equal efficacy but different potencies, being i.t. paracetamol 11.84 times more potent than i.p. paracetamol, and i.t. tramadol 3.54 times more potent than the i.p. tramadol. The isobolographic analysis indicates a synergistic interaction between the coadministration of i.p. or i.t. paracetamol with tramadol. The interaction index values were similar for the i.p. and i.t. coadministration with values of 0.414 and 0.364, respectively. The different mechanisms of action of paracetamol and tramadol strongly explain the analgesic synergism between them, in agreement with the general theory of drug interaction. This synergic interaction was not modified by the non selective opioid antagonist, naltrexone. This association could be of clinical significance in the treatment of pain with a reduction of doses and adverse effects.

EFFECT OF CARVEDILOL AND NEBIVOLOL ON OXIDATIVE STRESS-RELATED PARAMETERS AND ENDOTHELIAL FUNCTION IN PATIENTS WITH ESSENTIAL HYPERTENSION.

BASIC CLIN PHARMACOL TOXICOL. 2012 NOV;111(5):309-16.

Zepeda RJ, Castillo R, Rodrigo R, Prieto JC, Aramburu I, Brugere S, Galdames K, Noriega V, Miranda HF.

Oxidative stress and endothelial dysfunction have been associated with essential hypertension (EH) mechanisms. The purpose of this study was to evaluate the effect of carvedilol and nebivolol on the oxidative stress-related parameters and endothelial function in patients with EH. The studied population included 57 patients, either sex, between 30 and 75 years of age, with mild-to-moderate EH complications. Participants were randomized to receive either carvedilol (12.5 mg) (n = 23) or nebivolol (5 mg) (n = 21) for 12 weeks. Measurements included; 24-hr ambulatory blood pressure (BP), flow-mediated dilatation, levels of nitric oxide estimated as nitrite - a nitric oxide metabolite (NO (2)) - in plasma, and oxidative stress-related parameters in plasma and erythrocyte. EH patients who were treated with nebivolol or carvedilol showed systolic BP reductions of 17.4 and 19.9 mmHg, respectively, compared with baseline values ($p < 0.01$). Diastolic BP was reduced by 13.7 and 12.8 mmHg after the treatment with ebivolol and carvedilol, respectively ($p < 0.01$) (fig. 2B). Nebivolol and carvedilol showed 7.3% and 8.1% higher endothelium-dependent dilatation in relation to baseline values ($p < 0.05$). Ferric-reducing ability of plasma (FRAP) and reduced glutathione/oxidized glutathione (GSSH) ratio showed 31.5% and 29.6% higher levels in the carvedilol group compared with basal values; however, nebivolol-treated patients did not show significant differences after treatment. On the other hand, the NO (2) plasma concentration was not modified by

the administration of carvedilol. However, nebivolol enhanced these levels in 62.1% after the treatment. In conclusion, this study demonstrated the antihypertensive effect of both beta-blockers. However, carvedilol could mediate these effects by an increase in antioxidant capacity and nebivolol through the raise in NO (2) concentration. Further studies are needed to determine the molecular mechanism of these effects.

THROMBIN-RECEPTOR ANTAGONIST VORAPAXAR IN ACUTE CORONARY SYNDROMES.

N ENGL J MED. 2012 JAN 5;366(1):20-33.

Tricoci P, Huang Z, Held C, Moliterno DJ, Armstrong PW, Van de Werf F, White HD, Aylward PE, Wallentin L, Chen E, Lokhnygina Y, Pei J, Leonardi S, Rorick TL, Kilian AM, Jennings LH, Ambrosio G, Bode C, Cequier A, Cornel JH, Diaz R, Erkan A, Huber K, Hudson MP, Jiang L, Jukema JW, Lewis BS, Lincoff AM, Montalescot G, Nicolau JC, Ogawa H, Pfisterer M, Prieto JC, Ruzyllo W, Sinnaeve PR, Storey RF, Valgimigli M, Whellan DJ, Widimsky P, Strony J, Harrington RA, Mahaffey KW; TRACER Investigators.

BACKGROUND: Vorapaxar is a new oral protease-activated-receptor 1 (PAR-1) antagonist that inhibits thrombin-induced platelet activation. METHODS: In this multinational, double-blind, randomized trial, we compared vorapaxar with placebo in 12,944 patients who had acute coronary syndromes without ST-segment elevation. The primary end point was a composite of death from cardiovascular causes, myocardial infarction, stroke, recurrent ischemia with rehospitalization, or urgent coronary revascularization. RESULTS: Follow-up in the trial was terminated early after a safety review. After a median follow-up of 502 days (interquartile range, 349 to 667), the primary end point occurred in 1031 of 6473 patients receiving vorapaxar versus 1102 of 6471 patients receiving placebo (Kaplan-Meier 2-year rate, 18.5% vs. 19.9%; hazard ratio, 0.92; 95% confidence interval [CI], 0.85 to 1.01; P=0.07). A composite of death from cardiovascular causes, myocardial infarction, or stroke occurred in 822 patients in the vorapaxar group versus 910 in the placebo group (14.7% and 16.4%, respectively; hazard ratio, 0.89; 95% CI, 0.81 to 0.98; P=0.02). Rates of moderate and severe bleeding were 7.2% in the vorapaxar group and 5.2% in the placebo group (hazard ratio, 1.35; 95% CI, 1.16 to 1.58; P<0.001). Intracranial hemorrhage rates were 1.1% and 0.2%, respectively (hazard ratio, 3.39; 95% CI, 1.78 to 6.45; P<0.001). Rates of nonhemorrhagic adverse events were similar in the two groups. CONCLUSIONS: In patients with acute coronary syndromes, the addition of vorapaxar to standard therapy did not significantly reduce the primary composite end point but significantly increased the risk of major bleeding, including intracranial hemorrhage. (Funded by Merck; TRACER ClinicalTrials.gov number, NCT00527943.).

SYNERGISM BETWEEN FENTANYL AND TRAMADOL IN TONIC INFLAMMATORY PAIN: THE OROFACIAL FORMALIN TEST.

INFLAMMATION. 2012 JUN; 35(3): 1132-7.

Miranda HF, Noriega V, Zepeda RJ, Sierralta F, Prieto JC.

Opioids have been used for long time to management of pain, the coadministration of two opioids may induce synergism. The present study was conducted to determine the antinociceptive interaction between the dual mechanism of action of tramadol compared to the main of fentanyl antinociception in the orofacial formalin which represents a model of persistent cutaneous nociception in the region innervated by the trigeminal nerve. The i.p. administration of tramadol and fentanyl induced a dose-dependent antinociception with an ED(50) of 2.97 ± 0.32 mg/kg for phase I and 1.79 ± 0.30 mg/kg for phase II and 0.062 ± 0.0040 mg/kg in phase I and 0.041 ± 0.0039 mg/kg in phase II, respectively. The coadministration of fentanyl with tramadol induced synergism in both phases of the test with an interaction index of 0.343 and 0.163 for phase I and phase II, respectively. This finding could be explained by the more complex pharmacology of tramadol compared to fentanyl.

RELATIONSHIP BETWEEN MECHANICAL AND METABOLIC DYSSYNCHRONY WITH LEFT BUNDLE BRANCH BLOCK: EVALUATION BY 18-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY IN PATIENTS WITH NON-ISCHEMIC HEART FAILURE.

J HEART LUNG TRANSPLANT. 2012 OCT; 31(10):1096-101.

Castro P, Winter JL, Verdejo H, Orellana P, Quintana JC, Greig D, Enríquez A, Sepúlveda L, Concepción R, Sepúlveda P, Rossel V, Chiong M, García L, Lavandero S.

BACKGROUND: Ventricular dyssynchrony is a common finding in patients with heart failure (HF), especially in the presence of conduction delays. The loss of ventricular synchrony leads to progressive impairment of contractile function, which may be explained in part by segmental abnormalities of myocardial metabolism. However, the association of these metabolic disarrangements with parameters of ventricular dyssynchrony and electrocardiography (ECG) findings has not yet been studied. METHODS: Our aim was to determine the correlation between the presence of left bundle branch block (LBBB) with left ventricular (LV) mechanical synchrony assessed by multiple-gated acquisition scan (MUGA) and with patterns of 18-fluorodeoxyglucose (18FDG) uptake in patients with non-ischemic heart failure. Twenty-two patients with non-ischemic cardiomyopathy, LV ejection fraction (LVEF) ≤45% and New York Heart Association (NYHA) Functional Class II or III symptoms under standard medical therapy were included, along

with 10 healthy controls matched for age and gender. A 12-lead ECG was obtained to measure the length of the QRS. Mechanical LV synchrony was assessed by MUGA using phase analysis. All patients and controls underwent positron emission tomography with 18FDG to determine the distribution of myocardial glucose uptake. The standard deviation of peak (18)FDG uptake was used as an index of metabolic heterogeneity. Student's t-test and Pearson's correlation were used for statistical analysis. RESULTS: The mean age of the patients with HF was 54 ± 12 years and 72% were male. The length of the QRS was 129 ± 31 milliseconds and LBBB was present in 9 patients. Patients with HF had decreased LV 18FDG uptake compared with controls (7.56 ± 3.36 vs. 11.63 ± 4.55 standard uptake value; p = 0.03). The length of the QRS interval correlated significantly with glucose uptake heterogeneity (r = 0.62; p = 0.002) and mechanical dyssynchrony (r = 0.63; p = 0.006). HF patients with LBBB showed marked glucose uptake heterogeneity compared with HF patients without LBBB (41.4 ± 10 vs 34.7 ± 4.9 ml/100 g/min, respectively; p = 0.01). CONCLUSIONS: Patients with non-ischemic heart failure exhibit a global decrease in myocardial glucose uptake. Within this group, subjects who also have LBBB exhibit a marked heterogeneity in segmental glucose uptake, which directly correlates with QRS duration.

DEPARTAMENTO DE CIRUGÍA

RADIOLOGIC AND ENDOSCOPIC CHARACTERISTICS OF LAPAROSCOPIC ANTIREFLUX WRAP: CORRELATION WITH OUTCOME.

INT SURG. 2012 JUL;97(3): 189-97.

Braghetto I, Korn O, Csendes A, Valladares H, Davanzo C, Debandi A.

After antireflux surgery for gastroesophageal reflux disease, 10% to 15% of patients may have unsuccessful results as a result of abnormal restoration of the esophagogastric junction. The purpose of this study was to evaluate the postoperative endoscopic and radiologic characteristics of the antireflux barrier and their correlation with the postoperative results. After surgery, endoscopic and radiologic features of the antireflux wrap were evaluated in 120 consecutive patients. Jobe's classification of the postoperative valve was used for the definition of a "normal" or "defective" wrap. Patients were evaluated 3 to 5 years later in order to determine the clinical and objective failed fundoplication. A "normal" antireflux wrap was associated with successful results in 81.7% of the patients. On the contrary, defective radiologic or endoscopic antireflux wrap was observed in 19% of cases. Among these patients, hypotensive lower esophageal sphincter was observed in 50% to 65% of patients, abnormal 24-hour pH monitoring in 91%, and recurrent postoperative erosive esophagitis in 50% of patients, respectively (P < 0.001). "Defective" antireflux fundoplication is associated with recurrent reflux symptoms, presence of endoscopic esophagitis, hypotensive lower esophageal sphincter, and abnormal acid reflux.

IS LAPAROSCOPIC SLEEVE GASTRECTOMY AN ACCEPTABLE PRIMARY BARIATRIC PROCEDURE IN OBESE PATIENTS? EARLY AND 5-YEAR POSTOPERATIVE RESULTS.

SURG LAPAROSC ENDOSC PERCUTAN TECH. 2012 DEC; 22(6):479-86.

Braghetto I, Csendes A, Lanzarini E, Papapietro K, Cárcamo C, Molina JC.

In this paper, we analyze and discuss the possibility of Laparoscopic sleeve gastrectomy being accepted as a primary and definitive procedure for obese patients with comorbidities. This is based on our postoperative and 5 years of follow-up result and comparing them with the data reported in the international literature. For comparison of the results, a narrative revision of the literature was performed, using the Medline, Pubmed, and data base publications (Medline, Lilacs, and Cochrane Library), looking for the term "Sleeve gastrectomy," "Obesity," "Bariatric surgery," "Laparoscopic surgery" including "Review" articles and also other 42 selected papers. The current results demonstrate very low morbidity (<10%), nil mortality (<1%), mean % weight loss after 5 years of follow-up of 57%, very satisfactory results regarding comorbidities or improvement. However, gastroesophageal reflux manifestation after the operation (20% to 31%) and the possibility of regaining weight after 5 years (15% to 75%) appear as points for analysis.

