A large number of patients suffering from asthma or chronic obstructive pulmonary disease (COPD) can show overlapping features of both diseases. Several subjects affected by asthma-COPD overlap (ACO) may be at a severe stage, poorly responsive to triple therapy including inhaled corticosteroids, long-acting β2 agonists and muscarinic antagonists. This review tries to explore whether omalizumab can be used in poorly controlled severe ACO patients. According to the few studies available, omalizumab may improve asthma outcomes in ACO, although the magnitude of improvements may be lower in comparison to those obtained in subjects affected only by severe asthma. Omalizumab, by acting on IgE, might improve the eosinophilic pattern which is characteristic of the ACO asthma inflammation component. It can be hypothesized that a prevalence of Th1/Th17 airway inflammation pathways can modulate a lower response to anti-IgE while a Th2 pattern can lead to a higher effectiveness to omalizumab in ACO. High levels of IgE, FeNO and blood eosinophil count may be markers of a better response to omalizumab. In conclusion, on the basis of the few studies available, omalizumab could be effective in poorly-controlled severe ACO, although to a reduced extent in comparison to patients affected only by asthma.
EDITORIAL

IMPACT OF MOLD ON MAST CELL-CYTOKINE IMMUNE RESPONSE

S.K. KRITAS¹, C.E. GALLENGA², C. D’OVIDIO³, G. RONCONI⁴, A.L. CARAFFA⁵, E. TONIATO⁶, D. LAURITANO⁷ and P CONTI⁸

¹Department of Microbiology and Infectious Diseases, Aristotle University of Thessaloniki, Macedonia, Greece; ²Department of Biomedical Sciences and Specialist Surgery, Section of Ophthalmology, University of Ferrara, Italy; ³Section of Legal Medicine, Department of Medicine and Aging Sciences, “G. d’Annunzio” University of Chieti-Pescara, Italy; ⁴UOS Clinica dei Pazienti del Territorio, Policlinico Gemelli, Rome, Italy; ⁵Department of Pharmacology, University of Perugia, Perugia, Italy; ⁶Department of Medical, Oral and Biotechnological Sciences, University “G. d’Annunzio” of Chieti-Pescara, Chieti, Italy; ⁷University of Milano Bicocca, Milan, Italy; ⁸Immunology Division, Postgraduate Medical School, University of Chieti-Pescara, Chieti, Italy

Received May 23, 2018 - Accepted July 18, 2018

Molds include all species of microscopic fungi, the spores of which are small molecules, ubiquitous, mostly found in soil with higher rainfall and high humidity, in the atmosphere of urban and rural settings and in decaying vegetation. They originate from pathogenic fungi and have a crucial role in inflammatory response, causing a broad range of diseases. Immune suppressed subjects may develop mycoses caused by opportunistic common pathogenic fungi. Mast cells (MCs) are immune cells involved in the pathophysiology of infected skin, lung, and organs, where there is an increase of angiogenesis. Airways fungi infections can induce allergic lung disease mediated by MCs and other immune cells. In addition, fungal infection may cause and/or aggravate asthma inflammation. Spores are able to navigate in the airways of the lung and can be recognized trough toll-like receptor (TLR) signaling by the innate immune cells including MCs. Activated MCs release preformed mediators including histamine, proteases (tryptase, chimase), pro-inflammatory cytokines/chemokines and they also generate arachidonic acid products. MCs activated by fungi provoke an increases of PGD2 levels and lead to hypersensitivity diseases which present signs such as irritation of the respiratory tract and eyes, recurrent sinusitis, bronchitis, cough and neurological manifestations including fatigue, nausea, headaches and brain fog. Therefore, fungi activate the innate immune response through the TLRs, leading to the release of myeloid differentiation factor 88 (MyD88) which, with a series of cascade reactions, induces the stimulation of AP-1 and NF-kB with subsequent activation of inflammatory IL-1 family members. Here, we report that fungi can activate MCs to secrete pro-inflammatory cytokines which may be inhibited by IL-37, a new anti-inflammatory IL-1 family member.
A RAT OSTEOPOROSIS MODEL INDUCED BY OVARIECTOMY AND GLUCOCORTICOID

J.H. LEE\textsuperscript{1,2,3} and Y-Z. JIN\textsuperscript{1}

\textsuperscript{1}Department of Orthopedic Surgery, College of Medicine, Seoul National University, Seoul, Korea; \textsuperscript{2}Department of Orthopedic Surgery, SMG-SNU Boramae Medical Center, Seoul, Korea; \textsuperscript{3}Institute of Medical and Biological Engineering, Seoul National University Medical Research Center, Seoul, Korea

Received October 28, 2017 – Accepted May 17, 2018

Osteoporosis is characterized by reduced bone mineral density (BMD) and changes in bone morphometry, which increases the risk of fracture. However, the lack of proper models of significant osteoporosis limits our study of related medications and fracture mechanisms. The objective of this study was to determine whether a combination of ovariectomy (OVX) and glucocorticoid injection was appropriate for establishing an osteoporosis animal model. Female Sprague-Dawley rats were divided into sham, an OVX group, a glucocorticoid injection osteoporosis (GIO) group, and an OVX + GIO group. All animals were sacrificed in their 26\textsuperscript{th} week and their spines and bilateral femurs were harvested and analyzed. Their bone quality elements, including BMD, trabecular bone architecture, and cortical bone thickness were analyzed via micro-CT, and mechanical strength of the spines was measured with a Universal testing machine, TO-101G. Femur neck and total femur mean BMD (g/cm\textsuperscript{2}) in the OVX + GIO group (0.307, 0.439) was significantly lower than the sham group (0.518, 0.644) and the GIO group (0.485, 0.587). Femur neck cortical bone thickness (cm) in OVX + GIO group (0.369) were significantly less than those in the OVX group (0.421) or the GIO group (0.510). Furthermore, the OVX + GIO group had significantly lower mechanical strength than the other groups in the spine. In conclusion, OVX combined glucocorticoid injection could induce significant bone loss that had poorer bone quality and less mechanical strength than simple OVX or glucocorticoid injection had, without significantly increased mortality. Therefore, OVX + GIO might be an appropriate osteoporosis animal model.
The purpose of this study was to concomitantly determine oxidative DNA damage and bone resorption following a rapid body mass reduction in association with energy restriction and exercise training, considering 17β-estradiol level, in female collegiate judokas. Eighteen nationally ranked university female judokas were enrolled as participants in this study. All participants continuously managed to reduce their body mass 8 days just before a competition. To detect cumulative effects of oxidative DNA damage and bone resorption, urinary samples were collected in the morning on three different days (Day 1 = the beginning of body mass reduction; Day 4 = mid-term of body mass reduction; Day 7 = the day before the competition) for the later analysis of 8-hydroxy-2’- deoxyguanosine (8-OHdG) as well as cross-linked N-terminal telopeptides of Type I collagen (NTx). Urinary 8-OHdG and NTx levels were determined with high performance liquid chromatography and enzyme-linked immunosorbent assay, respectively. No significant alterations were observed in urinary 8-OHdG or NTx levels over a rapid body mass reduction period. The findings of the present study indicate that female judokas appear to have relatively less oxidative DNA damage determined by quantification of 8-OHdG and bone resorption over a rapid body mass reduction period, potentially due to the enhanced endogenous defense responses (training adaptation). These data can provide athletes and coaches with valuable information in considering an optimal body mass management program to avoid detrimental physiological and biological conditions.
GENDER AND AGE-RELATED VARIABILITY OF MACROPHAGE REPRESENTATION IN THE INTERNAL THORACIC ARTERY WALL: DOES IT MATTER?

