EDITORIAL

mTORC2-Akt SIGNALING AXIS IS IMPLICATED IN MYOCARDIAL COMPENSATION AND FIBROSIS

M. DANY¹, H.H. RIMMANI¹, S.A. MATAR¹ and I. HAJJ HUSSEIN²

¹College of Medicine, Medical University of South Carolina, Charleston, USA; ²School of Medicine, Oakland University William Beaumont, Rochester, USA

Received October 4, 2015 – Accepted October 27, 2015

mTOR signaling has long been implicated in the mechanisms of cardiomyocyte survival in response to volume or pressure overload. Several studies have focused on the significance of mTORC1 in cardiomyocyte survival, questioning the role of mTORC2. mTORC2–Akt signaling is an emerging axis implicated in cardiomyocyte compensation and thus heart failure. Upon being subjected to chronic stress, cardiomyocytes activate mTORC2–Akt signaling pathway to promote survival by activating the ubiquitin proteasome system, inducing the degradation of pro-apoptotic proteins, and altering the actin cytoskeleton. Given the importance of mTORC2 in cardiomyocyte survival, studies suggest that loss of mTORC2 signaling would result in loss of cardiomyocytes, fibrosis, and heart failure. This review serves to elaborate on how mTORC2-Akt signaling plays a role in cardiomyocyte growth and survival under stress and how the loss of the axis would result in fibrosis and heart failure.
Obesity incidence has reached pandemic levels, and is accompanied by high incidence and poor prognosis of various types of cancers including gastrointestinal ones. Underlying mechanisms include elevated levels of insulin, IGF-I, and altered adipokine concentration, mainly towards leptin and adiponectin levels. However, it is not yet thoroughly understood. It is now widely known that obesity is associated with chronic low-grade inflammation, characteristic of altered immune cell infiltration in adipose tissue, and changed inflammatory cytokines and chemokines: tumor necrosis factor alpha (TNF-α), IL-6, and the chemoattractant monocyte chemoattractant protein 1 (MCP-1) and others, all together eventually promoting cancer pathogenesis. Moreover, accumulating reports have shown that excess adipose tissue in obese individuals resulted in elevated levels of systematic oxidative stress, another way of promoting cancer development and progression. In general, altered immunological milieu and oxidative stress in obesity are important determinants for tumorigenesis.

Key words: obesity, gastrointestinal cancer, inflammation, oxidative stress
EDITORIAL

CLINICAL APPLICATION OF SHOCK WAVE THERAPY IN MUSCULOSKELETAL DISORDERS: PART II RELATED TO MYOFASCIAL AND NERVE APPARATUS

R. SAGGINI¹, A. DI STEFANO², A. SAGGINI³ and R.G. BELLOMO⁴

¹Department of Medical Science Oral and Biotechnology “G. D’Annunzio” University, Chieti, Italy; ²School of Specialties in Physical Medicine and Rehabilitation “G. D’Annunzio” University, Chieti, Italy; ³Department of Dermatology, University of Rome Tor Vergata, Rome, Italy; ⁴Department of Medicine and Science of Aging, “G. D’Annunzio” University, Chieti, Italy

Received May 4, 2015 – Accepted October 26, 2015

Shock waves have been widely recognized in literature as a biological regulator; accordingly we carried out a review on the effect of shock waves on the mesenchymal cells in their various expressions: bone, muscle, ligament and tendon tissue. To date, the application of Shock Wave Therapy (SWT) in musculoskeletal disorders has been primarily used in the treatment of tendinopathies (proximal plantar fasciopathy, lateral elbow tendinopathy, calcific tendinopathy of the shoulder, and patellar tendinopathy, etc.) and bone defects (delayed and non-union of bone fractures, avascular necrosis of femoral head, etc.). Although the mechanism of their therapeutic effects is still unknown, the majority of published papers have shown the positive and beneficial effects of using SWT as a treatment for musculoskeletal disorders, with a success rate ranging from 65% to 91%, while the complications are low or negligible. The purpose of this paper is to present the published data on the clinical application of SWT in the treatment of myofascial and nerve disorders. With the help of the relevant literature, in this paper we outline the indications and success rates of SWT, as well as the adequate SWT parameters (e.g., rate of impulses, energy flux density) defined according to the present state of knowledge.
Inflammatory mediators, such as cytokines, chemokines and arachidonic acid compounds, lead to vascular permeability and dilation and increase sensitization and pain receptors. Proinflammatory cytokines, including tumor necrosis factor, are involved in the etiology of clinical neurological disorders. These cytokines activate nuclear factor-κB (NF-κB) which leads to the activation of different inflammatory genes. TNF implicated in neurological disorders has an important role in the activation of microglia and astrocytes. The inhibition of TNF may lead to the decrease of microglia activation and can be useful for therapeutic intervention. TNF, at the site of nerve injury may activate mast cells (MCs) which mediate pathologic events such as headache and pain. TNF is the only cytokine stored in mast cells and can be rapidly released along with biogenic amines after MC stimulation. Activation of MCs leads to NF-κB and AP1 generation with release of many cytokines including TNF, IL-33 and IL-1. In this paper we discuss the role of TNF in MC activation, mediating pain and neurological disorders.
SELECTIVE INHIBITORS OF AURORA KINASES INHIBIT PROLIFERATION, REDUCE CELL VIABILITY AND IMPAIR CELL CYCLE PROGRESSION IN PAPILLARY THYROID CARCINOMA CELLS