CLASSIFICATION AND MANAGEMENT OF LEAKS AFTER GASTRIC BYPASS FOR PATIENTS WITH MORBID OBESITY: A PROSPECTIVE STUDY OF 60 PATIENTS.

OBES SURG. 2012 JUN; 22(6):855-62.

Csendes A, Burgos AM, Braghetto I.

The most important and frequent major complication after gastric bypass is the appearance of a leak, which can result in death of a patient. The purpose of this prospective study was to determine the incidence of a postoperative leak, to propose a classification and to evaluate the results of conservative or surgical treatment. All patients submitted to gastric bypass either laparotomic or

laparoscopic were included in a prospective protocol. In all radiological evaluation at 4(th) day after surgery was performed. The presence of a leak was evaluated according to the day of appearance, its location and its severity. Results of medical or surgical treatment were analyzed. From 1764 patients submitted to Roux-en-Y gastric bypass, 60 had a postoperative leak (3.4%). This leak appeared early after surgery (before 4 days) in 20%. It was a localized subclinical leak in 20% and clinical - septic in 80%. There were 7 possible anatomic location of a leak, being the gastrojejunal anastomosis the most frequent location (53%) followed by gastric pouch. The highest mortality was associated to the jejuno-jejunal anastomosis. Conservative treatment was employed in near 65% of the patients: The mean time of closure of a leak was 34 days. The appearance of a postoperative leak is a major and serious complication. It can be classified according to the day of appearance, its severity and its location. Conservative or surgical treatment can be employed properly if these 3 parameters are carefully evaluated.

LAPAROSCOPIC TREATMENT OF OBESE PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE AND BARRETT'S ESOPHAGUS: A PROSPECTIVE STUDY.

OBES SURG. 2012 MAY;22(5):764-72.

Braghetto I, Korn O, Csendes A, Gutiérrez L, Valladares H, Chacón M.

BACKGROUND: Short-segment Barrett's esophagus (SSBE) or long-segment Barrett's esophagus (LSBE) is the consequence of chronic gastroesophageal reflux disease (GERD), which is frequently associated with obesity. Obesity is a significant risk factor for the development of GERD symptoms, erosive esophagitis, Barrett's esophagus, and esophageal adenocarcinoma. Morbidly obese patients who submitted to gastric bypass have an incidence of GERD as high as 50% to 100% and Barrett's esophagus reaches up to 9% of patients. METHODS: In this prospective study, we evaluate the postoperative results after three different procedures--calibrated fundoplication + posterior gastropexy (CFPG), fundoplication + vagotomy + distal gastrectomy + Roux-en-Y gastrojejunostomy (FVDGRYGJ), and laparoscopic resectional Roux-en-Y gastric bypass (LRRYGBP)--among obese patients. RESULTS: In patients with SSBE who submitted to CFPG, the persistence of reflux symptoms and endoscopic erosive esophagitis was observed in 15% and 20.2% of them, respectively. Patients with LSBE were submitted to FVDGRYGJ or LRRYGBP which significantly improved their symptoms and erosive esophagitis. No modifications of LESP were observed in patients who submitted to LRRYGBP before or after the operation. Acid reflux diminished after the three types of surgery were employed. Patients who submitted to LRRYGBP presented a significant reduction of BMI from 41.5 ± 4.3 to 25.7 ± 1.3 kg/m(2) after 12 months. CONCLUSIONS: Among patients with LSBE, FVDGRYGJ presents very good results in terms of improving GERD and Barrett's esophagus, but the reduction of weight is limited. LRRYGBP improves GERD disease and Barrett's esophagus with proven reduction in body weight and BMI, thus becoming the procedure of choice for obese patients.

PROSPECTIVE SEQUENTIAL ENDOSCOPIC AND HISTOLOGIC STUDIES OF THE GASTRIC POUCH IN 130 MORBIDLY OBESE PATIENTS SUBMITTED TO ROUX-EN-Y GASTRIC BYPASS.

ARQ BRAS CIR DIG. 2012 DEC;25(4):245-249.

Csendes A, Smok G, Burgos AM, Canobra M.

BACKGROUND: Roux-en-Y gastric bypass is the most common performed bariatric surgery. A small gastric pouch is created, leaving a narrow gastrojejunal anastomosis, with a long jejunal limb. Very little is known regarding the behavior of this pouch years after surgery. AIM: To determine through prospective sequential endoscopic studies the size of the gastric pouch, the diameter of the anastomosis, and the behavior of H. pylori infection after surgery. METHODS: In 130 patients subjected to resectional gastric bypass, several routine sequential endoscopic (until 120 months) and histological evaluations of the gastric pouch were performed. RESULTS: After surgery, a mean of 3.6 endoscopies/patient were performed. Macroscopically nearly 95% of the small gastric pouches were normal, and the main pathological finding was a marginal ulcer. Erosive esophagitis disappeared in 93% of the patients. There was no increase in the orocaudal size of the pouch during this period of observation. There was no dilatation of the diameter of gastrojejunal anastomosis. Near 54% of all patients had normal fundic mucosa, while 18% had chronic active gastritis, coincident with H. pylori infection. Five patients had intestinal metaplasia. CONCLUSION: Based on this sequential endoscopic evaluation, there was no increase in the orocaudal size of the gastric pouch nor increase in the diameter of the gastrojejunal anastomosis. H. pylori behavior was inconsistent and difficult to interpret.

HEME- AND NONHEME-IRON ABSORPTION AND IRON STATUS 12 MO AFTER SLEEVE GASTRECTOMY AND ROUX-EN-Y GASTRIC BYPASS IN MORBIDLY OBESE WOMEN.

AM J CLIN NUTR. 2012 OCT; 96(4):810-7.

Ruz M, Carrasco F, Rojas P, Codoceo J, Inostroza J, Basfi-Fer K, Valencia A, Csendes A, Papapietro K, Pizarro F, Olivares M, Westcott JL, Hambidge KM, Krebs NF.

BACKGROUND: The effect of bariatric surgery on iron absorption is only partially known. OBJECTIVE: The objective was to study the

effects of sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGBP) on heme- and nonheme-iron absorption and iron status. DESIGN: Fifty-eight menstruating women were enrolled in this prospective study [mean (±SD) age: 35.9 ± 9.1 y; weight: 101.7 ± 13.5 kg; BMI (in kg/m^2): 39.9 ± 4.4]. Anthropometric, body-composition, dietary, and hematologic indexes and heme- and nonheme-iron absorption-using a standardized meal containing 3 mg Fe-were determined before and 12 mo after surgery. Forty-three subjects completed the 12-mo follow-up. Iron supplements were strictly controlled. RESULTS: Heme-iron absorption was 23.9% before and 6.2% 12 mo after surgery ($P < 0.0001$). Nonheme-iron absorption decreased from 11.1% to 4.7% ($P < 0.0001$). No differences were observed by type of surgery. Iron intakes from all sources of supplements were 27.9 ± 6.2 mg/d in the SG group and 63.2 ± 21.1 mg/d in the RYGBP group ($P < 0.001$). Serum ferritin and total-body iron decreased more after RYGBP than after SG. CONCLUSIONS: Iron (heme and nonheme) absorption is markedly reduced after SG and RYGBP. The magnitude of the decrease in heme-iron absorption is greater than that of nonheme iron. The amounts suggested as iron supplements may need to be increased to effectively prevent iron-status impairment.

CHANGES IN GHRELIN CONCENTRATIONS ONE YEAR AFTER RESECTIVE AND NON-RESECTIVE GASTRIC BYPASS: ASSOCIATIONS WITH WEIGHT LOSS AND ENERGY AND MACRONUTRIENT INTAKES.

NUTRITION. 2012 JUL; 28(7-8):757-61.

Carrasco F, Rojas P, Csendes A, Codoceo J, Inostroza J, Basfi-fer K, Papapietro K, Watkins G, Rojas J, Ruz M.

OBJECTIVE: Ghrelin is a potent stimulator of appetite and synthesized in the stomach. Its role in weight loss after gastric bypass (GBP) is still controversial. The aim of this study was to evaluate the relation between weight loss and food intake and between weight loss and changes in serum ghrelin concentrations 1 y after GBP with resection of the bypassed stomach (R-GBP) and without resection (NR-GBP). METHODS: Of 50 women (37.6 ± 10.2 y old, body mass index 43.8 ± 4.8 kg/m^2) with GBP, 26 had R-GBP and 24 had NR-GBP. Body weight, body composition (dual energy x-ray absorptiometry), food intake, and serum ghrelin at baseline and 12 mo after GBP were measured. RESULTS: The percentage of excess weight loss was 68.9 ± 12.8% at 12 mo after GBP. At 12 mo, the decrease of serum ghrelin was greater in the R-GBP group (-25.3 ± 22.5%) compared with the NR-GBP group (+11.2 ± 50.9%, $P < 0.005$). After adjustment by the baseline excess of body weight, there was a greater percentage of excess weight loss in the R-GBP group only at 6 mo (61.8% versus 54.9%, $P = 0.011$). After controlling for the baseline intake, a significant lower carbohydrate intake was observed in the R-GBP group 6 mo after surgery ($P < 0.05$). CONCLUSION: A greater decrease in ghrelin levels was observed only in patients who underwent R-GBP at 12 mo after surgery. This difference was not associated with differences in dietary intakes or weight loss at the same time point. Therefore, the small gastric pouch is probably more important than decreased ghrelin levels in producing long-term weight loss after R-GBP.

FREQUENCY AND USE OF PAIN ASSESSMENT TOOLS IMPLEMENTED IN RANDOMIZED CONTROLLED TRIALS IN THE ADULT BURNS POPULATION: A SYSTEMATIC REVIEW.

BURNS. 2012 MAR; 38(2):147-54.

Mahar PD, Wasiak J, O'Loughlin CJ, Christelis N, Arnold CA, Spinks AB, Danilla S.

INTRODUCTION: Pain continues to be an ongoing issue of concern in adult burn patients. Inadequate pain assessment hinders meaningful research, and prevents the optimal management of burn pain. The objective of this study was to examine the content of existing research in burn pain with the frequency and context of pain assessment tool use in randomized clinical trials in order to further inform their use for future researchers and clinicians. METHODS: Electronic searches of MEDLINE, CINAHL, EMBASE and The Cochrane Library databases from 1966 onwards were used to identify English articles related to clinical trials utilising pain assessment in adult burns patients. RESULTS: The systematic literature search identified 25 randomized clinical trials utilising pain assessment tools. Unidimensional pain assessment tools were most frequently used pain assessment tools, with multidimensional tools used less often, despite the multifaceted and complex nature of burn pain. CONCLUSION: The review highlights the lack of consistency of pain assessment tool use in randomized clinical trials with respect to managing burn pain. We recommend a broader but consistent use of multidimensional pain assessment tools for researchers undertaking clinical trials in this field. The review supports the need for an international expert consensus to identify the necessary critical outcomes and domains for clinicians and researchers undertaking further research into burn pain.

EVOLUCIÓN DE LA INGESTA Y DEL ESTADO NUTRICIONAL DE ZINC, HIERRO Y COBRE EN MUJERES SOMETIDAS A CIRUGÍA BARIÁTRICA HASTA EL SEGUNDO AÑO POSTOPERATORIO.

NUTR HOSP. 2012 OCT; 27(5):1527-35.

Basfi-Fer K, Rojas P, Carrasco F, Valencia A, Inostroza J, Codoceo J, Pizarro F, Olivares M, Papapietro K, Csendes A, Rojas J, Adjemian D, Calderón E, Ruz M.

Introduction: Bariatric surgery allows a significant reduction in weight and improvement of comorbidities associated with obesity in the

long term, but it can also adversely affect the nutritional status of some micronutrients. Objectives: To evaluate changes in intake and parameters of nutritional status of zinc, iron and copper in patients undergoing Roux-en-Y gastric bypass (GBP) or sleeve gastrectomy (SG), until the second postoperative year. Methods: We prospectively studied 45 women undergoing GBP or SG (mean age 35.2 ± 8.4 years, mean BMI 39.8 ± 4.0 kg/m^2), every 6 months We measured intake and status indications nutritional zinc, iron and copper, and annually evaluated body composition. The contribution of minerals through supplements represented twice the recommended intake for a healthy woman in patients undergoing GT and three times for GBP. Results: 20 women underwent GBP and 25 SG. In both groups there was a significant reduction in weight and body fat percentage, which was maintained until the second postoperative year. Women who have had a greater commitment GBP nutritional status of zinc, iron and copper, that patients undergoing SG. Conclusions: Gastric bypass Roux-Y produces a greater commitment of nutritional status of zinc, iron and copper sleeve gastrectomy. It should evaluate whether administration of supplementation fractional improve the absorption of these nutrients.