B. PEREK1, K. KOWALSKA2, B. KEMPISTY2,3,4, M. NOWICKI1, M. DYSZKIEWICZ-KONWIŃSKA3, M. PUŚLECKI1,5, D. OSTALSKA-NOWICKA6, M. JEMIELITY1, M. JANKOWSKI1, M.J. NAWROCKI1 and A. MALIŃSKA2,7

1Department of Cardiac Surgery and Transplantology, Poznan University of Medical Sciences, Poznan, Poland; 2Department of Histology and Embryology, Poznan University of Medical Sciences, Poznan, Poland; 3Department of Anatomy, Poznan University of Medical Sciences, Poznan, Poland; 4Department of Obstetrics and Gynecology, University Hospital and Masaryk University, Brno, Czech Republic; 5Department of Medical Rescue, Poznan University of Medical Science, Poznan, Poland; 6Department of Pediatric Cardiology and Nephrology, Poznan University of Medical Science, Poznan, Poland; 7Department of Anatomy and Histology, Faculty of Medicine and Health Sciences, University of Zielona Gora, Poland

Received March 9, 2018 – Accepted June 12, 2018

Some recent reports suggested that elderly and female patients did not benefit from implantation of the second internal thoracic artery (ITA) during coronary artery bypass surgery (CABG). Macrophages, among other cells, were described to be involved in both atherosclerosis and aortocoronary grafts failure. The aim of the study was to examine the age and gender association with different distribution of CD68+ cells within the layers of ITA wall. This study involved 158 consecutive patients (95 male and 63 female), with the mean age of 64.5±9.5 years, who underwent elective CABG procedures. During surgery, the surplus distal segments of ITA were harvested for immunohistochemical analysis. The number and distribution of CD68+ cells was calculated and plotted against the age and gender of the study participants. CD68+ cells were present in all of the harvested ITA fragments (median 44), more in women (55) than in men (42) (p<0.001). However, this difference was of statistical significance exclusively in the tunica intima. Approximately 70% of macrophages were found in the tunica adventitia. The total number of CD68+ cells the in arterial wall as well as in the tunica intima and adventitia correlated positively with the age of patients (r=0.544, r=501 and r=0.462, respectively). The lack of significant advantages of the use of two thoracic arteries, in elderly patients and women, might have resulted from the larger population of CD68+ cells in their walls, especially the tunica intima. However, this result from immunohistochemical analysis needs validation in long-term clinical research on a larger cohort of patients.
Spinal cord ischemia-reperfusion injury (IRI) results in overproduction of reactive oxygen species leading to tissue oxidative stress which impacts the neuronal network in the spinal cord as well as glial cells. We investigated the expression of Nuclear factor erythroid 2-related factor 2 (Nrf2) in neurons and glial cells after occlusion of the abdominal aorta followed by IRI as well as the time-dependent expression of Nrf2 in the same cells. The experimental method of transient aortic occlusion was carried out on rats by cross-clamping of the abdominal aorta for 45 minutes. The animals used for this study were sacrificed 1 h, 6 h, and 48 h after reperfusion to determine time-related changes of Nrf2 expression, as well as changes of astrocyte activity in the spinal cord. Immunofluorescence results showed an increase in the staining intensity of Nrf2 expression in the neurons following ischemia with highest intensity 48 h post-reperfusion and an increase in a number of reactive astrocytes. Western blot analysis showed that Nrf2 protein expression increased in a cytoplasmic and nuclear fraction as early as 1 h after reperfusion and remained active 48 h after, resulting in increased expression of the main Nrf2 target gene HO-1. In conclusion, substances that enhance expression of Nrf2 may have the potential to prevent cellular damage to the spinal cord caused by IRI.
BIOLOGICAL CHARACTERISTICS OF OSTEOCLAST EXOSOMES AND THEIR ROLE IN THE OSTEOGENIC DIFFERENTIATION OF SOMATIC CELLS PRIOR TO OSTEOGENESIS

C. CHEN, RQ. ZHENG, XC. CAO and GC. ZHANG

Department of Orthopaedics, General Hospital of Jinan Military Command, Jinan, Shandong Province, China

Received April 24, 2018 – Accepted June 18, 2018

This study aimed to investigate the biological characteristics of osteoclast exocrine bodies and their role in the differentiation of somatic cells, so as to find out the key factors involved in osteoclast exosomal growth and osteogenesis. RANKL (Receptor Activator for Nuclear Factor-κ B Ligand) induced factor was used to induce the osteoclast differentiation of Raw 264.7 cells, and TRAP(Tartrate resistant acid phosphatase) staining was employed to identify induced cells. Ultra-filtration centrifugation was used to separate OC-exosomes from osteoclast supernatant, while Western blot was employed to detect the expression characteristics of exosomal proteins CD9 and CD63. PKH67 labeled exosomes were observed to target kusao cells, which were divided into 3 groups, i.e., the complete medium group (group A), the osteoblast induced group (group B), and the osteogenesis induced liquid + OC-exosomes group (group C). The medium was changed on the next day and after 14-day culture. Using Western blot, alizarin red staining and Von Kossa silver staining, the role of OC-exosomes in the differentiation of kusao cells was clarified. Results showed that TRAP staining showed osteoclasts as irregular and TRAP positive giant cells with a red multicore and a large volume. Microcapsule membrane structures with a uniform size were detected in osteoclast supernatant, and the expression of CD9 and CD63 proteins was confirmed by Western blot. In addition, the Western blot results showed that the expression of RUNX2 (Runt-related transcription factor 2) protein in group B was 1.254 times of that in group A and 2.636 times of that in group C. Furthermore, alizarin red staining showed that the ratios of calcium salt deposition area to the total area in group A, group B and group C were 0.208%, 3.469%, and 20.724%, respectively. Von Kossa silver staining showed that the ratios of calcium salt deposition area to the total area in group A, group B and group C were 0.064%, 2.636%, and 20.872%, respectively. To sum up, OC-exosomes can promote the osteogenic differentiation of osteoblast cells (kusao cells).
Differential Expression and Analysis of Target Regulation of microRNAs in Alcohol-Dependent Rats

F. Xin\(^1\), X.M. Ye\(^1\), H.B. Liu\(^2\), L.P. Liu\(^3\), L.J. Yan\(^4\) and J. Hu\(^1\)

\(^1\)The First Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang, China; \(^2\)College of Bioinformatics Science and Technology, Harbin Medical University, Harbin, Heilongjiang, China; \(^3\)Harbin First Specialist Hospital, Heilongjiang, China; \(^4\)The Fourth Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang, China

Received April 12, 2018 – Accepted June 8, 2018

This study analyzed the differential expression of miRNAs related to alcohol dependence in rats undergoing continued consumption and withdrawal. Furthermore, miRNAs were sought and evaluated for potential use as biomarkers for diagnosis. This study used Exiqon miRCURY\(^\text{TM}\) LNA miRNA microarray on alcohol-dependent and normal rats for the expression of microRNAs in perfluorinated compounds, and the stem-loop qPCR method to validate its expression in brain tissue. We forecast the relevant target genes of differentially expressed miRNA and drew the regulatory network. Comparison of the differential expression between brain tissue and plasma was carried out and the correlation and analyzed. 65 miRNA with differential expression with threshold of 1.5 were screened out; among them, most miRNA with differential expression in the dependent group had relatively high expression values. The target genes were found with great confidence: PIK3CA, MAPK, NTF, BDNF, NGFR, IGF-1, and the pair consisting of miRNA- mRNA. Among the three groups, the expression levels of miR-101b (F=8.12, P<0.05) showed significant difference; no significant difference was found in the expression levels of miRNA in plasma among the groups (F=1.23, P>0.05). No consistency was shown in the changing trend of miRNA in PFC and plasma (r= -.004, p>0.05). The genetic regulatory network of neurotrophic factors, its receptors and the protein kinases that influence metabolism may mediate the incidence of alcohol-dependence. There is a lack of conformity between the expression of miR-101b in the prefrontal cortex and the plasma.
THE EXPRESSION OF CIRCULATING TUMOR CELLS IN PERIPHERAL BLOOD OF PATIENTS WITH NON-SMALL CELL LUNG CANCER AND ITS DETECTION

X-M. BU¹, F-F. XU¹, J. MA² and B. JIANG³

¹Department of Pathology, Jining No.1 People’s Hospital, Jining City, Shandong, China; ²Department of Oncology, Jining No.1 People’s Hospital, Jining City, Shandong, China; ³Department of Thoracic Surgery, Affiliated Hospital of Jining Medical University, Jining City, Shandong, China

Received February 22, 2018 - Accepted June 26, 2018

This study aimed to investigate the expression of circulating tumor cells (CTCs) in peripheral blood and relevant detection methods as well as the clinical values of determination of CTCs for the diagnosis of non-small cell lung cancer (NSCLC). Peripheral blood specimens were acquired from the patients with NSCLC who came to the Thoracic Surgery Department of Jining No.1 People’s Hospital, Shandong, China for the first visit between January 2015 and November 2016. Whether there was metastasis of CTCs or not was determined by detecting the number of epithelial cell adhesion molecules (EpCAM) which had expression in the CTCs of the peripheral blood with fluorescence polymerase chain reaction. Moreover, the correlation between the expression level of EpCAM of patients with NSCLC during postoperative adjuvant treatment and the efficacy of adjuvant therapy was initially explored. The expression level of EpCAM of the NSCLC patients was remarkably different to that of the patients with benign lung diseases. The expression level of EpCAM of the patients with NSCLC was notably different with that of the healthy volunteers. The expression level of EpCAM of the patients with NSCLC was much higher than that of patients with benign lung diseases and the volunteers. Moreover, the expression level of NSCLC at stages I, II and IIIA had significant differences; the expression level of EpCAM tended to increase as the stage of NSCLC developed. The expression level of EpCAM in CTCs of peripheral blood can be regarded as a reference for the early diagnosis and detection of NSCLC before and after surgery.
ACY 1215, A HISTONE DEACETYLASE 6 INHIBITOR, INHIBITS CANCER CELL GROWTH IN MELANOMA