E. BALDINI\textsuperscript{1}, C. TUCCILLI\textsuperscript{1}, N. PRINZI\textsuperscript{1}, S. SORRENTI\textsuperscript{2}, A. ANTONELLI\textsuperscript{3}, P. FALLAH\textsuperscript{3}, C. MIAN\textsuperscript{4}, S. BAROLLO\textsuperscript{4}, A. CATANIA\textsuperscript{2}, S. MORRONE\textsuperscript{1}, F. TARTAGLIA\textsuperscript{2}, D. MASCAGNI\textsuperscript{1}, C. COCCARO\textsuperscript{1}, M. PEPE\textsuperscript{1}, A. FILIPPINI\textsuperscript{2}, M. D’ARMIENTO\textsuperscript{1} and S. ULISSE\textsuperscript{1}

\textsuperscript{1}Department of Experimental Medicine, “Sapienza” University of Rome, Italy; \textsuperscript{2}Department of Surgical Sciences, “Sapienza” University of Rome, Italy; \textsuperscript{3}Department of Internal Medicine, University of Pisa, Italy; \textsuperscript{4}Department of Medicine, University of Padua, Italy

Received June 17, 2015 – Accepted August 7, 2015

The three members of the Aurora kinase family, Aurora-A, -B and -C, regulate several aspects of the mitotic process, and their aberrant expression and/or function causes mitotic abnormalities leading either to cell death or aneuploidy. They are found overexpressed in several human malignancies, including the papillary thyroid carcinoma (PTC). In the present study, we sought to establish whether Aurora kinase inhibition could be of any therapeutic value in the treatment of aggressive forms of PTC, enduring to radioactive iodide (RAI) ablation. To this end, the effects of selective inhibitors of Aurora-A (MLN8237) and Aurora-B (AZD1152) were analyzed on 3 human PTC cell lines expressing either wild-type (K1 and TPC1) or mutant p53 (BCPAP). The two inhibitors were capable of reducing cell proliferation in a time- and dose-dependent manner, with IC\textsubscript{50} comprised between 65.4 and 114.9 nM for MLN8237, and between 26.6 and 484.6 nM for AZD1152. Immunofluorescence experiments confirmed that AZD1152 inhibited Aurora-B phosphorylation of histone H3 on Ser10, however, it did not affect Aurora-A autophosphorylation. MLN8237 inhibited Aurora-A autophosphorylation as expected, but at concentrations required to achieve the maximum antiproliferative effects it also abolished H3 (Ser10) phosphorylation. Time-lapse videomicroscopy evidenced that both inhibitors prevented the completion of cytokinesis, and cytofluorimetric analysis showed accumulation of cells in G2/M phase and/or polyploidy. Apoptosis was induced in all the cells by both inhibitors independently from the p53 status. In conclusion, in the present preclinical study MLN8237 and AZD1152 have emerged as promising drug candidates for RAI-insensitive PTC.
LYMPHATIC EDEMA OF THE LOWER LIMBS AFTER ORTHOPEDIC SURGERY: RESULTS OF A RANDOMIZED, OPEN-LABEL CLINICAL TRIAL WITH A NEW EXTENDED-RELEASE PREPARATION

G. LESSIANI¹, P. IODICE², E. NICOLUCCI³ and M. GENTILI³

¹Vascular Medicine Unit, Private Hospital “Villa Serena”, Città Sant’Angelo (PE), Italy; ²Orthopedic Rehabilitation Unit, Private Hospital “Villa Serena”, Città Sant’Angelo (PE), Italy; ³Institute of Cognitive Sciences and Technologies, National Research Council, Rome, Italy