INCREASED PRODUCTION OF SOLUBLE TLR2 BY LAMINA PROPRIA MONONUCLEAR CELLS FROM ULCERATIVE COLITIS PATIENTS.

IMMUNOBIOLOGY. 2012 JUN; 217(6):634-42.

Candia E, Díaz-Jiménez D, Langjahr P, Núñez LE, de la Fuente M, Farfán N, López-Kostner F, Abedrapo M, Alvarez-Lobos M, Pinedo G, Beltrán CJ, González C, González MJ, Quera R, Hermoso MA.

Toll-like receptor 2 (TLR2) is a type I pattern recognition receptor that has been shown to participate in intestinal homeostasis. Its increased expression in the lamina propria has been associated with the pathogenesis in inflammatory bowel disease (IBD), such as ulcerative colitis (UC) and Crohn's disease (CD). Recently, soluble TLR2 (sTLR2) variants have been shown to counteract inflammatory responses driven by the cognate receptor. Despite the evident roles of TLR2 in intestinal immunity, no study has elucidated the production and cellular source of sTLR2 in IBD. Furthermore, an increase in the population of activated macrophages expressing TLR2 that infiltrates the intestine in IBD has been reported. We aimed first to assess the production of the sTLR2 by UC and CD organ culture biopsies and lamina propria mononuclear cells (LPMCs) as well as the levels of sTLR2 in serum, and then characterize the cell population from lamina propria producing the soluble protein. Mucosa explants, LPMCs and serum were obtained from UC, CD patients and control subjects. The level of sTLR2 was higher in conditioned media from organ culture biopsies and LPMCs from UC patients in comparison to CD and controls. Moreover, an inverse correlation between the content of intestinal and serum sTLR2 levels was observed in UC patients. Additionally, when characterizing the cellular source of the increased sTLR2 by LPMCs from UC patients, an increase in TLR2(+)/CD33(+) cell population was found. Also, these cells expressed CX3CR1, which was related to the increased levels of intestinal FKN in UC patients, suggesting that a higher proportion of TLR2(+) mononuclear cells infiltrate the lamina propria. The increased production of sTLR2 suggests that a differential regulating factor of the innate immune system is present in the intestinal mucosa of UC patients.

DEPARTAMENTO DE DERMATOLOGÍA

5% LIDOCAINE MEDICATED PLASTER USE IN CHILDREN WITH NEUROPATHIC PAIN FROM BURN SEQUELAE.

PAIN MED. 2012 DEC 28.

Orellana Silva M, Yañez V, Hidalgo G, Valenzuela F, Saavedra R.

OBJECTIVE: Neuropathic pain is a challenge in children with burn sequelae. Although relatively infrequent, the intensity and chronicity of neuropathic pain negatively impact functionality and quality of life. The use of 5% lidocaine medicated plaster has not previously been reported in children. We explored the effectiveness and safety of 5% lidocaine medicated plaster to treat neuropathic pain in children with burn sequelae. DESIGN: Three-month prospective, uncontrolled study. SETTING: Corporation of Aid to Burned Children (COANIQUEM), a nonprofit pediatric burn rehabilitation center in Chile. SUBJECTS: Fourteen pediatric patients with burn sequelae neuropathic pain. OUTCOME MEASURES: Demographics, burn and pain evolution (type, intensity [using Wong-Baker FACES], and Douleur Neuropathique 4 [DN4]), and patient functionality. Plasma lidocaine levels were measured at 0, 12, 36, and 60 hours after treatment commencement. RESULTS: Fourteen patients were evaluable for plasma lidocaine levels. Twelve patients were available for clinical assessment (two patients lost to follow-up) [mean (standard deviation)]: age, 11 years 7 months (2 years 6 months); weight, 45 kg (11.9 kg); burn evolution, 5 years 6 months (4 years); time between burn and pain onset, 3 years 6 months (3 years 2 months); time between pain onset and treatment, 5.1 months (4.8 months); lidocaine, between < and ½ plaster; initial pain intensity (FACES), 6.8 (1.6); final pain intensity, 0 in 11/12 patients; DN4, initial-6, final-2.3. All patients reported improved functionality. Plasma lidocaine levels were ≤27.45 ng/mL (>180 times below critical levels). No adverse reactions occurred. CONCLUSIONS: These are the first published data suggesting that 5% lidocaine medicated plaster improves patient functionality, and is effective and safe for the treatment of neuropathic pain in pediatric patients with burn sequelae.

COMMON APPLICATIONS OF DERMATOLOGIC SONOGRAPHY.

J ULTRASOUND MED. 2012 JAN; 31(1):97-111.

Wortsman X.

In recent years, there has been growing use of sonography in the dermatologic field. Thus, this review analyzes the most common dermatologic applications of sonography with some technical considerations for performing this type of examination. Moreover, the sonographic findings in common benign and malignant skin tumors, inflammatory dermatologic diseases, and ungual and cosmetic conditions, among others, are considered. Thus, this noninvasive technique may be a potent adjunctive tool in the diagnosis and management of dermatologic conditions in daily practice, delivering critical information otherwise unavailable to the clinical naked eye.

EARLY DIAGNOSIS OF A CALIBRE PERSISTENT LABIAL ARTERY IN A CHILD: USEFULNESS OF ULTRASONOGRAPHY.

AUSTRALAS J DERMATOL. 2012 MAY; 53(2):E18-9.

Arellano J, Antoniazzi C, Wortsman X.

Calibre persistent labial artery is a vascular lesion in which a large diameter artery penetrates the submucosal tissue of the lip and continues without division or decreasing its size. Usually, a calibre persistent artery of the lip presents as a pulsatile papule and is easily misdiagnosed. Although the diagnosis can be clinical, the development of high-resolution colour Doppler ultrasound is a useful non-invasive tool for evaluating the lesion. We report a case of a 2-year-old male patient presenting with a congenital pulsatile lesion on his upper lip. Clinical diagnosis of a calibre persistent artery of the lip was confirmed by colour Doppler ultrasound. Images are provided to highlight findings of the physical and ultrasound examinations.

ULTRASOUND DETECTION AND IDENTIFICATION OF COSMETIC FILLERS IN THE SKIN.

J EUR ACAD DERMATOL VENEREOL. 2012 MAR; 26(3):292-301.

Wortsman X, Wortsman J, Orlandi C, Cardenas G, Sazunic I, Jemec GB.

BACKGROUND: While the incidence of cosmetic filler injections is rising world-wide, neither exact details of the procedure nor the agent used are always reported or remembered by the patients. Thus, although complications are reportedly rare, availability of a precise diagnostic tool to detect cutaneous filler deposits could help clarify the association between the procedure and the underlying pathology. OBJECTIVES: The aim of this study was to evaluate cutaneous sonography in the detection and identification of cosmetic fillers deposits and, describe dermatological abnormalities found associated with the presence of those agents. METHODS: We used ultrasound in a porcine skin model to determine the sonographic characteristics of commonly available filler agents, and subsequently applied the analysis to detect and identify cosmetic fillers among patients referred for skin disorders. RESULTS: Fillers are recognizable on ultrasound and generate different patterns of echogenicity and posterior acoustic artefacts. Cosmetic fillers were identified in 118 dermatological patients; most commonly hyaluronic acid among degradable agents and silicone oil among non-degradable. Fillers deposits were loosely scattered throughout the subcutaneous tissue, with occasional infiltration of local muscles and loco-regional lymph nodes. Accompanying dermatopathies were represented by highly localized inflammatory processes unresponsive to conventional treatment, morphea-like reactions, necrosis of fatty tissue and epidermal cysts; in the case of non-degradable agents, the associated dermatopathies were transient, resolving upon disappearance of the filler. CONCLUSIONS: Cosmetic filler agents may be detected and identified during routine ultrasound of dermatological lesions; the latter appear to be pathologically related to the cosmetic procedure.

SONOGRAPHY IN PATHOLOGIES OF SCALP AND HAIR.

BR J RADIOL. 2012 MAY; 85(1013):647-55.

Wortsman X, Wortsman J, Matsuoka L, Saavedra T, Mardones F, Saavedra D, Guerrero R, Corredoira Y.

Disorders of the scalp often result in severe cosmetic interference with quality of life, creating the need for optimal medical surveillance. We tested the latest generation of ultrasound machines in patients with scalp pathology and prepared a cross-sectional library encompassing a wide assortment of conditions. Normative data on the sonographic anatomy of scalp and human hair, and important methodological considerations, are also included.

FINGER RETRONYCHIAS DETECTED EARLY BY 3D ULTRASOUND EXAMINATION.

J EUR ACAD DERMATOL VENEREOL. 2012 FEB; 26(2):254-6.

Wortsman X, Calderon P, Baran R.

BACKGROUND: A new pattern of ingrown nail, called retronychia is involved in the posterior translation of the whole nail unit producing paronychia. OBJECTIVE: To demonstrate an unusual case of paronychia that affected three of the fingers on the right

hand. METHODS: We used 3D ultrasound to study the whole nail unit in the fingers of both the affected (right) and non affected (left) hand. RESULTS: Backward motion of the nail unit with decreased distance between the origin of the nail plates and the distal interphalangeal joint was clearly demonstrated by 3D ultrasound in the affected fingers. CONCLUSION: 3D ultrasound provides non invasive and more understandable information about the physiopathological changes in retronychia.

CLINICAL EFFICACY OF ADAPALENE (DIFFERIN(®)) 0.3% GEL IN CHILEAN WOMEN WITH CUTANEOUS PHOTOAGING.

J DERMATOLOG TREAT. 2012 FEB; 23(1):57-64.

Herane MI, Orlandi C, Zegpi E, Valdés P, Ancić X.

Skin photoaging is a concern for many patients today, and it is important for dermatologists to evaluate new therapeutic approaches. This 6-month open-label study evaluated the effectiveness and safety of adapalene 0.3% gel in 40 Latin American women with signs of facial photoaging. Assessments at baseline, week 12, and week 24 included clinical severity grading, measurement of transepidermal water loss, hydration, and elasticity (Cutometer MPA 850®), evaluation of general skin tone and number of wrinkles (VISIA®) Complexion Analysis System), and ultrasonography to measure changes in skin thickness. There were significant improvements in clinical grading of wrinkles ($p < 0.01$) with a reduction in mean severity score of 40% in forehead wrinkles, 52% in periorbital wrinkles, and 29% in perioral wrinkles. Melanin, transepidermal water loss, and hydration were improved, as were general skin tone and the number of wrinkles ($p < 0.05$). Measurement of skin thickness showed a non-significant improvement in the epidermis and dermis and a significant decrease of the elastosis band (11.6% at week 12 and 15.1% at week 24). Adapalene was well tolerated overall, although three patients discontinued the study due to skin irritation in the first month. We conclude that adapalene 0.3% gel is a new safe and effective approach to photoaging.

DEPARTAMENTO DE MEDICINA

GASTROENTEROLOGÍA

GENOMIC DETERMINANTS OF HEPATITIS C VIRUS ANTIVIRAL THERAPY OUTCOMES: TOWARD INDIVIDUALIZED TREATMENT.

ANN HEPATOL. 2012 NOV-DEC; 11(6):827-37.

Venegas M, Brahm J, Villanueva RA.

Hepatitis C virus (HCV) is an important global health problem with an estimated prevalence of more than 170 million infected individuals worldwide. Currently, the standard antiviral therapy, based on pegylated interferon alpha and ribavirin, can achieve a virological response in only nearly 50% of the patients infected with HCV genotype 1, the most widely distributed globally. During the last years, relevant data from genome-wide association studies (GWAS) about the impact and contribution of the patient genomics on viral infection outcomes has suggested the possibility that an individualized antiviral therapy can be considered. In this review, we analyze the existing information on single nucleotide polymorphisms (SNPs) of several host genes and viral factors that influence, as a whole, the outcome of the standard antiviral therapy, and that might be used to predict an individualized antiviral response. We also discuss the clinical data within the most recent context of the triple antiviral therapy.

THE VIRAL TRANSACTIVATOR HBX PROTEIN EXHIBITS A HIGH POTENTIAL FOR REGULATION VIA PHOSPHORYLATION THROUGH AN EVOLUTIONARILY CONSERVED MECHANISM.

INFECT AGENT CANCER. 2012 OCT 18; 7(1):27.

Hernández S, Venegas M, Brahm J, Villanueva RA.