F. WANG1*, B. ZHONG2* and Z. ZHAO3

1 Plastic Surgery Department, Daqing Oilfield General Hospital, Daqing, P.R.China; 2 Ophthalmology Department, Daqing Oilfield General Hospital, Daqing, P.R.China; 3 The Eastern Division Plastic and Cosmetic Surgery Department, The First Hospital of Jilin University, Changchun, P.R.China

Received September 29, 2017 – Accepted April 27, 2018

*These Authors contributed equally to this work

Histone deacetylase 6 (HDAC6) plays critical roles in dozens of malignant cancers, including melanoma. Therefore, inhibition of HDAC6 can be a potential strategy of targeting melanoma. ACY 1215 (ricolinostat), a selective HDAC6 inhibitor, is currently being clinically trialed in multiple cancers but not in melanoma. In this study, we tested the pre-clinical efficacy of ACY 1215 in melanoma cell lines. First, we found higher HDAC6 expression in melanoma cell lines than in an epidermal melanocyte cell line. Then, we observed the dose- and time-dependent reduction of cell proliferation caused by ACY 1215 treatment. Proliferation inhibition by ACY 1215 was associated with accumulation of acetylated tubulin but did not affect histone H3K9 acetylation. In addition, ACY 1215 induced cell apoptosis and G0/G1 cell cycle arrest. Finally, we show that ACY 1215 reduced tumor burden and increased survival in an in vivo mouse cell line xenograft model. All of these pre-clinical data indicate that HDAC6 is a potential target in melanoma, and that targeting HDAC6 in melanoma using ACY 1215 may be translationally relevant.
LETTER TO THE EDITOR

STUDY OF SELECTED THERAPEUTIC POTENTIALS OF MOMORDICA CHARANTIA FRUIT

F. HUSSAIN, A. IRSHAD and M. SHAHID

Clinico-Medical Biochemistry Laboratory, Department of Biochemistry, Faculty of Sciences, University of Agriculture, Faisalabad, Pakistan

Received September 30, 2017 – Accepted April 27, 2018

*M. charantia* extract partitioned in different solvents was assessed for antioxidant (2, 2-diphenyl 1-picrylhydrazyl), total phenolic contents (TPC), total flavonoid contents (TFC), antiglycation, alpha amylase and acetylcholinesterase inhibitory activities along with cytotoxic, thrombolytic and antibiofilm potentials. Most effective antioxidant fraction was *n*-hexane with TPC and TFC, highest in *n*-butanol and ethanol fractions, respectively. Ethyl acetate fraction showed maximum glycation and alpha amylase inhibitions and optimum acetylcholinesterase inhibition was by ethanol fraction. Fractions exhibited significant hemolytic and thrombolytic efficacies and bacterial growth restraint. The present research reveals some medicinal potency of *M. charantia*. 
LETTER TO THE EDITOR

PHENOLICS, TOCOPHEROLS AND FATTY ACID PROFILING OF WILD AND COMMERCIAL MUSHROOMS FROM PAKISTAN

S. SHARIF¹, S. RASHID², A. ATTA³, A. IRSHAD², M. RIAZ⁴, M. SHAHID² and G. MUSTAFA⁵

¹College of Biosystem, Engineering and Food Science, Zhejiang University, China; ²Department of Biochemistry, University of Agriculture, Faisalabad, Pakistan; ³Department of Biochemistry, Bahauddin Zakariya University Multan, Pakistan; ⁴Department of Allied Health Sciences, Sargodha Medical College, University of Sargodha, Pakistan; ⁵Department of Biochemistry, Government College University, Faisalabad, Pakistan

Received March 12, 2018 – Accepted May 2, 2018

Mushrooms can be used as nutraceutical or functional foods to maintain and promote good health. In the present study, wild Ganoderma lucidum and four commercial mushrooms, Pleurotus ostreatus, Volvariella volvacea, Hericium erinaceus and Lentinus edodes, collected from Pakistan were screened for phenolics, tocopherols and fatty acid contents. High performance liquid chromatography analysis of phenolic acids showed that chlorogenic acid, ferulic acid, gallic acid, p-Coumaric and caffeic acids were observed in selected mushrooms. H. erinaceus contained high amounts of chlorogenic acid (11.49±0.1 µg/g of dry weight) and ferulic acid (7.84±0.7 µg/g of dry weight). γ-tocopherol and lutein were present in all studied mushrooms. Lutein contents were higher in H. erinaceus (2.42±0.087 µg/g of DW) followed by V. volvacea > P. ostreatus > L. edodes. γ-tocopherol was observed in the range of 74.25±3.01 to 29.65±1.2 µg/g of dry weight. GC/MS analysis of fatty acids showed that linoleic acid (18’:2n6c), oleic acid (18’:1n9c), palmitic acid (C16:0), stearic acid (C18:0), linolenic acid (18’:3n3) and nonadecanoic acid (C19-0), were the main fatty acids found in selected mushrooms. The unsaturated fatty acids were predominated over saturated fatty acids. It is concluded that selected mushrooms are good sources of antioxidant compounds and unsaturated fatty acids.
LETTER TO THE EDITOR

COMPARISON OF NURSING METHODS OF PEDIATRIC EPILEPSY

L.B. JIA¹, L. TANG² and Y. CAI³

¹Department of Neurology, Xuzhou Children’s Hospital, Xuzhou, Jiangsu, China; ²Intensive Care Unit, Xuzhou Children’s Hospital, Xuzhou, Jiangsu, China; ³Department of Nursing, Xuzhou Children’s Hospital, Xuzhou, Jiangsu, China

Received August 21, 2017 – Accepted April 24, 2018

We evaluated a modified clinical nursing procedure applied in pediatric epilepsy treatment. A total of 120 sick children were randomly selected and evenly divided into control and observation groups. The control group was treated with a conventional epilepsy nursing protocol, while the observation group was treated with a modified clinical nursing protocol including establishment of a nursing care quality control group, designing a standardized nursing workflow using unified tables, adjusting nursing intensity according to different types of epilepsy, and extension of nursing care post-hospitalization. The clinical effects of the two groups were compared. The cure rate of epilepsy in the observation group was significantly higher than that in the control group (P<0.05). The duration of treatment was shortened and the incidence of complications was reduced in the observation group compared to the control group with statistical significance (P<0.05). The satisfaction for nursing care and treatment compliance were significantly improved in the observation group compared with controls (P<0.05). In conclusion, a relevant clinical nursing method can significantly enhance pediatric epilepsy therapy through improvement of nursing care quality.
LETTER TO THE EDITOR

EFFECT OF RADIAL SHOCK WAVE THERAPY ON LONG BONE FRACTURE REPAIR

T. SCHNURRER-LUKE-VRBANIĆ, V. AVANCINI-DOBROVIĆ, I. SOSA, O. CVIJANOVIC and D. BOBINAC

1University Hospital Centre Rijeka, Department of Physical and Rehabilitation Medicine, Rijeka, Croatia; 2University of Rijeka, Medical Faculty, Department of Forensic Medicine and Criminalistics, Rijeka, Croatia; 3University of Rijeka, Medical Faculty, Department of Anatomy, Rijeka, Croatia

Received February 1, 2018 – Accepted May 9, 2018

Nowadays, various diseases of the locomotor system are treated by extracorporeal shock wave therapy (ESWT) for instance: acute fracture and pseudoarthrosis, nonunion, chronic tendinitis. Unfocused (radial) pressure wave therapy (RPWT) primarily affects superficial tissues, so justifiability of its medicinal employment is uncertain. We aimed to observe time sequence of the long bone fracture healing using RPWT. Forty-eight female Wistar rats were divided into an RPWT group (n=36) and a control group (n=12). The RPWT group had the largest cross-sectional area (CSA) of the bone trabeculae compared to controls. Post-hoc analyses revealed the largest cross-sectional area (CSA) of the bone trabeculae (1.7 mm²) and the smallest CSA of the cartilage (0.04 mm²) of the RPWT group on the 22nd day. Conclusively, long bone fracture repair is enhanced by RPWT, suggesting that it strongly stimulates the processes of callus ossification.
ASSOCIATION BETWEEN Ca/Mg/P STATUS AND SUPPURATIVE TONSILLITIS IN CHILDREN

S. MAO, F. LIU, X-P. WANG, L-X. WU and J-H. ZHANG

Department of Pediatrics, Shanghai Jiao Tong University Affiliated Sixth People’s Hospital, Shanghai, China

Received October 9, 2017 – Accepted May 2, 2018

Suppurative tonsillitis (ST) is a common respiratory disease in children. This study aims to investigate the association between calcium (Ca)/magnesium (Mg)/phosphorus (P) and the risk of onset of suppuration in tonsillitis in children. Seventy children with ST and 61 age- and sex-matched children with non-ST were enrolled in this study. The association between Ca/Mg/P and suppuration risk in tonsillitis was investigated. The relationship between Ca/Mg/P and the potential risk factors for ST were also studied. White blood cell (WBC), platelet (PLT), c-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels were significantly higher in the ST group than those in the non-ST group (p<0.05). Mg and P levels were significantly lower in the ST group than those in the non-ST group (p<0.05). There was no obvious difference in Ca level between the ST group and the non-ST group (p=0.762). A significantly negative association between P and PCT was noted (r=-0.236, p=0.035). The results indicated that Mg/P disorder may be associated with the susceptibility to suppuration in children with tonsillitis, inflammatory indexes may reflect this risk.
LETTER TO THE EDITOR