Received February 5, 2015 – Accepted September 4, 2015

The lymphedema is a high interstitial protein concentration edema, caused by impaired lymphatic transport capacity. It can be primary or secondary. The secondary form may be caused by a lesion of the lymphatic vessels and/or lymph nodes during diagnostic or therapeutic procedures such as surgical interventions. Often, in clinical practice, there is lymphedema after orthopedic surgery, even in minor orthopedic surgery. Lymphedema, typically presents symptoms of swelling, pain, inflammation, and itching, and it can generate, over the years, acute disability in the affected limbs. The standard therapy is mainly represented by medical treatment, such as manual lymphatic drainage and compression with bandages and stockings. In literature it is documented that lymphedema is responsive to alpha and the gamma benzopyrones. The aim of this study was to determine the effectiveness of delayed extended-release formulation of a compound containing alpha-benzo-pyrone (Coumarin), benzo-gamma-pyrone (Troxuretina) and oligomeric proanthocyanidins from Vitis vinifera (OPC), in addition to compression therapy, in the reduction of lymphatic edema after prosthetic hip and knee surgery. In the group treated, after 30 days, a reduction was observed of the edema of 4.8% in the ankle area (p<0.008) and 2.7% in the calf area (p<0.013). The control group showed no significant reduction. The treated group showed a marked reduction of all the secondary symptoms considered in the study, although variations were not significant. The results show that the compound used was effective in reducing edema after major orthopedic surgery, and consequently in alleviating some related symptoms, such as pain, itching, and burning. As an edema has extensive inflammatory components in patients with reduced mobility, the final data seems interesting, however, further investigations and a better follow-up are required.
OSTEOGENIC DIFFERENTIATION AND GENE EXPRESSION OF DENTAL PULP STEM CELLS UNDER LOW-LEVEL LASER IRRADIATION: A GOOD PROMISE FOR TISSUE ENGINEERING

A. BALLINI1, F. MASTRANGELO2, G. GASTALDI3, L. TETTAMANTI3, N. BUKVIC4, S. CANTORE1, T. COCCO1, R. SAINI5, A. DESIATE6, E. GHERLONE2 and S. SCACCO1

1Department of Basic Medical Sciences, Neuroscience and Sense Organs, University of Bari Aldo Moro Bari, Italy; 2Unit of Dentistry, IRCCS San Raffaele Scientific Institute, Vita e Salute San Raffaele University, Milano, Italy; 3Department of Periodontology and Oral Implantology, Rural Dental College Loni Maharashtra, India; 4University Hospital Bari-Policlinics, Medical Genetics Unit Bari, Italy; 5Department of Oral Science, Insubria University of Varese, Varese, Italy; 6Department of Interdisciplinary Medicine, University of Bari Aldo Moro Bari, Italy

Received September 18, 2015 – Accepted November 2, 2015

The effects of low-level laser therapy (LLLT) has been the focus of recent studies as being assumed responsible for promoting photostimulatory and photobiomodulatory effects in vivo and in vitro, increasing cell metabolism, improving cell regeneration and invoking an anti-inflammatory response. A positive effect of LLLT on the bone proliferation of some cell types has been observed, but little is known about its effect on dental pulp stem cells (DPSCs). Here, we accurately describe the technical procedure to isolate mesenchymal DPSCs, and assay their osteogenic capacity when irradiated with an LLLT source. These preliminary results show that LLLT irradiation influences the in vitro proliferation of DPSCs and increases the expression of essential proteins for bone formation, although it is necessary to carry out further experiments on other cell types and to uniform the methodological designs.
LETTER TO THE EDITOR

THE PROFILE OF MELATONIN RECEPTORS GENE EXPRESSION AND GENES ASSOCIATED WITH THEIR ACTIVITY IN COLORECTAL CANCER: A PRELIMINARY REPORT

E. ZIÓŁKO1, T. KOKOT1, A. SKUBIS2, B. SIKORA2, J. SZOTA-CZYŻ2, C. KRUSZNIEWSKA-RAJS2, J. WIERZGOŃ3, U. MAZUREK2, E. GROCHOWSKA-NIEDWOROK4 and M. MUC-WIERZGOŃ1

1School of Public Health in Bytom, Silesian Medical University, Department of Internal Medicine, Poland; 2Department of Molecular Biology, School of Pharmacy with the Division of Laboratory Medicine in Sosnowiec, Silesian Medical University, Poland; 3Department of Oncologic and Reconstructive Surgery Gliwice, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Poland; 4Department of Human Nutrition, School of Public Health, Silesian Medical University, Poland