BACKGROUND: Hepatitis B virus (HBV) encodes an oncogenic factor, HBx, which is a multifunctional protein that can induce dysfunctional regulation of signaling pathways, transcription, and cell cycle progression, among other processes, through interactions with target host factors. The subcellular localization of HBx is both cytoplasmic and nuclear. This dynamic distribution of HBx could be essential to the multiple roles of the protein at different stages during HBV infection. Transactivational functions of HBx may be exerted both in the nucleus, via interaction with host DNA-binding proteins, and in the cytoplasm, via signaling pathways. Although there have been many studies describing different pathways altered by HBx, and its innumerable binding partners, the molecular mechanism that regulates its different roles has been difficult to elucidate. METHODS: In the current study, we took a bioinformatics approach to investigate whether the viral protein HBx might be regulated via phosphorylation by an evolutionarily conserved mechanism. RESULTS: We found that the phylogenetically conserved residues Ser25 and Ser41 (both within the negative regulatory domain), and Thr81 (in the transactivation domain) are predicted to be phosphorylated. By molecular 3D modeling of HBx, we further show these residues are all

predicted to be exposed on the surface of the protein, making them easily accesible to these types of modifications. Furthermore, we have also identified Yin Yang sites that might have the potential to be phosphorylated and O-β-GlcNAc interplay at the same residues. CONCLUSIONS: Thus, we propose that the different roles of HBx displayed in different subcellular locations might be regulated by an evolutionarily conserved mechanism of posttranslational modification, via phosphorylation.

LACTULOSE HYDROGEN BREATH TEST AND FUNCTIONAL SYMPTOMS IN PEDIATRIC PATIENTS.

DIG DIS SCI. 2012 MAY; 57(5):1330-5.

Madrid AM, Landskron G, Klapp G, Reyes A, Pizarro C, Defilippi C.

BACKGROUND: The role of small intestinal bacterial overgrowth (SIBO) in functional digestive disorders in the pediatric population is a matter of controversy, since methods currently used to establish this diagnosis are difficult to interpret. The aim of this work was to analyze the characteristics of the lactulose H(2) breath test (LHBT) in children with functional gastrointestinal symptoms according to more recent criteria. METHODS: Seventy-two patients and 17 controls were enrolled. A questionnaire was administered regarding digestive symptoms (abdominal pain, bloating, vomiting, and bowel-movement disorders). A lactose hydrogen breath test was performed to rule out lactose malabsorption and a LHBT was used to measure the time elapsed between lactulose oral ingestion and an increment of H(2) concentration of 20 ppm over basal. RESULTS: There were no differences of age and gender between patients and controls. Mean time to 20-ppm change was shorter in patients (56.3 ± 3 min) compared to healthy children (74.7 ± 5 min), p\0.05. In 39% of patients, rise of H(2) occurred during the first 40 min after lactulose ingestion, and in almost all controls, an increment was observed between 50 and 90 min (p\0.05). Symptoms were unrelated to time to 20-ppm change. CONCLUSIONS: An abnormal LHBT was found in children with functional symptoms of the digestive tract, but the exact mechanism involved, accelerated intestinal transit or SIBO, needs to be confirmed by an additional method.

GENÉTICA

GENÉTICA DE LA SORDERA CONGÉNITA

MED CLIN (BARC). 2012; 139:446-51.

Faundes, Víctor; Pardo, Rosa Andrea; Castillo Taucher, Silvia

La sordera congénita se define como la pérdida auditiva que se presenta en el momento del nacimiento y, por lo tanto, antes del desarrollo del habla. Es el trastorno sensorioneural más prevalente en países desarrollados, con una incidencia de 1-3 niños por cada 1.000 recién nacidos vivos, de los cuales más del 50% son atribuibles a causas genéticas. La sordera se puede clasificar como sindrómica o no sindrómica. En el primer caso, está asociada con malformaciones del oído externo y/o alteraciones en otros órganos y sistemas. Se han descrito más de 400 síndromes que presentan déficit auditivo, que dan cuenta del 30% de los casos genéticos. El 70% restante corresponde a casos no sindrómicos, dentro de los cuales el 75-85% son de herencia autosómica recesiva, el 15-24% autosómica dominante y el 1-2% ligada al cromosoma X. La evaluación de un niño con sordera requiere de la participación de diversos especialistas, quienes deben coordinarse y entregar la información a la familia. Los objetivos de establecer un diagnóstico son predecir otros hallazgos clínicos que sugieran algún síndrome y anticiparse en su tratamiento y proveer consejo genético a los padres e individuos afectados.

WHEAT FLOUR FORTIFICATION WITH FOLIC ACID: CHANGES IN NEURAL TUBE DEFECTS RATES IN CHILE

AM J MED GENET A. 2012 AUG; 158A(8):1885-90.

Cortés F, Mellado C, Pardo RA, Villarroel LA, Hertrampf E.

In January 2000, Chilean Ministry of Health mandated the addition of folic acid (FA) to wheat flour in order to reduce the risk of neural tube defects (NTDs). This policy resulted in significant increases in serum and red cell folate in women of fertile age 1 year after fortification. To evaluate the effect of wheat flour fortification on the prevalence of NTDs in Chile we designed a prospective hospital-based surveillance program to monitor the frequency of NTDs in all births (live and stillbirths) with birth weight≥500 g at the nine public maternity hospitals of Santiago, Chile from 1999 to 2009. During the pre-fortification period (1999-2000) the NTD rate was 17.1/10,000 births in a total of 120,566 newborns. During the post-fortification period (2001-2009) the NTD rate decreased to 8.6/10,000 births in a total of 489,915 newborns, which translates into a rate reduction of 50% (RR: 0.5; 95% CI: 0.42-0.59) for all NTDs. The rate reduction by type of NTD studied was: 50% in anencephaly (RR: 0.5; 95% CI: 0.38-0.67), 42% in cephalocele (RR: 0.58; 95% CI: 0.37-0.89), and 52% in spina bifida (RR: 0.48; 95% CI: 0.38-0.6). Rates showed significant reduction both in stillbirths and live births: 510.3 to 183.6/10,000 (RR=0.36; 95% CI: 0.25-0.53) and 13.3 to 7.5/10,000 (RR=0.56; 95% CI: 0.47-0.68), respectively. In Chile, fortification of wheat flour with FA has proven to be an effective strategy for the primary prevention of NTDs.

MEDICINA NUCLEAR

ENDOGENOUS THYROID-STIMULATING HORMONE AND RADIOACTIVE IODINE UPTAKE IN NORMAL SUBJECTS.

CLIN NUCL MED. 2012 JUN; 37(6):584-6.

González P, Jaimovich R, Araya V, Massardo T, Carmona A.

In 105 normal volunteers, 52 male and 53 female, mean age 45 (range, 20-68), serum thyroid-stimulating hormone (TSH) (1.46 ± 0.7; range, 0.43-3.87 microUI/mL) and 24-hour thyroid radioactive iodine uptake (RAIU) (16.15% ± 4.78% range, 6.45%-30.08%) were measured. Additionally, TSH was 1.18 ± 0.5 microUI/mL for 20 to 29 year-olds and 1.59 ± 0.9 microUI/mL for 60 to 68 year old (P = 0.037). RAIU was 18.30 ± 4.5 for 20 to 29-year-olds and 14.92 ± 3.1 for 60 to 68 year-olds (P = 0.009). TSH trends positively and RAIU at 24 hours correlates negatively with aging of the pituitary axis.

REUMATOLOGÍA

WEAK CD4+ T-CELL RESPONSES TO CITRULLINATED VIMENTIN IN RHEUMATOID ARTHRITIS PATIENTS CARRYING HLA-DR9 ALLELES.

RHEUMATOL INT. 2012 JUN; 32(6):1819-25.

Catalán D, Aravena O, Zúñiga R, Silva N, Escobar A, Sabugo F, Wurmann P, Soto L, González R, Alfaro J, Larrondo M, Cuchacovich M, Aguillón JC.

Citrullinated vimentin (cVIM) is one of the antigens specifically targeted by anti-citrullinated protein antibodies (ACPA) in rheumatoid arthritis (RA) patients. The association between ACPA and certain HLA-DRB1 alleles, those coding for the shared epitope (SE), suggests that this response could be T-cell mediated. HLA-DR9 alleles, which do not code for the SE, have recently been associated with ACPA (+) RA. The objective of this work was to study CD4+ T cell responses to cVIM in RA patients and healthy controls carrying HLA-DR9 alleles. Fourteen RA patients and ten healthy controls previously genotyped for HLA-DRB1 were studied for the presence of serum anti-cVIM antibodies by Western blot and ELISA. Peripheral blood mononuclear cells were stimulated with native vimentin and cVIM, and CD4+ T cells proliferation was assessed by flow cytometry. Citrulline-specific CD4+ T cells proliferation was found not only in RA patients but also in healthy controls. Although most patients carrying HLA-DR9 alleles present anti-cVIM antibodies, HLA-DR9 alleles were associated with weaker cVIM-driven CD4+ T-cell responses among RA patients. These results suggest that HLA-DR9 alleles could exert a protective effect on the recognition of cVIM epitopes by CD4+ T cells. In this context, other citrullinated proteins may break T and B cell tolerance, with cVIM only acting as a cross-reactive target for ACPA.

RESPIRATORIO

ROLE OF NEUTRALIZING ANTIBODIES IN ADULTS WITH COMMUNITY-ACQUIRED PNEUMONIA BY RESPIRATORY SYNCYTIAL VIRUS.

CLIN INFECT DIS. 2012 APR; 54(7):905-12.

Luchsinger V, Piedra PA, Ruiz M, Zunino E, Martínez MA, Machado C, Fasce R, Ulloa MT, Fink MC, Lara P, Avendaño LF.

BACKGROUND: Respiratory syncytial virus (RSV) has been implicated in the etiology of adult community-acquired pneumonia (CAP). We investigated RSV infection in Chilean adults with CAP using direct viral detection, real-time reverse-transcription polymerase chain reaction (rtRT-PCR), and serology (microneutralization assay). METHODS: RSV, other respiratory viruses, and bacteria were studied by conventional and molecular techniques in adults aged ≥18 years presenting with CAP to the healthcare facilities in Santiago, Chile from February 2005 through December 2007. RESULTS: All 356 adults with CAP enrolled had an acute blood sample collected at enrollment, and 184 had a convalescent blood sample. RSV was detected in 48 cases (13.4%). Immunofluorescence assay and viral isolation each detected only 1 infection (0.2%), whereas rtRT-PCR was positive in 32 (8.9%) cases and serology was positive in 20 (10.8%) cases. CAP clinical characteristics were similar in RSV-infected and non-RSV-infected cases. RSV-specific geometric mean serum-neutralizing antibody titer (GMST) was significantly lower at admission in the 48 RSV-infected cases compared with 308 non-RSV-infected adults (GMST in log(2): RSV/A 8.1 vs 8.9, and RSV/B 9.3 vs 10.4; P < .02). CONCLUSIONS: RSV infection is frequent in Chilean adults with CAP. Microneutralization assay was as sensitive as rtRT-PCR in detecting RSV infection and is a good adjunct assay for diagnostic research. High RSV-specific serum-neutralizing antibody levels were associated with protection against common and severe infection. The development of a vaccine could prevent RSV-related CAP in adults.

DEPARTAMENTO DE NEUROLOGÍA Y NEUROCIRUGÍA

OLFACTORY DEFICITS AND COGNITIVE DYSFUNCTION IN PARKINSON'S DISEASE.

NEURODEGENER DIS. 2012; 10(1-4):179-82.

Parrao T, Chana P, Venegas P, Behrens MI, Aylwin ML.

BACKGROUND: Olfactory deficits and executive dysfunction have been reported in Parkinson's disease (PD). However, the association between these deficits has not been thoroughly examined. METHODS: We studied 44 PD subjects and 17 age-matched controls. In PD subjects, symptoms were assessed with the Unified Parkinson's Disease Rating Scale and the Hoehn and Yahr scale. Cognition in both groups was assessed by a neuropsychological battery. Olfactory identification and sensitivity was evaluated with the Sniffin' Sticks® test and olfactory detection threshold, respectively. RESULTS: PD subjects showed significant deficits in olfactory function and working memory, executive function, speed of information processing, visuospatial skills and phonological verbal fluency tests when compared with the control group. Moreover, there was a significant correlation between olfactory sensory deficits and executive dysfunction. In PD patients with up to 12 months of motor symptoms, results were equivalent. CONCLUSION: Our preliminary results suggest a significant association between olfactory deficits and impairments of executive functions in PD.