GASTROSCOPY-GUIDED PLACEMENT OF INTRANASAL JEJUNUM NUTRIENT CANAL AND ANALYSIS OF NUTRIENT ABSORPTION EFFICIENCY

LH. XIA¹, YX. SUN², HW. YAN³, Y. MENG⁴ and XX. MA⁵

¹Section of Gastroscopy, Central Hospital of Linyi City, Shandong Province, China; ²Division of Emergency, Center Hospital of Binzhou City, Shandong Province, China; ³Section of Thyroid and Breast Surgery, Center Hospital of Binzhou City, Shandong Province, China; ⁴Department of Medicine, Center Hospital of Binzhou City, Shandong Province, China; ⁵Section of Gastroscopy, Centre Hospital of Ji’nan City, Shandong Province, China

Received August 21, 2017 – Accepted May 17, 2018

This study investigated and analyzed using both a pair of clamping pliers to place intranasal-jejunum nutrient canal under the guidance of gastroscope and using a guide wire to place the canal under the guidance of gastroscope. Ninety critically ill patients were randomly divided into a control (n=45) and an observation (n=45) group. The observation group had the intranasal-jejunum nutrient canal placed under the guidance of gastroscope by using a pair of clamping pliers while patients in the control group had the same canal placed under the guidance of gastroscope but using the guide wire. An intergroup comparison was conducted on the success rate of intranasal-jejunum nutrient canal placement and the incidence of complications. The results showed that the comparison yielded no significant difference in the success rate between observation (95.56 %) and control (97.78 %) groups (P > 0.05). When compared with control group, the A/G ratio and BMI level in the observation group increased significantly (P < 0.05). The intergroup comparison also yielded no significant difference in the incidence of complications. It was concluded that the method of gastroscopy-guided placement of intranasal jejunum nutrient canal produced better clinical results. The operating steps were simple and it had very low incidence of complications, therefore this method can be widely promoted for clinical practices.
LETTER TO THE EDITOR

LIMB-SALVAGE TREATMENT OF MALIGNANT TUMORS OF THE LIMBS

G. LI¹, J. LI¹, CY. HU², L. TIAN¹, CA. LV³ and LJ. JIN²

¹Orthopedic Department, Affiliated Hong Qi Hospital of Mu Dan Jiang Medical University, Mudanjiang City, China; ²Anesthesiology Department, Affiliated Hong Qi Hospital of Mu Dan Jiang Medical University, Mudanjiang City, China; ³ICU Department, Affiliated HongQi Hospital of Mu Dan Jiang Medical University, Mudanjiang City, China

Received February 20, 2018 – Accepted April 16, 2018

The aim of this study was to explore the clinical efficacy of limb-salvage therapy for malignant bone tumors of the limbs using two surgical methods. This investigation presents a retrospective study of malignant bone tumors of the limbs in 42 patients. Participants were divided into two groups: group A of 25 patients who were treated with artificial prosthetic replacement, and group B of 17 patients treated with bone inactivation. By collection of clinical data, the survival rate, surgical complications, quality of life, pain relief and postoperative limb function following artificial prosthesis replacement and tumor inactivation were comprehensively evaluated in patients with malignant bone tumors of the limbs. Group A had significantly higher Karnofsky quality of life scores compared to group B after six months (P=0.027). The Enneking scores of limb functions in group A were significantly higher than those of group B (P=0.022). In group A the postoperative limb function score was good and excellent in 92% and in group B in 64.7%. There were significantly more postoperative complications in group B compared with group A (P=0.027), but no significant difference in the recurrence rate in the two group (P=0.976). The study results can provide reference for surgical treatment of the patients with malignant bone tumors.
LETTER TO THE EDITOR

EVALUATION OF FUNCTIONAL PROPERTIES OF ZEIN EXTRACTED FROM VARIOUS MAIZE VARIETIES

T. SIDDIQUE¹, A. ASGHAR¹, I. PASHA¹ and M. SHAHID²

¹National Institute of Food Science and Technology, University of Agriculture, Faisalabad, Pakistan; ²Department of Biochemistry, University of Agriculture, Faisalabad, Pakistan

Received February 8, 2018 – Accepted May 18, 2018

Zein is the major storage protein of maize and was identified initially on the basis of solubility in aqueous alcohol solution. It is comprised of 45-50% grain portion and has a wide range of application as a functional ingredient in the food industry. In the current study, five different maize varieties were analyzed and compared for the physicochemical, mineral and functional characteristics. Zein protein was extracted at different concentrations of ethanol and was further characterized for its antioxidant and functional properties. Significant variations in the characteristics were observed in different varieties related to their mineral and chemical composition. Likewise, antioxidant properties of zein extracted from Agaiti-2002 variety were 32.61% and minimum value (30%) was observed in the Pearl variety. Zein protein has the potential to be used as encapsulating material for controlled release of different bioactive compounds.
LETTER TO THE EDITOR
THE ROLE OF COLOR DOPPLER CARDIAC OUTPUT INDEX IN THE CLASSIFICATION OF HEART DISEASE

F. LI¹, J. XU² and W. LI¹

¹CT Department, Xinxiang Central Hospital, Xinxiang, Henan Province, China; ²Ultrasonic Department, Xinxiang Central Hospital, Xinxiang, Henan Province, China

Received June 24, 2017 – Accepted April 23, 2018

This study aims to investigate the relationship between the value of cardiac output index (COI) and pathological Gleason score of heart disease by color Doppler. The dynamic contrast-enhanced color Doppler data of 312 patients with heart disease were collected. Multi-parameter oxygen concentration images based on color Doppler were used to detect the COI of heart disease. Multi spin relaxation time editing sequence and weak diffusion model were used to estimate the oxygen saturation level and pO2. The biological behavior and prognosis of the patients were determined according to the haematoxylin and eosin staining of the cardiac pathological tissues and Gleason score, and the relationship between the COI and Gleason score level of heart disease was evaluated. Of the 312 patients, 28 cases had a Gleason score 10, 112 had score 9, 56 had score 8, and 116 had score ≤ 7. According to the degree of differentiation, they were divided into middle-high differentiation group (Gleason scores ≤ 7) and low differentiation group (Gleason scores 8-10). Multi-parameter oxygen concentration images based on color Doppler were successfully built, the COI was measured, and the Gleason scores and classification for the patients were made. There was a positive correlation between the value of COI and Gleason score ($r_s=0.349$, $P<0.05$). There was significant difference in the value of COI between the middle-high differentiation group and the low differentiation group ($P<0.05$). In conclusion, the value of COI is positively associated with Gleason score; COI values may be used to evaluate the classification of heart disease and the prognosis of patients.
LETTER TO THE EDITOR

A CASE OF METASTATIC CUTANEOUS MELANOMA TO THE LIVER

Y. CHEN¹, S. YU², H. LI³, J.H. YANG²* and C.Y. E²*

¹Department of Hepatobiliary and Pancreas Surgery, The Second Hospital of Jilin University, Changchun, China; ²Department of Neurology, China-Japan Union Hospital of Jilin University, Changchun, Jilin, P.R. China, Changchun, China; ³Department of Cerebral Surgery, Jilin Cancer Hospital, Changchun, Jilin, China

Received March 6, 2018 – Accepted April 19, 2018

*These Authors contributed equally to this study

Cutaneous melanoma (CM) with liver lesions is uncommon in Asia and found in only 14-20% of all cases. Here, we report the case of a 70-year-old male patient with cutaneous melanoma with metastases to the liver. Computerized tomography (CT) revealed multiple hepatic cystic lesions, and hepatic puncture biopsy was used for definitive diagnostics. The primary lesion was found on the patient’s scalp. We briefly reviewed the literature to summarize the recent progress in diagnosis and treatment of metastatic cutaneous melanoma. Examination of pathology data is still considered the gold standard of diagnosis, while imaging is used to detect metastases, assess the stage of disease and monitor the patients. Metastasectomy, whenever possible, may benefit most patients. Systemic therapies remain the mainstay of the treatment, with some important breakthroughs reported in the recent years. New treatments, such as adult-to-adult living donor liver transplantation, are still in the early stages.
LETTER TO THE EDITOR

POLYMORPHISM OF THE ANDROGEN RECEPTOR GENE CAG REPEAT SEQUENCE AND MALE CLIMACTERIC SYNDROME

ZL. HONG, Q. XU, YF. MAO, YZ. YE, JG. MAO, MF. WAN and MY. JIANG

Department of Urinary Surgery, The First People’s Hospital of Tonglu, Tonglu, Zhejiang Province, China

Received March 29, 2018 – Accepted May 3, 2018

The aim of this study was to analyze the association between polymorphism of the androgen receptor (AR) gene CAG repeat sequence and the climacteric syndrome in men. The study was performed in 103 males with climacteric syndrome and 111 males without the clinical syndrome of climacteric, aged between 40 and 70 years. DNA sequencing of the CAG repeat sequence in the N-terminal domain of the first exon of the AR gene was analyzed. The AR allele length ranged from 18-34 CAG repeats in males with climacteric syndrome. The average value of CAG repeat was 24.71 ± 2.58. However, the corresponding values ranged from 15-24 CAG repeat in control group and the average value of CAG repeat was 21.25±2.63. There was a significant difference of the number of CAG repeat between the two groups. The occurrence of male climacteric syndrome was related to the CAG repeat number of androgen receptor gene, and the male patients with more CAG repeats had higher risk of clinical syndrome of climacteric. The detection of CAG repeat number of AR gene might be helpful for the prediction of clinical syndrome of climacteric.
LETTER TO THE EDITOR

DRUG-LOADED NANOBUBBLES FOR ULTRASOUND-MEDIATED ANTITUMOR TREATMENT

CF. LIU¹, J. ZHOU², XR. CHEN² and J. YU³

¹Ultrasonic Department, The affiliated Hongqi Hospital of Mudanjiang Medical University, Mudanjiang, China; ²Ultrasonic Department, The Second affiliated Hospital of Mudanjiang Medical University, Mudanjiang, China; ³Outpatient Clinic, Affiliated Hongqi hospital of Mudanjiang Medical University, Mu Danjiang, China

Received February 25, 2018 – Accepted May 9, 2018

Polylactic acid (PLA) bubbles that can act both as ultrasound contrast agents and drug carriers have the disadvantage of low encapsulation efficiency and do not allow effective extravasation into the tumor tissue. In this regard, PLA and lecithin are considered drug carriers. The present study used a modified ultrasonic double emulsion-solvent evaporation technology in order to prepare paclitaxel-loaded PLA-lecithin nanobubbles. X-ray diffraction analysis (XRD) was used to investigate the state of the drug in the bubbles, whereas the tumor weight and the inhibition rate of tumor bearing mice in the ultrasound-mediated function were further examined. The results indicated that the nanobubbles prepared with a mass ratio of PLA and lecithin at 50:250 were characterized as inner hollow. The size of these particles was approximately 615 nm, and the drug loading and encapsulation reached 8.34±0.67% and 91.42±5.48%, respectively. Paclitaxel was distributed in the shell of the bubbles in an amorphous state, and the in vitro drug release was characterized by sustained release, zero release and ultrasound mediated drug release. The injection of H22 hematoma-bearing mice with ultrasound-mediated drug-loaded PLA-lecithin nano-scaled bubbles could reduce the toxicity and increase the antitumor efficacy compared with paclitaxel.
LETTER TO THE EDITOR

GENETIC DIVERSITY OF MYCOBACTERIUM TUBERCULOSIS IN NORTHERN GREECE

G. KAZDAGLIS1*, B. MOLINA-MOYA2*, K. MANIKA3, P. IOANNIDIS4, D. PAPAVENTSIS4, E. VOGIATZAKIS4, M. PANOPOLOU5, A. MELIDOU1, J. DOMÍNGUEZ2**, N. MALISIOVAS1** and G. GIOULA1***

1Microbiology Department, Medical School, Aristotle University of Thessaloniki, Greece; 2Microbiology Laboratory, University Hospital Germans Trias i Pujol, Institute of Investigation Germans Trias i Pujol, Badalona, Autonomous University of Barcelona, CIBERES, Spain; 3Pulmonary Department, Aristotle University of Thessaloniki, G. Papanikolaou Hospital, Greece; 4Microbiology Laboratory and National Reference Center for TB, Sotiria Chest Diseases Hospital, Athens, Greece; 5Microbiology Department, Medical School, Democritus University of Thrace, Greece

Received April 12, 2018 – Accepted May 15, 2018

*These authors contributed equally to this work ** Co-senior authors

The aim of the present study was to describe the genetic diversity of Mycobacterium tuberculosis (M. tuberculosis) strains circulating in the region of Northern Greece. A total of thirty-seven M. tuberculosis clinical isolates were analysed by the spoligotyping method. According to the results, six clusters comprising seventeen strains were detected, and the remaining twenty strains showed unique patterns. The M. tuberculosis families according to SITVITWEB were distributed as follows: Haarlem (H) (27.0%); T (24.3%); Beijing (13.5%); Latin-America and Mediterranean (LAM) (5.4%) and S (2.7%). The remaining isolates (27%) did not match any isolates within the database and they were characterized as orphans. Regarding GenoType MTBDRplus results, two strains (5.4%) were Multi-Drug-Resistant, four strains (10.8%), were isoniazid monoresistant, while the remaining thirty-one strains (83.8%) were susceptible. In conclusion, in the region of Macedonia-Thrace (Northern Greece), there was high phylogenetic diversity among M. tuberculosis isolates. Molecular tools used and data presented can have regional and national impact on tuberculosis control.
LETTER TO THE EDITOR

THE EFFECT OF TOPICAL MINOXIDIL TREATMENT ON FOLLICULAR SULFOTRANSFERASE ENZYMATIC ACTIVITY

A. GOREN1,2, J. MCCOY1, M. KOVACEVIC2, M. SITUM3, J. CHITALIA4, R. DHURAT4, T. NACCARATO1 and T. LOTTI2

1Applied Biology, Inc., Irvine, CA, USA; 2Department of Dermatology and Venereology, University of Rome “G. Marconi”, Rome, Italy; 3Department of Dermatology and Venereology, University Hospital Center “Sestre milosrdnice”, Zagreb, Croatia; 4Department of Dermatology, LTM Medical College & Hospital Sion, Mumbai, India

Received May 1, 2018 – Accepted June 11, 2018

Minoxidil is the only US FDA-approved topical drug for the treatment of female and male pattern hair loss. Previously, it was demonstrated that topical minoxidil is metabolized to its active metabolite, minoxidil sulfate, by sulfotransferase enzymes located in the outer root sheath of hair follicles. The expression of sulfotransferase in the scalp varies greatly between individuals, and this difference in expression explains the varied response to minoxidil treatment. Previously, we have demonstrated the clinical utility of detecting sulfotransferase in plucked hair follicles to predict minoxidil response in pattern hair loss patients. Typically, exogenous exposure to substrates affects the expression of the enzymatic system responsible for their metabolism. For example, Phase I metabolizing enzymes, such as the cytochrome P450 family of enzymes, are known to be up-regulated in the presence of xenobiotic substrates. However, it is not known if Phase II metabolizing enzymes, such as the sulfotransferase family of enzymes, are similarly affected by the presence of substrates. In this study, we recruited 120 subjects and analyzed their sulfotransferase enzymatic activity before and after treatment with topical minoxidil. Adjusting the results for biologic (within subject) variability, we discovered that the sulfotransferase enzymatic system expression is stable over the course of minoxidil treatment. To the best of our knowledge, this is the first study to demonstrate the stability of sulfotransferase, a Phase II metabolizing enzyme, over the course of minoxidil treatment.
LETTER TO THE EDITOR

DIAGNOSIS AND TREATMENT OF DISTAL LIMB MICROCIRCULATORY DISTURBANCE CAUSED BY STEROID INJECTION

Y. LIU, L. CHEN, Z-G. LIU and R-J. LI

Department of Hand Surgery, The First Hospital of Jilin University, Changchun, Jilin, China

Received March 8, 2018 – Accepted June 2018

Corticosteroid is commonly used for the clinical treatment of pain. It is safe, reliable and a simple procedure with other advantages. However, a possible potential catastrophic complication of corticosteroid injections in distal limbs (e.g., the wrist) is acute radial artery ischemia due to the injection into the radial artery. This may result from spasm attributed to the steroids. While the complication of corticosteroids in the wrist is rare, ischemia of the hand caused by corticosteroid injections in radial artery has been reported in several articles. We treated five patients with microcirculation disturbance of distal limb caused by corticosteroid treatment. Here, we report the two different treatment strategies adopted according to the severity of the disease which achieved good therapeutic effects.
LETTER TO THE EDITOR

COMBINED TREATMENT OF TRADITIONAL CHINESE MEDICINE AND WESTERN MEDICINE IN THE TREATMENT OF DIABETIC PERIPHERAL NEUROPATHY

JY. XU and HY. GAO

Department of Traditional Chinese Medicine, Binzhou City Center Hospital, Binzhou, China