MOTOR PATHWAY EXCITABILITY IN ATP13A2 MUTATION CARRIERS: A TRANSCRANIAL MAGNETIC STIMULATION STUDY.

PARKINSONISM RELAT DISORD. 2012 JUN; 18(5):590-4.

Zittel S, Kroeger J, van der Vegt JP, Siebner HR, Brüggemann N, Ramirez A, Behrens MI, Gerloff C, Bäumer T, Klein C, Münchau A.

OBJECTIVE: To describe excitability of motor pathways in Kufor-Rakeb syndrome (PARK9), an autosomal recessive nigro-striatal-pallidal-pyramidal neurodegeneration caused by a mutation in the ATP13A2 gene, using transcranial magnetic stimulation (TMS). METHODS: Five members of a Chilean family with an ATP13A2 mutation (one affected mutation carrier (MC) with a compound heterozygous mutation, 4 asymptomatic MC with a single heterozygous mutation) and 11 healthy subjects without mutations were studied. We measured motor evoked potentials (MEP), the contralateral silent period (cSP), short interval intracortical inhibition (SICI), intracortical facilitation (ICF), short latency afferent inhibition (SAI) as markers of intracortical intrahemispheric inhibition/facilitation and the ipsilateral silent period (iSP) and paired-pulse interhemispheric inhibition (IHI) to probe interhemispheric motor interactions. RESULTS: CSP duration was increased in the symptomatic ATP13A2 MC. The iSP measurements revealed increased interhemispheric inhibition in both the compound heterozygous and the heterozygous MC. CONCLUSION: A compound heterozygous mutation in the ATP13A2 gene is associated with increased intracortical inhibition. In addition, some aspects of interhemispheric inhibition are increased in the presence of a single ATP13A2 mutation.

INVERSE SUSCEPTIBILITY TO OXIDATIVE DEATH OF LYMPHOCYTES OBTAINED FROM ALZHEIMER'S PATIENTS AND SKIN CANCER SURVIVORS: INCREASED APOPTOSIS IN ALZHEIMER'S AND REDUCED NECROSIS IN CANCER.

J GERONTOL A BIOL SCI MED SCI. 2012 OCT; 67(10):1036-40.

Behrens MI, Silva M, Salech F, Ponce DP, Merino D, Sinning M, Xiong C, Roe CM, Quest AF.

A paucity of cancer in individuals with Alzheimer's disease (AD) and low rates of AD in cancer survivors has been reported in epidemiological studies. Deregulation in opposite directions of biological mechanisms, such as susceptibility to cell death, might be shared in the two disorders. We analyzed lymphocytes from AD and skin cancer patients as well as healthy controls and found significantly increased vulnerability of AD lymphocytes to H(2)O(2)-induced apoptotic death and higher resistance to death of skin cancer lymphocytes, due to reduced necrosis, as compared with healthy controls by pairwise comparisons adjusted for age and sex. H(2)O(2)-induced death in lymphocytes was caspase independent and significantly reduced by PARP-1 inhibition in all three groups. These differences in the susceptibility to cell death observed for lymphocytes from AD and skin cancer patients may be one of the mechanisms that help explain the inverse correlation detected between these diseases in epidemiological studies.

NFAT5 IS ACTIVATED BY HYPOXIA: ROLE IN ISCHEMIA AND REPERFUSION IN THE RAT KIDNEY.

PLOS ONE. 2012; 7(7):E39665.

Villanueva S, Suazo C, Santapau D, Pérez F, Quiroz M, Carreño JE, Illanes S, Lavandero S, Michea L, Irarrazabal CE.

The current hypothesis postulates that NFAT5 activation in the kidney's inner medulla is due to hypertonicity, resulting in cell protection. Additionally, the renal medulla is hypoxic (10-18 mmHg); however there is no information about the effect of hypoxia on NFAT5. Using in vivo and in vitro models, we evaluated the effect of reducing the partial pressure of oxygen (PO(2)) on NFAT5

activity. We found that 1) Anoxia increased NFAT5 expression and nuclear translocation in primary cultures of IMCD cells from rat kidney. 2) Anoxia increased transcriptional activity and nuclear translocation of NFAT5 in HEK293 cells. 3) The dose-response curve demonstrated that HIF-1α peaked at 2.5% and NFAT5 at 1% of O (2). 4) At 2.5% of O(2), the time-course curve of hypoxia demonstrated earlier induction of HIF-1α gene expression than NFAT5. 5) siRNA knockdown of NFAT5 increased the hypoxia-induced cell death. 6) siRNA knockdown of HIF-1α did not affect the NFAT5 induction by hypoxia. Additionally, HIF-1α was still induced by hypoxia even when NFAT5 was knocked down. 7) NFAT5 and HIF-1α expression were increased in kidney (cortex and medulla) from rats subjected to an experimental model of ischemia and reperfusion (I/R). 7) Experimental I/R increased the NFAT5-target gene aldose reductase (AR). 8) NFAT5 activators (ATM and PI3K) were induced in vitro (HEK293 cells) and in vivo (I/R kidneys) with the same timing of NFAT5. 8) Wortmannin, which inhibits ATM and PI3K, reduces hypoxia-induced NFAT5 transcriptional activation in HEK293 cells. These results demonstrate for the first time that NFAT5 is induced by hypoxia and could be a protective factor against ischemic damage.

MEMORY, FLUENCY, AND ORIENTATION: A FIVE-MINUTE SCREENING TEST FOR COGNITIVE DECLINE.

NEUROLOGIA. 2012 DEC 13.

Delgado Derio C, Guerrero Bonnet S, Troncoso Ponce M, Araneda Yañez A, Slachevsky Chonchol A, Behrens Pellegrino MI.

BACKGROUND: The prevalence of cognitive impairment (CI) will double in the next 20 years, making early detection a key priority. OBJECTIVES: Validation of a 5-minute CI screening test. METHODS: Adults aged 60 and older were recruited from memory clinics and the community at large in the Santiago, Chile metropolitan area. Based on clinical examination they were categorised as No CI (NCI), Mild CI (MCI) and dementia sufferers (DS). We measured the validity of a new test, MEFO, evaluating memory (5 points), phonetic verbal fluency (2 points) and orientation (6 points) by comparing its results with those from the MMSE. RESULTS: We evaluated 214 subjects, comprising 49 with dementia, 47 with MCI, and 118 with no CI. The MEFO differentiated between all 3 groups whereas the MMSE did not discriminate between the MCI and NCI groups. The area under the ROC curve (AUC) for the MEFO distinguishing NCI subjects from dementia sufferers was 0.97; for NCI vs CI (dementia+MCI), 0.89; and for NCI vs MCI, 0.80. On the MMSE these values were 0.95, 0.84, and 0.73, respectively. A cut-off score of 6/7 on the MEFO identified dementia sufferers with a sensitivity of 86% and a specificity of 96%. A cut-off score of 8/9 distinguished CI from NCI subjects with a sensitivity of 83% and a specificity of 75%. CONCLUSIONS: The MEFO is a valid and reliable test for discriminating between dementia and CI sufferers and subjects with no CI. Its validity is similar to that the MMSE under these conditions, but it is more effective for identifying subjects with MCI and its administration time is shorter.

PROGNOSIS OF CRYPTOGENIC ISCHEMIC STROKE: A PROSPECTIVE SINGLE-CENTER STUDY IN CHILE.

J STROKE CEREBROVASC DIS. 2012 NOV; 21(8):621-8.

Vallejos J, Jaramillo A, Reyes A, Illanes S, Orellana P, Manterola J, Díaz V.

Approximately 25%-40% of ischemic strokes are considered of unknown cause (ie, cryptogenic). The available information on associated risk factors, functional outcome, and recurrence of this subtype of stroke is limited, especially for the Chilean population. We conducted a prospective cohort study of 380 patients aged ≥ 18 years admitted consecutively to a stroke unit with demonstrated ischemic stroke. The stroke subtypes were classified according to the Trial of Org 10172 in Acute Stroke Treatment criteria. The modified Rankin Scale score and Barthel Index were used to assess functional outcome. The Kaplan-Meier product-limit method and Cox proportional hazards regression analysis were used to identify predictors of recurrent stroke during the follow-up period (mean, 2.1 years). Cryptogenic stroke (CS) was diagnosed in 76 patients (20%), 55.2% of them male, with a mean age of 62 ± 17 years. CS was the third most common stroke subtype after the large-artery disease (29%) and cardioembolic (24.4%) subtypes. After adjustment for age and sex, no vascular risk factors or laboratory parameters assessed at the time of admission were found to be predictive of CS. The CS subtype had the lowest rate of stroke recurrence at the end of the follow-up period (n = 4; 2.5% per year; odds ratio, 0.32; 95% confidence interval, 0.11-0.91; P = .022), a favorable functional outcome (mean modified Rankin Scale score, 2; mean Barthel Index, 77), and no increase in mortality risk (odds ratio, 0.73; 95% confidence interval, 0.29-1.77; P = .48). Our findings demonstrate that patients with no definite etiology identified after an extensive workup are at lower risk of recurrence and more likely to have a favorable outcome. No risk factors distinguish CS from other stroke subtypes in our study population.

DEPARTAMENTO DE OBSTETRICIA Y GINECOLOGÍA

RANDOMIZED TRIAL OF EARLY BUBBLE CONTINUOUS POSITIVE AIRWAY PRESSURE FOR VERY LOW BIRTH WEIGHT INFANTS.

J PEDIATR. 2012 JUL; 161(1):75-80.E1.

Tapia JL, Urzua S, Bancalari A, Meritano J, Torres G, Fabres J, Toro CA, Rivera F, Cespedes E, Burgos JF, Mariani G, Roldan L, Silvera F, Gonzalez A, Dominguez A; South American Neocosur Network.

OBJECTIVE: To determine whether very low birth weight infants (VLBWIs), initially supported with continuous positive airway pressure (CPAP) and then selectively treated with the INSURE (intubation, surfactant, and extubation to CPAP; CPAP/INSURE) protocol, need less mechanical ventilation than those supported with supplemental oxygen, surfactant, and mechanical ventilation if required (Oxygen/mechanical ventilation [MV]). STUDY DESIGN: In a multicenter randomized controlled trial, spontaneously breathing VLBWIs weighing 800-1500 g were allocated to receive either therapy. In the CPAP/INSURE group, if respiratory distress syndrome (RDS) did not occur, CPAP was discontinued after 3-6 hours. If RDS developed and the fraction of inspired oxygen (FiO(2)) was >0.35, the INSURE protocol was indicated. Failure criteria included FiO(2) >0.60, severe apnea or respiratory acidosis, and receipt of more than 2 doses of surfactant. In the Oxygen/MV group, in the presence of RDS, supplemental oxygen without CPAP was given, and if FiO(2) was >0.35, surfactant and mechanical ventilation were provided. RESULTS: A total of 256 patients were randomized to either the CPAP/INSURE group (n = 131) or the Oxygen/MV group (n = 125). The need for mechanical ventilation was lower in the CPAP/INSURE group (29.8% vs 50.4%; P = .001), as was the use of surfactant (27.5% vs 46.4%; P = .002). There were no differences in death, pneumothorax, bronchopulmonary dysplasia, and other complications of prematurity between the 2 groups. CONCLUSION: CPAP and early selective INSURE reduced the need for mechanical ventilation and surfactant in VLBWIs without increasing morbidity and death. These results may be particularly relevant for resource-limited regions.

NIFEDIPINE VERSUS FENOTEROL IN THE MANAGEMENT OF PRETERM LABOR: A RANDOMIZED, MULTICENTER CLINICAL STUDY.

GYNECOL OBSTET INVEST. 2012; 74(2):109-15.

Valdés E, Salinas H, Toledo V, Lattes K, Cuellar E, Perucca E, Díaz R, Montecinos F, Reyes A.

PURPOSE: To compare the efficacy of nifedipine and fenoterol in the management of threatened preterm labor (TPL). METHODS: A randomized and multicenter study assessing the tocolytic effect of nifedipine versus fenoterol in patients admitted to the participating maternity units with a diagnosis of TPL and a cost-savings study for economic assessment. For a power of 80% and an α error equal to 0.05, 132 consecutive patients were recruited during the study period; 66 patients were assigned to each group. A $\chi(2)$ analysis and a mean differences test were performed according to variable types and survival curves per intention-to-treat. RESULTS: Demographics were similar in both groups. The latency period was similar in both groups (26.7 vs. 25.6; p = 0.3). There were no differences in the results obtained. Nifedipine failed more frequently to obtain tocolysis when used as a first-line agent (80 vs. 90%, p = 0.0001). The group treated with fenoterol showed more drug adverse events (57.8 vs. 19.0%, p = 0.0001). The economic assessment did not evidence a significant difference in terms of cost savings between groups treated with either drug. CONCLUSION: The present study failed to demonstrate either clinical or economic superiority of any of the two drugs used in TPL management. The highest failure percentage of nifedipine when used as a first-line agent should encourage further research.