Received November 21, 2017 – Accepted May 24, 2018

Diabetic peripheral neuropathy (DPN), a common complication of diabetes, has a high morbidity, and currently there is no effective therapy. To investigate the clinical effect of traditional Chinese medicine in combination with Western medicine, 88 patients with early DPN who were admitted to Binzhou City Center Hospital, Shandong, China, between November 2015 and November 2016, were selected as the research subjects and were randomly divided into a control group and an observation. Patients in the control group were treated by conventional Western medicine, while patients in the observation group were treated by traditional Chinese medicine in addition to conventional Western medicine. The clinical effect was compared between the two groups. The results demonstrated that the overall effective rate of the observation group was much higher than that of the control group, and the difference was statistically significant (P<0.05). The vibration perception threshold (VPT) of nervus peroneus communis, nervus suralis and posterior tibial nerve of the two groups significantly declined after treatment (P<0.05), however, the decrease in the observation group was more obvious (P<0.05). The improvement of glycosylated hemoglobin (HbAlc) and blood glucose of the observation group was superior to that of the control group, and the difference had statistical significance (P<0.05). In conclusion, traditional Chinese medicine in combination with Western medicine has a remarkable effect in the treatment of DPN and can effectively relieve vital signs and clinical symptoms of patients and significantly improve nerve conduction velocity. The therapy is worth clinical application and promotion.
LETTER TO THE EDITOR

EFFECTS OF ASTRAGALUS GLYCOPROTEIN ON Th17/TREG CELLS IN MICE WITH COLLAGEN-INDUCED ARTHRITIS

ZH. WANG¹*, C. QIN¹*, T. RAN¹*, DQ. YANG² and JH. GUO³

¹Department of Orthopedics and Traumatology, Traditional Chinese Medicine Hospital, Dianjiang, Chongqing, China; ²Department of Cardiovascular, Traditional Chinese Medicine Hospital, Dianjiang, Chongqing, China; ³Department of Traumatology Center, Traditional Chinese Medicine Orthopaedic Hospital, Chongqing, China

Received April 11, 2018 – Accepted May 21, 2018

* These authors contribute equally to this work

In this study of Th17/Treg cells, the therapeutic effect of Astragalus glycoprotein on collagen-induced arthritis in mice (CIA) was explored, and a basis for the clinical treatment of rheumatoid arthritis is provided. Sixty mice were selected for the establishment of a CIA mouse model, and were then randomly divided into a CIA model group, a hydrocortisone control group, a low, medium, and high dose group of Astragalus glycoprotein, respectively. The same number of control groups with same number of mice was established and after basic immunization, intraperitoneal injections were given once daily for two weeks in the treatment. At the end of the treatment, the mice in each group were selected and the proportion of Th17/Treg cells was detected by flow cytometry. The expression and positive expression of RORγt, Foxp3, P-STAT3 and P-STAT5 protein were detected by Western blot and immunohistochemistry. Astragalus glycoprotein was shown to potentially improve the diet and mental state, reduce the arthritis index score and improve the pathological state of synovial membranes in the mice. Moreover, flow cytometry results showed that, compared with the CIA model group, the proportion of Th17 cells in the four other groups of mice decreased, while the proportion of Treg cells increased. This difference was statistically significant (P<0.05). From the experiment, the following conclusions were drawn: Astragalus glycoprotein can reduce Th17 cells and their transcription factors in the peripheral blood of CIA mice, up-regulate Treg cells and their transcription factors, and correct the balance of Th17/Treg cells so as to achieve an effective of treatment for CIA mice.
LETTER TO THE EDITOR

QUANTITATIVE DETERMINATION OF ENDOGENOUS CARDIOLIPIN IN RAT CEREBRAL TISSUES BY HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY USING STANDARD ADDITION METHOD

T. WU¹, Y. WANG¹, S. YIN², YS. CONG¹ and SH. QI¹

¹Department of Anesthesiology, The Fourth Affiliated Hospital, Harbin Medical University, Harbin, PR China; ²Department of Pharmacy, The Fourth Affiliated Hospital, Harbin Medical University, Harbin, PR China

Received April 12, 2018 – Accepted May 30, 2018

Cardiolipin is an important cellular component, and its normal level is a key prerequisite for maintaining the structure and function of mitochondria. To accurately quantify endogenous cardiolipin content in mitochondria, a standard addition method (SAM) was developed to establish a high-performance liquid chromatographic (HPLC) technique that is both reliable and accurate. Increasing amounts of cardiolipin standards were added to a constant amount of isolated mitochondria prior to the extraction procedure, and the two were extracted together. By limiting the interference effects that occur to within an acceptable range in an analytical system examined, this procedure ensures an ideal match of the sample composition in the standards, even if the composition is extremely complex or completely unknown. Then, the desired results can be obtained by extrapolation. As such, the authentic content of the endogenous cardiolipin can be obtained with greater accuracy than with classical detection methods, e.g. external standard calibration (ESC) and internal standard calibration (ISC). This method provides an excellent means of quantifying endogenous substances in living cells. The authors expect this method to be useful for researchers working on mitochondria-related mechanisms, cell survival-related mechanisms and similar topics.
LETTER TO THE EDITOR

GASTRIC REFLUX: THE THERAPEUTICAL ROLE OF MARIAL®

S.E. ARAGONA¹, G. MEREGHETTI¹ and G. CIPRANDI²

¹Center of Regenerative Medicine, Humanitas Mater Domini, Castellanza (VA), Italy; ²Ospedale Policlinico San Martino, Genoa, Italy

Received April 6, 2018 – Accepted April 19, 2018

The worldwide relevance of gastroesophageal reflux disease (GERD) has had a considerable increase in recent years. The guidelines for the diagnosis and treatment of GERD are well consolidated and continuously updated. Recently, the extra-esophageal manifestations of reflux have been considered from a multidisciplinary point of view, so the symptoms of the laryngo-pharyngeal reflux (LPR) have been precisely defined. At present, a new Medical Compound (Marial®) has the indication for the treatment of both GERD and LPR. Clinical experience has initially confirmed its effectiveness in both disorders.
EMERGING FROM GASTROESOPHAGEAL REFLUX (EMERGE): AN ITALIAN SURVEY - I THE VIEWPOINT OF THE GASTROENTEROLOGIST

M. BIANCHETTI¹, S. PERALTA², R. NICITA³, S.E. ARAGONA⁴, G. CIPRANDI⁴

and the EMERGE STUDY GROUP*

¹Gastroenterologia - Humanitas Mater Domini, Castellanza (VA), Italy; ²Endoscopia Digestiva – Policlinico P. Giaccone, Università di Palermo, Palermo, Italy; ³Gastroenterologia - ASP 5, Reggio Calabria, Italy; ⁴Center of Regenerative Medicine - Humanitas Mater Domini, Castellanza (VA), Italy; ⁵Ospedale Policlinico San Martino, Genoa, Italy


Received April 6, 2018 - Accepted April 23, 2018

Gastroesophageal reflux disease (GERD) is defined as a “disease that develops when the reflux of stomach contents induces troublesome symptoms and/or complications”. From a therapeutic point of view, many options have been proposed, including proton pump inhibitors (PPI), antihistamines (H₂-receptor antagonists), antacid chemical compounds, antireflux barrier (using alginates), prokinetics, inhibitors of gastric sphincters, protection of mucosal tissue, neuromodulators, nociceptor antagonists, lifestyle modification, and surgery. A new medical compound has been recently launched in Italy: Marial® (manufactured by Aurora, Milan, Italy) containing magnesium alginate and E-Gastryal®. The aim of this survey was to analyse the patients’ characteristics and the prescriptive approach considering both the past or current treatments and clinical features during a visit in 56 gastroenterological centers, distributed in the whole of Italy. One thousand eight hundred forty-nine patients (46.5% males, and 53.5% females, mean age 48.59 years) were visited. Patients with positive reflux symptoms index (RSI) had higher GIS scores than RSI- subjects. PPIs (both as monotherapy or plus add-on) were the most common medication prescribed before the visit. There was a significant change of prescription to Marial® at the visit. More precisely, Marial® was preferentially prescribed to about a quarter of the patients, particularly to those with lower GIS score, whereas PPI plus add-on option was preferred for patients with higher GIS score. In conclusion, the current experience demonstrated that GERD may be managed considering a patient-centred work-up by using the GIS questionnaire. GIS score may be able to define the medication choice that includes also the new medical compound Marial®.

Key words: gastroesophageal reflux, gastroenterologist, diagnosis, treatment
LETTER TO THE EDITOR

EMERGING FROM GASTROESOPHAGEAL REFLUX (EMERGE): AN ITALIAN SURVEY - II THE VIEWPOINT OF THE PATIENT

M. BIANCHETTI¹, S. PERALTA², R. NICITA³, S.E. ARAGONA⁴, G. CIPRANDI⁴

and the EMERGE STUDY GROUP*

¹Gastroenterologia, Humanitas Mater Domini, Castellanza (VA), Italy; ²Endoscopia Digestiva, Policlinico P. Giaccone, Università di Palermo, Palermo, Italy; ³Gastroenterologia, ASP 5, Reggio Calabria, Italy; ⁴Center of Regenerative Medicine, Humanitas Mater Domini, Castellanza (VA), Italy; ⁵Ospedale Policlinico San Martino, Genoa, Italy


Received April 6, 2018 – Accepted April 23, 2018

Gastroesophageal reflux disease (GERD) is a very common disease, as about a quarter of the Western population has GERD symptoms at least weekly and GERD is the most frequent reason for outpatient gastroenterology consultation. GERD treatment is based on proton pump inhibitor (PPI) use, but PPI may be ineffective in some patients and potentially unsafe if administered for very long time. A new medical compound (Marial®) has been introduced on the Italian market. This product contains magnesium alginate and a phytopolymer: it may be able to repair ulcer/erosion, protect mucosal tissue, and contrast acid contents. The current survey was conducted on a large group of GERD patients visited at 56 Italian gastroenterological offices. Patients were treated with PPI alone, PPI plus add-on, or Marial® for 4 weeks: the choice was decided by each gastroenterologist on the basis of the best practice criterion. A reflux symptoms index (RSI) questionnaire was used to weekly assess the clinical features. Marial® and PPI plus add-on significantly reduced RSI scores, from the second week. Noteworthy, Marial® was more effective than PPI plus add-on. In conclusion, the current survey demonstrated that patients with GERD perceived a significant improvement of GERD symptoms measured by the RSI questionnaire. Marial® was as effective as PPI plus add-on.

Key words: gastroesophageal reflux disease, patients, RSI, PPI, Marial®
LETTER TO THE EDITOR

CORRELATION BETWEEN THE REFLUX FINDING SCORE AND THE GERD IMPACT SCALE IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE

M. BIANCHETTI1, S. PERALTA2, R. NICITA3, S.E. ARAGONA4, G. CIPRANDI4
and the EMERGE STUDY GROUP*

1Gastroenterologia - Humanitas Mater Domini, Castellanza (VA), Italy; 2Endoscopia Digestiva - Policlinico P. Giaccone, Università di Palermo, Palermo, Italy; 3Gastroenterologia - ASP 5, Reggio Calabria, Italy; 4Center of Regenerative Medicine - Humanitas Mater Domini, Castellanza (VA), Italy; 5Ospedale Policlinico San Martino, Genoa, Italy


Received April 6, 2018 - Accepted April 23, 2018

Gastroesophageal reflux disease (GERD) is a very common disorder. As there is no gold standard diagnostic tool, patient-based strategy is adopted in clinical practice. In this regard, there are questionnaires able to easily and rapidly assess symptom severity directly by the patient. The GERD Impact Scale (GIS) and the Reflux Symptom Index (RSI) have been validated as diagnostic tools in routine clinical care. The present study aimed to correlate RIS values with GIS scores in a large cohort of GERD patients visited at gastroenterological clinics. Globally, 785 subjects (51.2% males, 48.8% females, mean age: 49.59 years) were visited in 56 Italian gastroenterological offices. The current study demonstrates that a GIS value >19 may be a reliable cut-off to define the positivity of the test, and GIS and RSI were significantly correlated. Therefore, both tests may be recommended for GERD patients in clinical practice.
LETTER TO THE EDITOR

FROM NEW SCIENTIFIC KNOWLEDGE ON ROSACEA TO ITS POSSIBLE MEDICO-LEGAL CONSEQUENCES

P. VELLANTE¹, M. AURIEMMA², P. AMERIO², A. CARNEVALE¹ and C. D’OVIDIO¹

¹Section of Legal Medicine, Department of Medicine and Aging Sciences, “G. d’Annunzio” University of Chieti–Pescara, Italy; ²Department of Dermatology, and Centre for Aging Studies (CeSI), University of Chieti–Pescara, Chieti, Italy

Received March 19, 2018 – Accepted May 10, 2018

New scientific knowledge of rosacea hides possible medico-legal consequences. Indeed, the solid molecular basis surrounding rosacea exacerbation and progression has been shown among genetically prone people who are exposed to trigger factors, such as moderately hot temperatures associated with employment. If this is ignored in the phase of prevention, then progression of rosacea might lead to medico-legal consequences.
LETTER TO THE EDITOR

AN INNOVATIVE PICK-UP IMPRESSION TECHNIQUE

G. DE MARCO*, A. LANZA* and F. DI FRANCESCO

Multidisciplinary Department of Medical, Surgical and Dental Sciences, Campania University
 Luigi Vanvitelli, Naples, Italy

Received February 27, 2018 – Accepted May 8, 2018

* These Authors contributed equally to this work

Precision of impression is one of the keys for the success of implant-prosthetic rehabilitation. The choice of correct techniques, performance materials, and operator skills, can improve the accuracy of impression. The proposed technique describes a modified pick-up impression technique, both for single and multiple implants, aiming to combine the advantages of direct technique (open-tray or pick-up impression) with those of indirect technique (closed-tray or transfer type impression technique) in order to improve the accuracy of implant impression.
LETTER TO THE EDITOR

PLASMA FATTY ACID PROFILE AS BIOMARKER OF CORONARY ARTERY DISEASE: A PILOT STUDY USING FOURTH GENERATION ARTIFICIAL NEURAL NETWORKS

E. DOZIO, E. VIANELLO, E. GROSSI, L. MENICANTI, G. SCHMITZ and M.M. CORSI ROMANELLI

1Department of Biomedical Sciences for Health, Università degli Studi di Milano, Milan, Italy; 2Villa Santa Maria Institute, Tavernerio, Como, Italy; 3Department of Cardiac Surgery, I.R.C.C.S. Policlinico San Donato, San Donato Milanese, Milan, Italy; 4Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Regensburg, Germany; 5Service of Laboratory Medicine 1-Clinical Pathology, I.R.C.C.S. Policlinico San Donato, San Donato Milanese, Milan, Italy

Received March 8, 2018 – Accepted April 27, 2018

*These authors contributed equally to this work

Many studies, focused on identifying new biomarkers for coronary artery disease (CAD) risk computation and monitoring, suggested a potential diagnostic role for fatty acids (FA). In the present study, we explored the potential diagnostic role of FA by using a data mining approach based on fourth generation artificial neural networks (ANN). Forty-one male subjects were enrolled. According to coronary angiography, 31 displayed CAD and 10 did not (non-CAD, control group). FA analysis was performed on plasma samples using a gas chromatography-mass spectrometry system and analyses were performed by an ANN method. The variables most closely related to CAD were low levels of alpha-linolenic acid, eicosapentaenoic acid, eicosatetraenoic and docosahexaenoic acids. High levels of 1,1-dimethoxyhexadecane, total dimethyl acetals and docosatetraenoic acid were related to non-CAD condition. This subset of variables, which were most closely correlated to the target diagnosis, achieved a consistent predictive rate. The average accuracy obtained was 76.5%, with 93% of sensitivity and 60% of specificity. The area under the ROC curve was equal to 0.79. In conclusion, our study highlighted the association between different plasma FA species, CAD and non-CAD conditions. The specific subset of variables could be of interest as a new diagnostic tool for CAD management.
LETTER TO THE EDITOR

MINIMALLY-INVASIVE OSTEOTOME SINUS FLOOR ELEVATION COMBINED WITH SHORT IMPLANTS AND PLATELET-RICH PLASMA FOR EDENTULOUS ATROPHIC POSTERIOR MAXILLA: A FIVE-YEAR FOLLOW-UP PROSPECTIVE STUDY

S. TASCHIERI1,2, L. KARANXHA1,2, L. FRANCETTI1,2, R. WEINSTEIN3, A.B. GIANNÌ1,4 and M. DEL FABBRO1,2

1Department of Biomedical, Surgical and Dental Sciences, Università degli Studi di Milano, Milan, Italy; 2Dental Clinic, IRCCS Galeazzi Orthopaedic Institute, Milan, Italy; 3Scientific Director D&S ICH Humanitas Dental Center, Rozzano, Milan, Italy; 4Division of Maxillofacial Surgery, Fondazione Ca’ Granda IRCCS Ospedale Maggiore Policlinico, Milan, Italy

Received October 24, 2017 – Accepted November 23, 2017

The aim of this study was to investigate the success of the combination of short implants, osteotome sinus floor elevation technique (OSFE) and pure platelet rich plasma (P-PRP), for the rehabilitation of atrophic posterior maxilla. Fifty-one patients were included in this study, receiving a total of 88 short implants in three different lengths (6.5 mm, 7.5 mm, 8.5 mm), depending on the residual bone height level. A total of 39 standard implants were also inserted when judged necessary, and splinted with one or more short implants in order to support a fixed prosthesis. Data were recorded in a one-year and five-year follow-ups. No statistically significant difference was found between short implants with different length, nor between short and standard length implants in terms of both bone level change and bone height. Based on the present results, the use of short implants combined with OSFE technique for the rehabilitation of atrophic posterior maxilla can be recommended.
LETTER TO THE EDITOR