OXIDATIVE DAMAGE TO PRE-ECLAMPTIC PLACENTA: IMMUNOHISTOCHEMICAL EXPRESSION OF VEGF, NITROTYROSINE RESIDUES AND VON WILLEBRAND FACTOR.

J MATERN FETAL NEONATAL MED. 2012 NOV; 25(11):2339-45.

Bosco C, González J, Gutiérrez R, Parra-Cordero M, Barja P, Rodrigo R.

OBJECTIVE: To determine the relationship of biomarkers of placental damage by oxidative stress in pre-eclamptic placenta. METHODS: A case-control study was performed on a population of 14 pregnant women with PE and 12 women with normal pregnancies. Immunohistochemical expressions of VEGF, vWF distribution, (Na + K)-ATPase activity, and abundance of nitrotyrosine residues, were assessed in the placental tissue. RESULTS: Women with pre-eclampsia showed increased VEGF expression and abundance of nitrotyrosine residues in placental villous, and plasma vWF levels ($p < 0.05$), whereas placental (Na + K)-ATPase activity were significantly reduced. The syncytiotrophoblast and the maternal space of pre-eclamptic placenta showed diminished and increased vWF expression, respectively, but no significant differences in its expression were found in the placental endothelium and stroma ($p < 0.05$). CONCLUSIONS: It could be suggested that increased oxidative stress and VEGF contribute to enhance the impairment of placental perfusion by increasing peroxynitrite formation, product of the NO and superoxide reaction, thereby partly contributing to account for the pathophysiology of this disease. The presence of vWF in the maternal space and its diminished expression in syncytiotrophoblast of pre-eclamptic placenta also might have pathogenic implications.

RISK OF PERINATAL DEATH IN EARLY-ONSET INTRAUTERINE GROWTH RESTRICTION ACCORDING TO GESTATIONAL AGE AND CARDIOVASCULAR DOPPLER INDICES: A MULTICENTER STUDY.

FETAL DIAGN THER. 2012; 32(1-2):116-22.

Cruz-Lemini M, Crispi F, Van Mieghem T, Pedraza D, Cruz-Martínez R, Acosta-Rojas R, Figueras F, Parra-Cordero M, Deprest J, Gratacós E.

OBJECTIVE: To assess the value of gestational age and cardiovascular Doppler indices in predicting perinatal mortality in a multicenter cohort of early-onset intrauterine growth-restricted (IUGR) fetuses. METHODS: A multicenter prospective cohort study including 157 early-onset (<34 weeks) IUGR cases with abnormal umbilical artery (UA) Doppler was conducted. Cardiovascular assessment included the ductus venosus (DV), the aortic isthmus flow index (IFI), and the myocardial performance index (MPI). Isolated and combined values to predict the risk of perinatal death were evaluated by logistic regression and by decision tree analysis, where the gestational age at delivery, UA, and middle cerebral artery (MCA) were also included as covariates. RESULTS: Perinatal mortality was 17% (27/157). All parameters were significantly associated with perinatal death, with individual odds ratios (OR) of 25.2 for gestational age below 28 weeks, 12.1 for absent/reversed DV atrial flow, 5.3 for MCA pulsatility index <5th centile, 4.6 for UA absent/reversed diastolic end-flow, 1.8 for IFI <5th centile, and 1.6 for MPI >95th centile. Decision tree analysis identified gestational age at birth as the best predictor of death (<26 weeks, 93% mortality; 26-28 weeks, 29% mortality, and >28 weeks, 3% mortality). Between 26 and 28 weeks, DV atrial flow allowed further stratification between high (60%) and low risk (18%) of mortality. CONCLUSIONS: Gestational age largely determines the risk of perinatal mortality in early-onset IUGR before 26 weeks and later than 28 weeks of gestation. The DV may improve clinical management by stratifying the probability of death between 26 and 28 weeks of gestation.

LABORATORIO DE ENDOCRINOLOGÍA

NERVE GROWTH FACTOR INDUCES THE EXPRESSION OF CHAPERONE PROTEIN CALRETICULIN IN HUMAN EPITHELIAL OVARIAN CELLS.

HORM METAB RES. 2012 JUL; 44(8):639-43.

Vera C, Tapia V, Kohan K, Gabler F, Ferreira A, Selman A, Vega M, Romero C.

Epithelial ovarian cancer is highly angiogenic and high expression of Nerve Growth Factor (NGF), a proangiogenic protein. Calreticulin is a multifunctional protein with anti-angiogenic properties and its translocation to the tumor cell membrane promotes recognition and engulfment by dendritic cells. The aim of this work was to evaluate calreticulin expression in human normal ovaries, benign and borderline tumors, and epithelial ovarian cancer samples and to evaluate whether NGF regulates calreticulin expression in human ovarian surface epithelium and in epithelial ovarian cancer cell lines. Calreticulin mRNA and protein levels were analyzed using RT-PCR, Western blot and immunohistochemistry in 67 human ovarian samples obtained from our Institution. Calreticulin expression induced by NGF stimulation in cell lines was evaluated using RT-PCR, Western blot and immunocytochemistry. We found a significant increase of calreticulin mRNA levels in epithelial ovarian cancer samples as compared to normal ovaries, benign tumors, and borderline tumors. Calreticulin protein levels, evaluated by Western blot, were also increased in epithelial ovarian cancer with respect to benign and borderline tumors. When HOSE and A2780 cell lines were stimulated with Nerve Growth Factor, we found an increase in calreticulin protein levels compared to controls. This effect was reverted by GW441756, a TRKA specific inhibitor. These results suggest that NGF regulates calreticulin protein levels in epithelial ovarian cells through TRKA receptor activation.

PROTEIN EXPRESSION OF PKCZ (PROTEIN KINASE C ZETA), MUNC18C, AND SYNTAXIN-4 IN THE INSULIN PATHWAY IN ENDOMETRIA OF PATIENTS WITH POLYCYSTIC OVARY SYNDROME (PCOS).

REPROD BIOL ENDOCRINOL. 2012 MAR 5; 10:17.

Rivero R, Garin CA, Ormazabal P, Silva A, Carvajal R, Gabler F, Romero C, Vega M.

BACKGROUND: Polycystic Ovary Syndrome (PCOS) is an endocrine-metabolic disorder commonly associated with insulin resistance (IR). Previous studies indicate about the expression of molecules involved in the insulin pathway in endometria of women with PCOS-IR. Therefore, the aim of the present study was to evaluate the effect of insulin and testosterone in the expression of these proteins in the endometria and immortal endometrial stromal cell line (T-HESCs). METHODS: We examined the protein levels of Munc18c, PKC zeta, phospho-PKC Zeta, and Syntaxin-4. Protein levels were assessed by Western Blot and/or immunohistochemistry in proliferative endometria (NPE = 6) and in PCOS endometria with insulin resistance (PCOSE-IR = 6). We also evaluated whether high concentrations of insulin (100 nM) and/or testosterone (100 nM), during a 24 h stimulatory period, affected the expression of these proteins in an immortal endometrial stromal cell line (T-HESCs). Once stimulated, proteins were extracted from cells and were assessed by Western Blot analysis. Immunocytochemistry was performed to detect AR in T-HESC cells. RESULTS: Western Blot

data showed decreased expression (p < 0,05) of Munc18c and phospho-PKC Zeta in PCOS-IR endometria (PCOSE-IR) with respect to the control (NPE). In the in vitro study, Western Blot analysis showed decreased levels of Munc18c, PKC Zeta and phospho-PKC Zeta with the different hormonal treatments when compared to the control condition (no hormonal stimulation) (p < 0,05). The AR was present in the endometrial stromal cell line (T-HESC). CONCLUSION: The conditions of hyperinsulinism and hyperandrogenism present in PCOS-IR patients modulate the expression and/or phosphorylation of the proteins involved in the insulin pathway at the endometrial level. These data extend to the T-HESCs cells results, where insulin and testosterone exert an effect on both the expression and phosphorylation of proteins present in the pathway.

NERVE GROWTH FACTOR STIMULATES CELLULAR PROLIFERATION OF HUMAN EPITHELIAL OVARIAN CANCER.

HORM METAB RES. 2012 SEP; 44(9):656-61.

Urzua U, Tapia V, Geraldo MP, Selman A, Vega M, Romero C.

Due to its ability to induce vascular endothelial growth factor expression and proliferation, migration, and vasculogenesis of endothelial cells, nerve growth factor (NGF) has been considered as an angiogenic factor in epithelial ovarian cancer (EOC). In this work, we evaluated the angiogenic and proliferative mRNA expression profiles of EOC and addressed the responsiveness of EOC explants to NGF stimulation. Twenty EOC samples were obtained from Obstetrics and Gynecology Department, University of Chile's Clinical Hospital. Global gene expression profiles of selected poorly differentiated serous EOC samples were obtained with DNA oligonucleotide microarrays. In addition, EOC explants were subjected to NGF stimulation and levels of p-AKT, BAX, BCL2, Ki-67, c-MYC, and FOXL2 proteins were determined by immunohistochemistry. Results showed that mRNAs coding for specific transcriptional regulators and antiapoptotic components of the NGF signaling pathway were upregulated in EOC cells. At the protein level, key members of the NGF pathway including p-AKT, BCL2/BAX, Ki-67, and c-MYC were found increased, while FOXL2 was decreased in response to NGF stimulation. These findings strongly suggest that NGF stimulates cellular proliferation of human EOC.

DECREASED PHOSPHORYLATION OF Y14CAVEOLIN-1 IN ENDOMETRIAL TISSUE OF POLYCYSTIC OVARY SYNDROME PATIENTS MAY BE RELATED WITH AN INSULIN RESISTANT STATE IN THIS TISSUE.

HORM METAB RES. 2012 DEC 7.

Ormazabal P, Romero C, Gabler F, Quest AF, Vega M.

Endometrial tissue of patients with polycystic ovary syndrome (PCOS) shows an impaired expression of insulin signaling molecules. Tyrosine phosphorylation of the insulin receptor (IR) by insulin promotes glucose uptake by activating the PI3K/Akt pathway. IR stability and function depend on the presence of the protein caveolin-1. Activation of IR increases phosphorylation of Y14caveolin-1. Since the endometrium of PCOS patients is proposed to be insulin resistant, we evaluated the phosphorylation of IR and caveolin-1 in endometria of patients with insulin resistance (PCOSE-IR) compared to controls (CE). To explore the mechanism associated with this condition, cultured endometrial cells (T-HESC) were exposed to high glucose (25 mM, 24 h), an experimental condition that leads to insulin resistance in other cell types. Endometrial protein levels of phospho-Y972IR, phospho-Y14caveolin-1 and caveolin-1 were determined by Western blotting. In cultured cells, protein levels of caveolin-1, IR, and Akt were evaluated by Western blotting. After acute insulin stimulation, phospho-S473Akt, phospho-Y14caveolin-1, and 2-deoxyglucose (2-DOG) uptake were determined. PCOSE-IR samples showed high protein levels of caveolin-1, but reduced phospho-Y14caveolin-1 compared to CE. No differences were observed for phospho-Y972IR between both groups. Cells pretreated with glucose showed a reduction in protein levels of IR and caveolin-1 and were unable to increase 2-DOG uptake, phospho-S473Akt and phospho-Y14caveolin-1 after insulin stimulation. In conclusion, in PCOSE-IR the impaired phosphorylation of IR downstream molecules such as phospho-Y14caveolin-1 suggests a diminished insulin sensitivity in endometria, condition that could be supported in vitro by the ability of T-HESCs to become insulin resistant when they are exposed to high glucose.

DEPARTAMENTO DE PSIQUIATRÍA Y SALUD MENTAL

LESSONS FROM SCALING UP A DEPRESSION TREATMENT PROGRAM IN PRIMARY CARE IN CHILE.

REV PANAM SALUD PUB. 2012 SEP; 32(3):234-40.

Araya R, Alvarado R, Sepúlveda R, Rojas G.