PROANTHOCYANIDIN MAY IMPROVE THE SHEAR BOND STRENGTH AT THE COMPOSITES/DENTINE INTERFACE

G. AUTIERI¹, F. MUSSANO¹, M. PETRUZZI², M. CAROSSA¹, T. GENOVA¹, M. CORSALINI² and S. CAROSSA¹

¹Department of Surgical Sciences, Dental School, Università degli Studi di Torino, Torino, Italy; ²Interdisciplinary Department of Medicine, Dental School, Università degli Studi di Bari, Bari, Italy

Received February 25, 2018 – Accepted May 3, 2018

This study aimed at assessing whether proanthocyanidin, a collagen cross-linker, affects the adhesion strength of resin composites on the dentine surface. Freshly extracted, caries-free, human molars (N=55) were embedded in transparent resin and bisected. The halves were then assigned to either a treated or a non-treated group, where the treatment consisted of a 10 min incubation in a 6.5% proanthocyanidin solution in PBS. A resin composite cylinder was polymerized perpendicularly to the dentinal surfaces and shear tests were made, using an Instron-like machine. The fracture surfaces were characterized by optical (Picro-Sirius Red stain) and electron microscopy (FESEM EDX analysis). Mean bond strength values were 10.73 MPa (SD 3.70) for the treated group and 8.69 MPa (SD 3.20) for the non-treated group (p<0.05 Student’s t-test). No constant fracture patterns could be found within the two groups. Proanthocyanidin treatment may improve the adhesion properties of the dentine-bonding interface.
LETTER TO THE EDITOR

DIGITAL FLOW IN MEDICINE AND DENTISTRY: WHAT’S NEW?

L. PACIFICI and A. PACIFICI

Department of Oral and Maxillofacial Sciences, Sapienza University of Rome Italy

Received June 1, 2018 – Accepted June 8, 2018

Both Authors contributed equally to this work

The increasing requirements of standardization in medical applications have led physicians towards a deep revision of their protocols. The phenomenon of ‘digital health’ has revolutionized the way a patient accesses medical information, but it has also improved the way the doctor handles the surgical and clinical phases. In digital dentistry, the working steps are mainly reported as digital image acquisition, preparation and/or processing of data, device production and clinical application on patients; the new technologies have brought significant benefits to both the dentist and the patient. Digital processing of anatomical data uses virtual models, which represent a precise representation of the patient’s anatomy. Recent advances in digital image acquisition technologies and the enormous complexity of modern software have made intraoral scans possible to realize digital dental arch models, however, the digital model is able to report substantial information to the clinician. Therefore, both complex surgeries and less invasive local therapies can be easily planned, with an accurate analysis of biological regulators improving the regenerative procedures, to achieve the best results in a shorter treatment.
LETTER TO THE EDITOR

IMMUNOHISTOCHEMICAL STUDY OF OSTEOPONTIN IN ORAL SQUAMOUS CELL CARCINOMA ALLIED TO FRACTAL DIMENSION

G. D’ADDAZIO1, L. ARTESE1, T. TRAINI1, C. RUBINI2, S. CAPUTI1 and B. SINJARI1

1Department of Medical, Oral and Biotechnological Sciences, University “G. d’Annunzio” Chieti-Pescara, Chieti, Italy; 2Department of Pathology, Polytechnic University of the Marche, Ancona, Italy

Received January 9, 2018 – Accepted June 6, 2018

The aim of the study was to consider a possible correlation between the intensity of expression of osteopontin and grading established by the pathologist. Furthermore, a correlation was investigated between the increase of fractal dimension and osteopontin in order to use this marker as an early and reliable diagnostic tool for the degree of cell transformation in oral squamous carcinoma. Ten histologically healthy oral samples and sixty-four primary oral squamous cell carcinomas specimens were analysed by a single pathologist. Immunohistochemical analysis and Fulgen stain were performed in order to evaluate intensity of expression of osteopontin and fractal dimension. Data obtained were presented as mean and standard deviation and processed for the statistical analysis. Osteopontin expression revealed a statistical significance between groups (P < 0.001). Fractal dimension in oral squamous cell carcinoma groups vs controls revealed statistically significant differences (P < 0.001). The fractal dimension value and the osteopontin expression were compared, using two-dimensional scatter. The correlation was relevant in the G3 group. The results demonstrated a correlation between the growths of osteopontin expression and nuclear abnormality measured by fractal dimension. These results support the hypothesis that the level of osteopontin expression might be used as a marker for the evaluation of oral squamous cell carcinoma differentiation. Osteopontin and fractal dimension could support the histological grading to increase the predictability of the diagnosis, choices of treatment procedure and long-term prognosis.
The altered expression levels of S100 proteins can lead to four different categories of diseases: diseases of the heart and of the central nervous system, inflammatory disorders and cancer. Various studies have shown the lack of harmonization of the results obtained with different methods, mainly due to different performances and measurements of S100B. The purpose of this work was to compare quantitatively the fully automated Elecsys® immunoassay with the reference immunoenzymatic method CanAg® EIA for serum S100B protein. In the study serum samples were analyzed of 161 patients: 85 females (aged 22-83 years) and 76 males (aged 16-90 years), affected by oncological and non-oncological pathologies. Passing–Bablok regression was used to analyze the comparison between the assays; it showed a strong interassay correlation: $r = 0.9350$ (95% CI = 0.9122 – 0.9520), with an intercept of 0.02063 (95% CI = -0.02850 – 0.01400) and a slope of 1.1125 (95% CI = 1.0200 – 1.2417). Elecsys® S100 assay should be preferred to CanAg® S100 for better standardization, good reliability and precision but also with the aim to reduce costs and obtain results in a shorter time.
LETTER TO THE EDITOR

THE USE OF CASEIN IN SPORT MOUTHGUARDS: MICROBIOLOGICAL AND ECOLOGICAL VARIATIONS IN ORAL CAVITY

D. TRIPODI, D. MARTINELLI, C. CIARAVINO, D. FULCO, M. TIERI and S. D’ERCOLE

Department of Medical, Oral and Biotechnological Sciences, University “G. D’Annunzio” of Chieti-Pescara, Chieti, Italy

Received January 25, 2018 – Accepted June 8, 2018

Sport mouthguards have the potential to become a microbial reservoir, produce oral and systemic diseases and cause negative changes in the oral cavity. The aim of this study was to monitor oral environmental changes caused by casein and sport-mouthguard in vivo, through clinical, salivary and bacterial markers of young athletes. Forty-eight active young athletes in different disciplines were selected and analysed at different times: baseline (T0); after three months of casein application on the mouthguard (T1); and after six months of application (T2). The product used was GC Tooth Mousse®. At T0, clinical monitoring was performed and the following parameters were recorded: Decay-Missing-Filled Teeth (DMFT) index, Plaque index (PL+) and Gingival Bleeding (BOP+). Saliva-Check Buffer GC® and Saliva-CheckMutans GC® salivary tests were then performed. At T0 the athletes demonstrated DMFT 0.03±0.01. PL value was positive in 100% of subjects at T0, T1, and T2. The BI value was always negative. At the three time-points, a significant change in baseline hydration values was observed; baseline viscosity was normal in 50% of cases while it increased in the remaining 50% at T0; it was normal and constant at T1 and T2. The value of the baseline pH underwent an not statistically significant increase at T1 (7.6±0.08) while remaining constant at T2. The amount of saliva produced after 5-min stimulation ranged significantly and gradually from T0 to T1 and T2, with a statistically significant difference. Plaque indicator tests highlighted that at T0 a plaque with a pH of 6.0±0.5 prevailed; at T1 it was 6.25±0.75 while at T2, pH was equal to 6. Tests for the detection of S. mutans resulted constant in all subjects at the various observation times, resulting in 67% of patients in whom S. mutans was present. The application of casein, within custom-made ethylene-vinyl acetate (EVA) mouthguards, positively influences salivary flow, the increase of pH values, the amount of stimulated saliva and the buffering capacity of the athlete, improving their state of oral health, which is negatively affected by the use of common mouthguards.
LETTER TO THE EDITOR

THE RELEVANCE OF THE MOMETASONE FUROATE NASAL SPRAY IN CLINICAL PRACTICE

G. CIPRANDI and A. VARRICCHIO

Associazione Italiana Vie Aeree Superiori, Frattamaggiore, Naples, Italy

Received March 9, 2018 – Accepted June 19, 2018

Allergic rhinitis (AR) is characterized by mucosal inflammation, therefore anti-inflammatory drugs are indicated for its treatment, mainly concerning intranasal administration. Mometasone furoate nasal spray (MFNS) has been on the market under the brand Nasonex® for 20 years and has high effectiveness and an excellent safety profile. From a clinical point of view, an ideal topical medication should respect a series of requirements, including handy device, good sensory characteristics, aptitude to the reach posterior nasal cavity, long residence time, and optimal pharmacokinetic and pharmacodynamic activities. MFNS fully satisfies these claims, as underlined by 20 years of worldwide prescriptions.