In Chile, the National Depression Detection and Treatment Program (Programa Nacional de Diagnóstico y Tratamiento de la Depresión, PNDTD) in primary care is a rare example of an evidence-based mental health program that was scaled up to the national level in a low- or middle-income country. This retrospective qualitative study aimed to better understand how policymakers made the decision to scale up mental health services to the national level, and to explore the elements, contexts, and processes that

facilitated the decision to implement and sustain PNDTD. In-depth semistructured interviews with six key informants selected through intentional sampling were conducted in August-December 2008. Interviewees were senior officers at the Ministry of Health who were directly involved in the decision to scale up the program. Results yielded four elements pivotal to the decisionmaking process: scientific evidence, teamwork and leadership, strategic alliances, and program institutionalization. Each element contributed to building consensus, securing funding, attracting resources, and gaining lasting support from policymakers. Additionally, a review of available documentation led the authors to consider sociopolitical context and use of the media to be important factors. While research evidence for the effectiveness of mental health services in the primary care setting continues to accumulate, low- and middle-income countries should get started on the lengthy process of scaling up by incorporating the elements that led to decisionmaking and implementation of the PNDTD in Chile.

AFFECTIVE TEMPERAMENTS IN CLINICAL PRACTICE: A VALIDATION STUDY IN MOOD DISORDERS.

J AFFECT DISORD. 2012 FEB; 136(3):577-80.

Vöhringer PA, Whitham EA, Thommi SB, Holtzman NS, Khrad H, Ghaemi SN.

BACKGROUND: We sought to examine correlations between clinical validators and temperaments in clinical practice. METHODS: We provided the self-report TEMPS-A (50 item long) to 123 consecutive patients seen in the Mood Disorders Program of Tufts Medical Center. Temperament was assessed as cyclothymia, dysthymia, irritable or hyperthymia. Cut-offs were tested using (50%) and (75%) thresholds of affirmative responses, as well as highest percent for dominant temperament. We reported no dominant temperament at 75% cut-off. Multivariate regression modeling was conducted to assess confounding bias. RESULTS: Using clinical and demographic validators, cyclothymia was the most strongly validated temperament, followed by dysthymia and hyperthymia. Irritable temperament did not appear to be valid in this sample. A 75% item endorsement cut-off appeared to identify clinically important temperaments in slightly less than half of this sample. Those without any temperament at 75% cut-off had better prognostic features. 50% cut-off was highly nonspecific, and poorly correlated with diagnostic validators. CONCLUSIONS: Affective temperaments correlate with clinical validators, most robustly for cyclothymia. 75% cut-off on the TEMPS may provide a useful categorical definition of abnormal affective temperaments in mood disorders. With that definition, slightly less than one-half of patients with mood disorders have affective temperaments. Those without abnormal affective temperaments have better prognostic features.

FROM GLUTAMATERGIC DYSFUNCTION TO COGNITIVE IMPAIRMENT: BOUNDARIES IN THE THERAPEUTIC OF THE SCHIZOPHRENIA.

CURR PHARM BIOTECHNOL. 2012 JUN; 13(8):1543-8.

Gaspar PA, Bustamante ML, Rojo LE, Martinez A.

Cognitive deficits are trait markers in schizophrenia and the improvement of these dysfunctions has been considered as a new frontier of treatment in this disease. A current model for the patophysiology of schizophrenia states that N-methyl-D-aspartate receptor (NMDAR) hypofunction leads to a dysregulation of gamma-amino butyric acid (GABA) fast- spiking interneurons, consequently disinhibiting pyramidal glutamatergic output and disturbing signal-to-noise ratio. In this way, the modulation of the glutamate activity might constitute a highly promising target for future therapeutic interventions of this disease. In the present review, we discuss key regulatory elements for glutamatergic neurotransmission and provide new insights into their potential role in developing pharmacological treatments. Also, we emphasize the role of certain chemical families as potential sources of new lead compounds with affinity for metabotropic glutamate receptors (mGluRs) with cognitive enhancing properties.

MIXED DEPRESSION: A STUDY OF ITS PHENOMENOLOGY AND RELATION TO TREATMENT RESPONSE.

J AFFECT DISORD. 2012 FEB; 136(3):1059-61.

Pae CU, Vöhringer PA, Holtzman NS, Thommi SB, Patkar A, Gilmer W, Ghaemi SN.

BACKGROUND: Mixed depression reflects the occurrence of a major depressive episode with subsyndromal manic symptoms. Not recognized in DSM-IV, it is included in the proposed changes for DSM-5. Observational and cross-sectional studies have suggested that mixed depression is present in up to one-half of major depressive episodes, whether in MDD or bipolar disorder. Based on observational studies, antidepressants appear to be less effective, and neuroleptics more effective, in mixed than pure depression (major depressive episodes with no manic symptoms). In this report, we examine the specific manic symptoms that are most present in mixed depression, especially as they correlate with prospectively assessed treatment response. METHODS: In 72 patients treated in a randomized clinical trial (ziprasidone versus placebo), we assessed the phenomenology of manic symptom type at study entry and their influence as predictors of treatment response. RESULTS: The most common symptom

presentation was a clinical triad of flight of ideas (60%), distractibility (58%), and irritable mood (55%). Irritable mood was the major predictor of treatment response. DSM-based diagnostic distinctions between MDD and bipolar disorder (type II) did not predict treatment response. CONCLUSION: In this prospective study, mixed depression seems to be most commonly associated with irritable mood, flight of ideas, and distractibility, with irritability being an important predictor of treatment outcome with neuroleptic agents. If these data are correct, in the presence of mixed depression, the DSM-based dichotomy between MDD and bipolar disorder does not appear to influence treatment response.

A 6 WEEK RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF ZIPRASIDONE FOR THE ACUTE DEPRESSIVE MIXED STATE.

PLOS ONE. 2012;7(4):E34757.

Patkar A, Gilmer W, Pae CU, Vöhringer PA, Ziffra M, Pirok E, Mulligan M, Filkowski MM, Whitham EA, Holtzman NS, Thommi SB, Logvinenko T, Loebel A, Masand P, Ghaemi SN.

OBJECTIVE: To examine the efficacy of ziprasidone vs placebo for the depressive mixed state in patients with bipolar disorder type II or major depressive disorder (MDD). METHODS: 73 patients were randomized in a double-blinded, placebo-controlled study to ziprasidone (40-160 mg/d) or placebo for 6 weeks. They met DSM-IV criteria for a major depressive episode (MDE), while also meeting 2 or 3 (but not more nor less) DSM-IV manic criteria. They did not meet DSM-IV criteria for a mixed or manic episode. Baseline psychotropic drugs were continued unchanged. The primary endpoint measured was Montgomery-Åsberg Depression Rating Scale (MADRS) scores over time. The mean dose of ziprasidone was 129.7±45.3 mg/day and 126.1±47.1 mg/day for placebo. RESULTS: The primary outcome analysis indicated efficacy of ziprasidone versus placebo (p=0.0038). Efficacy was more pronounced in type II bipolar disorder than in MDD (p=0.036). Overall ziprasidone was well tolerated, without notable worsening of weight or extrapyramidal symptoms. CONCLUSIONS: There was a statistically significant benefit with ziprasidone versus placebo in this first RCT of any medication for the provisional diagnostic concept of the depressive mixed state.

THE VARIETIES OF DEPRESSIVE EXPERIENCE: DIAGNOSING MOOD DISORDERS.

PSYCHIATR CLIN NORTH AM. 2012 MAR; 35(1):73-86.

Ghaemi SN, Vöhringer PA, Vergne DE.

Biopsychosocial eclecticism has led, the authors believe, to a simplistic acceptance of a unitary view of MDD with little scientific solidity. The authors propose a return to careful psychopathology as the basis of all nosology, which has led to identifying four main types of depressive illness, and a method-based, existential approach to understanding depression.

OFICINA APOYO A LA INVESTIGACIÓN CLÍNICA

TOLL-LIKE RECEPTOR 4 GENE POLYMORPHISM INFLUENCES DENDRITIC CELL IN VITRO FUNCTION AND CLINICAL OUTCOMES IN VACCINATED MELANOMA PATIENTS.

CANCER IMMUNOL IMMUNOTHER. 2012 NOV; 61(11):2067-77.

Tittarelli A, González FE, Pereda C, Mora G, Muñoz L, Saffie C, García T, Díaz D, Falcón C, Hermoso M, López MN, Salazar-Onfray F.

Toll-like receptor 4 (TLR4) is expressed on dendritic cells (DCs), sensing environmental danger molecules that induce their activation and maturation. Recently, we reported a method for the production of therapeutic DCs against melanoma, called tumor antigen-presenting cells (TAPCells), using a heat-shocked allogeneic melanoma cell lysate (TRIMEL) as an activation factor and antigen provider. Since TRIMEL contains endogenous TLR4 ligands, we evaluated the role of TLR4 in TAPCells differentiation by antibody neutralization and the association of a Tlr4 polymorphism (896A/G) (Asp299Gly), determined by PCR-RFLP, with the in vitro activation capacity and the clinical outcome of TAPCells-vaccinated patients. Antibody blocking of monocyte TLR4 inhibited surface expression, determined by flow cytometry, of the major histocompatibility complex class I, CCR7, CD80, CD83 and CD86 on TAPCells, reduced interleukin (IL)-6 and tumor necrosis factor -α gene expression evaluated by qRT-PCR, and also inhibited the TAPCells-mediated interferon-γ (IFN-γ) secretion of melanoma-specific CD8(+) T cells determined by ELISpot ($p < 0.01$). Moreover, CD8(+) T-cell activation capacity was significantly reduced in TAPCells bearing the TLR4 Asp299Gly receptor ($p < 0.05$). Finally, TAPCells-vaccinated stage-IV melanoma patients bearing the Tlr4 896G allele showed a shortened post-therapy median survival rate compared with those carrying the Tlr4 896A allele ($p < 0.05$; log-rank test). Our results indicate that TLR4 is a key receptor for the tumor lysate-mediated in vitro generation of clinically efficient antigen-presenting cells. Further analysis of patients included in different vaccine protocols is necessary for definitively establishing a role for TLR4 polymorphism in clinical responses.

THE IMMUNOLOGICAL RESPONSE AND POST-TREATMENT SURVIVAL OF DC-VACCINATED MELANOMA PATIENTS ARE ASSOCIATED WITH INCREASED TH1/TH17 AND REDUCED TH3 CYTOKINE RESPONSES.

CANCER IMMUNOL IMMUNOTHER. 2012 DEC 15.

Durán-Aniotz C, Segal G, Salazar L, Pereda C, Falcón C, Tempio F, Aguilera R, González R, Pérez C, Tittarelli A, Catalán D, Nervi B, Larrondo M, Salazar-Onfray F, López MN.

INTRODUCTION: Immunization with autologous dendritic cells (DCs) loaded with a heat shock-conditioned allogeneic melanoma cell lysate caused lysate-specific delayed type hypersensitivity (DTH) reactions in a number of patients. These responses correlated with a threefold prolonged long-term survival of DTH(+) with respect to DTH(-) unresponsive patients. Herein, we investigated whether the immunological reactions associated with prolonged survival were related to dissimilar cellular and cytokine responses in blood. MATERIALS AND METHODS: Healthy donors and melanoma patient's lymphocytes obtained from blood before and after vaccinations and from DTH biopsies were analyzed for T cell population distribution and cytokine release. RESULTS/DISCUSSION: Peripheral blood lymphocytes from melanoma patients have an increased proportion of Th3 (CD4(+) TGF-β(+)) regulatory T lymphocytes compared with healthy donors. Notably, DTH(+) patients showed a threefold reduction of Th3 cells compared with DTH(-) patients after DCs vaccine treatment. Furthermore, DCs vaccination resulted in a threefold augment of the proportion of IFN-γ releasing Th1 cells and in a twofold increase of the IL-17-producing Th17 population in DTH(+) with respect to DTH(-) patients. Increased Th1 and Th17 cell populations in both blood and DTH-derived tissues suggest that these profiles may be related to a more effective anti-melanoma response. CONCLUSIONS: Our results indicate that increased proinflammatory cytokine profiles are related to detectable immunological responses in vivo (DTH) and to prolonged patient survival. Our study contributes to the understanding of immunological responses produced by DCs vaccines and to the identification of follow-up markers for patient outcome that may allow a closer individual monitoring of patients.

SERVICIO ANATOMÍA PATOLÓGICA

ARTICULAR CARTILAGE DEVELOPMENT: A MOLECULAR PERSPECTIVE.

ORTHOP CLIN NORTH AM. 2012 APR; 43(2):155-71

Las Heras F, Gahunia HK, Pritzker KP.

In this article, development of articular cartilage and endochondral ossification is reviewed, from the perspective of both morphologic aspects of histogenesis and molecular biology, particularly with respect to key signaling molecules and extracellular matrix components most active in cartilage development. The current understanding of the roles of transforming growth factor β and associated signaling molecules, bone morphogenic proteins, and molecules of the Wnt-β catenin system in chondrogenesis are described. Articular cartilage development is a highly conserved complex biological process that is dynamic and robust in nature, which proceeds well without incident or failure in all joints of most young growing individuals.

COMPARISON OF CARTILAGE HISTOPATHOLOGY ASSESSMENT SYSTEMS ON HUMAN KNEE JOINTS AT ALL STAGES OF OSTEOARTHRITIS DEVELOPMENT.

OSTEOARTHRITIS CARTILAGE. 2012 JUN; 20(6):476-85.

Pauli C, Whiteside R, Heras FL, Nesic D, Koziol J, Grogan SP, Matyas J, Pritzker KP, D'Lima DD, Lotz MK.

OBJECTIVE: To compare the MANKIN and OARSI cartilage histopathology assessment systems using human articular cartilage from a large number of donors across the adult age spectrum representing all levels of cartilage degradation. DESIGN: Human knees (n=125 from 65 donors; age range 23-92) were obtained from tissue banks. All cartilage surfaces were macroscopically graded. Osteochondral slabs representing the entire central regions of both femoral condyles, tibial plateaus, and the patella were processed for histology and Safranin O - Fast Green staining. Slides representing normal, aged, and osteoarthritis (OA) tissue were scanned and electronic images were scored online by five observers. Statistical analysis was performed for inter- and intra-observer variability, reproducibility and reliability. RESULTS: The inter-observer variability among five observers for the MANKIN system showed a similar good Intra-class correlation coefficient (ICC>0.81) as for the OARSI system (ICC>0.78). Repeat scoring by three of the five readers showed very good agreement (ICC>0.94). Both systems showed a high reproducibility among four of the five readers as indicated by the Spearman's rho value. For the MANKIN system, the surface represented by lesion depth was the parameter where all readers showed an excellent agreement. Other parameters such as cellularity, Safranin O staining intensity and tidemark had greater inter-reader disagreement. CONCLUSION: Both scoring systems were reliable but appeared too complex and time consuming for assessment of lesion severity, the major parameter determined in standardized

scoring systems. To rapidly and reproducibly assess severity of cartilage degradation, we propose to develop a simplified system for lesion volume.

ABERRANT CHONDROCYTE HYPERTROPHY AND ACTIVATION OF Β-CATENIN SIGNALING PRECEDE JOINT ANKYLOSIS IN ANK/ANK MICE.

J RHEUMATOL. 2012 MAR; 39(3):583-93

Las Heras F, Pritzker KP, So A, Tsui HW, Chiu B, Inman RD, Tsui FW.

OBJECTIVE: We assessed the role of Ank in the maintenance of postnatal articular cartilage using the ank/ank mouse (mice homozygous for progressive ankylosis). METHODS: We analyzed ank/ank mice and wild-type littermates (8, 12, and 18 weeks old). Sections from decalcified, paraffin-embedded joints were stained with hematoxylin and eosin. Articular chondrocyte size and cartilage thickness were determined using morphometric methods. Immuno-histochemical staining was performed with anticollagen X, antitissue nonspecific alkaline phosphatase (TNAP), and anti-ß-catenin antibodies on fixed joint sections. Axin2 expression in paw joint lysates in wild-type versus ank/ank mice were compared using Western blot analysis. RESULTS: In all age groups of normal mice studied, calcified cartilage (CC) chondrocyte areas were significantly larger than those of uncalcified cartilage (UC) chondrocytes. However, similar chondrocyte areas (UC vs CC) were found in 12-week and 18-week-old ank/ank mice, indicating that hypertrophic chondrocytes were present in the UC of these mutant mice. The ank/ank mice showed an increase in CC thickness. The ank/ank UC hypertrophic chondrocytes showed diffuse immuno-reactivity for collagen X and TNAP. Increased ß-catenin activation was demonstrated by nuclear localization of ß-catenin staining in ank/ank chondrocytes. Axin2 expression from paw lysates was downregulated in ank/ank mice. CONCLUSION: We identified a previously unrecognized phenotype in the articular cartilage of ank/ank mice: collagen X-positive hypertrophic chondrocytes in the UC. It is possible that consequent to downregulation of axin2 expression, ß-catenin signaling was activated, leading to accelerated chondrocyte maturation and eventual ankylosis in ank/ank joints. Our studies shed new light on the contribution of a key signaling pathway in this model of joint ankylosis.

MIXED EPITHELIAL AND STROMAL TUMOR OF THE KIDNEY (MEST).

ARCH ESP UROL. 2012 SEP; 65(7):713-6.

Lopez-Fontana G, Gallegos I, Sepúlveda F, Bonomo JI, Castillo OA.

OBJECTIVE: To report an unusual case of renal tumor and review the literature. METHODS: We present a 20 years old female with a history of acute right pyelonephritis. The ultrasound study revealed a tumor-like image in the lower pole of the right kidney. The CT-scan showed a mixed solid and cystic mass of 7 cm. in the lower pole of the right kidney. RESULTS: A right laparoscopic partial nephrectomy was performed. The total operative time was 90 minutes, with 24 minutes of warm ischemia. The estimated blood loss was 50 ml. and the length of stay (LOS) 36 hours. The pathology findings confirm a mixed epithelial and stromal tumor (MEST) of the kidney. CONCLUSION: Mixed epithelial and stromal tumor (MEST) of the kidney is a benign and rare condition that doesn't show a clear difference with other renal tumors in image studies. Nephron-sparing surgery with margin study is the standard treatment when is feasible.

SERVICIO DENTOMAXILOFACIAL

DETERMINATION OF SUSCEPTIBILITY TO SENSITIZATION TO DENTAL MATERIALS IN ATOPIC AND NON-ATOPIC PATIENTS.

MED ORAL PATOL ORAL CIR BUCAL. 2012 MAR 1; 17(2):E320-4.

Rojas-Alcayaga G, Carrasco-Labra A, Danús P, Guzmán MA, Morales-Bozo I, Urzúa B, Ortega-Pinto A.

INTRODUCTION: Some studies report that atopic patients have a greater frequency of delayed-type sensitization than non-atopic patients. Objective: To determine the influence of the atopic condition on delayed sensitization to dental materials. DESIGN: cross-sectional study. METHODS: Forty (40) atopic subjects and forty (40) non-atopic subjects, of both sexes, between 20 and 65 years of age were included. The determination of delayed sensitization to dental materials was performed using patch test. An oral exam was also carried out to check for lesions of the oral mucosa. RESULTS: 61.25% of the patients were positive for delayed-type sensitization to one or more allergens, being palladium chloride (21.25%), ammoniated mercury (20%), benzoyl peroxide (12.5%) and amalgam (10%) the most frequent. The frequency of sensitization was 67.5% in the group of atopic patients, compared to 55% in the non atopic group ($p>0.05$). The materials with the greatest difference of sensitization in atopic compared to non-atopic patients were ammoniated mercury, benzoyl peroxide, amalgam and Bisphenol A Dimethacrylate (BIS-GMA). CONCLUSION: The atopic condition is not related to a higher frequency of delayed sensitization to a battery of dental materials.

SERVICIO UROLOGÍA

PHARMACOPERONE IN3 ENHANCES THE APOPTOTIC EFFECT OF LEUPROLIDE IN PROSTATE CANCER CELLS BY INCREASING THE GONADOTROPIN-RELEASING HORMONE RECEPTOR IN THE CELL MEMBRANE.

ANTICANCER DRUGS. 2012 OCT; 23(9):959-69.

Sánchez CA, Mercado AJ, Contreras HR, Cabezas JC, Huidobro CC, Castellón EA.

Gonadotropin-releasing hormone (GnRH) agonists are widely used for the treatment of advanced prostate cancer (PCa). Agonists activate the GnRH receptor (GnRH-R), triggering apoptosis in PCa cells. In gonadotropes, the amount of GnRH-R in the plasma membrane is regulated by protein folding and endoplasmic reticulum retention, mechanisms that can be overcome by the pharmacoperone IN3. Our aim was to describe the intracellular distribution of GnRH-R in PCa cells and its relation to response to GnRH analog treatments. The expressions of GnRH-R in PCa biopsies were evaluated by immunohistochemistry and the intracellular distribution was determined by immunofluorescence in primary cell cultures from human PCa samples. Cultured cells were pretreated with IN3 and then with leuprolide. Cell survival was evaluated by 1-(4,5-dimethylthiazol-2-yl)-3,5-diphenylformazan (MTT) thiazolyl blue formazan and cell cycle and apoptosis by flow cytometry. We observed that the expression of GnRH-R decreased according to malignant progression. Most GnRH-R are located inside the cell, colocalizing with endoplasmic reticulum markers. The treatment with IN3 decreased cellular GnRH-R retention, increasing plasma membrane expression in approximately 60%. Pretreatment with IN3 decreased PCa cell survival compared with leuprolide-alone treatment, primarily because of an increase in apoptosis. We conclude that the response of PCa cells to leuprolide is related to the amount of GnRH-R in the plasma membrane. Therefore, pretreatment evaluation of the amount of these receptors may be a predictor of the outcome of leuprolide treatment in PCa patients. Assessment of systemic IN3 effect would be necessary to determine its utility as an adjuvant treatment in hormone-resistant tumors.

UPC

EVOLUTION OF PERIPHERAL VS METABOLIC PERFUSION PARAMETERS DURING SEPTIC SHOCK RESUSCITATION. A CLINICAL-PHYSIOLOGIC STUDY.

J CRIT CARE. 2012 JUN; 27(3):283-8.

Hernandez G, Pedreros C, Veas E, Bruhn A, Romero C, Rovegno M, Neira R, Bravo S, Castro R, Kattan E, Ince C.

PURPOSE: Perfusion assessment during septic shock resuscitation is difficult and usually complex determinations. Capillary refill time (CRT) and central-to-toe temperature difference (Tc-toe) have been proposed as objective reproducible parameters to evaluate peripheral perfusion. The comparative evolution of peripheral vs metabolic perfusion parameters in septic shock resuscitation has not been studied. We conducted a prospective observational clinical-physiologic study to address this subject. METHODS: Patients with sepsis-related circulatory dysfunction were resuscitated according to a standard local algorithm. Perfusion assessment included serial determinations of metabolic (central venous O (2) saturation [Scvo(2)] and central venous to arterial Pco(2) gradient [P(cv-a)co(2)]) and peripheral perfusion parameters (CRT and Tc-toe, among others). Successful resuscitation was defined as a normal plasma lactate at 24 hours. RESULTS: Forty-one patients were included. The presence of normal values for both CRT and Tc-toe considered together at 6 hours was independently associated with a successful resuscitation (P = .02), as compared with the behavior of metabolic parameters. Capillary refill time was the first parameter to be significantly normalized. CONCLUSION: Early recovery of peripheral perfusion anticipates a successful resuscitation compared with traditional metabolic parameters in septic shock patients. Our findings support the inclusion of serial peripheral perfusion assessment in multimodal monitoring strategies for septic shock resuscitation.

CLÍNICA UNIVERSITARIA QUILÍN

IS FIBROMYALGIA PART OF THE CLIMACTERIC SYNDROME?

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Blümel JE, Palacios S, Legorreta D, Vallejo MS, Sarra S.

Fibromyalgia syndrome (FMS) is a disorder usually affecting middle aged women, who complain of diffuse musculoskeletal aches, pains or stiffness associated with tiredness, anxiety and poor sleep. Neurotransmission disorders linked both to pain perception as well as mood, sleep and cognition modulation are involved in FMS etiopathogenesys. Treatments that may be

effective to decrease pain and fatigue include tricyclic antidepressants, dual reuptake inhibitors of serotonin/noradrenalin and pregabalin. The climacteric syndrome is a set of symptoms caused by the decline of ovarian hormone levels, which alters brain neurotransmission and provokes musculoskeletal pains, mood disorders, poor sleep quality and hot flushes. The hormone therapy reverses those symptoms and its risks are marginal if women's own hormones are used through transdermal route. Some antidepressants may be useful for patients with climacteric symptoms. We have found it surprising the epidemiological, etiopathogenic, symptomatic and therapeutic similarity between FMS and climacteric that could lead us to hypothesize that FMS is a part of the climacteric syndrome. However, the existence of FMS non-climacteric patients points out that hormone deficit is not the only physiopathological mechanism involved in this syndrome's etiopathogenesys. Nevertheless, it is likely that hormone disorders are involved in the symptoms genesis of most middle aged women with FMS. Keeping this in mind, we see the point in considering the use of HT in climacteric patients with FMS. Studies assessing the FMS clinical response to HT in a prospective manner and with the current diagnose criteria are still required.