Received May, 25, 2015 – Accepted August 5, 2015

The antiproliferative and immunomodulatory effects of melatonin (MLT) have been demonstrated in a variety of neoplasms including colorectal cancer (CRC). In humans and other mammals, MLT acts on target tissues through membrane and retinoid nuclear receptors. The aim of this study was to evaluate transcription activity of melatonin receptors and genes associated with regulation of their activity in colorectal adenocarcinoma tissues in relation to clinical stage of cancer. A total of 24 pairs of surgically removed tumoral and healthy (marginal) tissue samples from colorectal cancer patients at clinical stages I-II and III-IV were collected. As an additional control, twenty normal samples were taken from people whose large intestine tissues were reported as non-tumoral after colonoscopy. Expression of mRNA genes was studied by microarray HG-U133A analysis. The analysis of gene expression profile was performed using commercially available oligonucleotide microarrays of HG-U133A. High increase of MT1 mRNA expression levels in all cancerous samples vs non-cancerous tissues was observed. The MT2 mRNA expression levels increased slightly in marginal and malignant samples. Among the genes participating in the cascade of signal transfer in cells activated by MLT via melatonin receptors, we found encoding genes (GNA11, OXTR, TPH1) only for differentiating stage III - IV of CRC. Monitoring the expression levels of genes that are related to melatonin receptors may offer a strategy to anticipate tumour development and estimate the molecular changes that occur during carcinogenesis. The mechanism behind this association needs further elucidation.
LRIG1 EXPRESSION DURING HOMEOSTASIS AND SKIN WOUND HEALING IN MICE

S. MURAD\textsuperscript{1}, A. ANWAR\textsuperscript{1}, Z.Z. PIRACHA\textsuperscript{1} and A. SULTAN\textsuperscript{2}

\textsuperscript{1}Molecular Immunology Laboratory, Health Care Biotech, Atta-ur-Rahman School of Applied Biosciences, National University of Sciences and Technology (NUST), Islamabad, Pakistan; \textsuperscript{2}Biochemistry Department, Quaid-e-Azam University, Islamabad, Pakistan

Received May 18, 2015 – Accepted August 28, 2015

Leucine-rich repeats and immunoglobulin-like domains (LRIG)-1 belong to the family of proteins known to be expressed in skin. Ablation of LRIG1 in mice results in epidermal hyperplasia and its aberrant expression levels have been reported in pathological conditions such as psoriasis, thus evident of an indispensible role of LRIG1 in maintaining epidermal homeostasis. In order to gain insight into the homeostatic expression of LRIG1 and in various stages of cutaneous wound healing, LRIG1 expression was immunohistochemically analyzed in full thickness skin wounds in mice. The full thickness skin wounds were established on the dorsal back of Balb/c mice (n=6). LRIG1 expression at various post wounding days (1, 2, 3, 6 and 14) was determined through Immunohistochemical analysis (IHC) of the murine skin sections. The injury caused a sharp decline in LRIG1 expression in the basal epidermal cells and appendages surrounding the wound which correlates with the re-epithelialization phase of healing. LRIG1 expression remained down regulated during most of the wound healing stages. LRIG1\textsuperscript{+} cells were found to re-populate the neo-epidermis on day 14, suggesting an important homeostatic role of LRIG1 in skin.
LETTER TO THE EDITOR

EFFECTS OF VASCULAR ENDOTHELIAL GROWTH FACTOR-B ON THE BIOELECTRIC ACTIVITY OF RAT ATRIAL MYOCARDIUM UNDER NORMAL CONDITIONS AND DURING GRADUAL STRETCHING

R.S. OVCHINNIKOV$^{1,2}$, V.M. MITROKHIN$^{1*}$ and M.I. MLADENOV$^{1,3*}$

$^1$Department of Fundamental and Applied Physiology, Russian National Research Medical University, Moscow, Russia; $^2$Federal Scientific Clinical Center for Specialized Types of Medical Assistance and Medical Technologies of the Federal Medical and Biological Agency, Russia, Moscow, Russia; $^3$Faculty of Natural Sciences and Mathematics, Institute of Biology, “Ss. Cyril and Methodius” University, Skopje, Macedonia

Received May 25, 2015 – Accepted November 11, 2015

*These authors contributed equally as senior authors to this paper

Using a microelectrode technique we studied the effects of vascular endothelial growth factor-B on the activity of rat atrial myocardium under normal conditions and after gradual stretching of the tissue. It was shown that vascular endothelial growth factor-B increased duration of the action potential only at the level of 90% re-polarization. Effects on the frequency and force of contraction were absent. The repetition frequency of the action potentials did not change. Close observation of the vascular endothelial growth factor-B-induced mechanisms and stretch-induced alteration in action potential durations to 90% of repolarization, confirmed the existence of a link between the examining growth factor-B and stretch induced mechanisms.
Traumatic shock is a serious threat to life and health. The aim of this study is to investigate the effect of different resuscitation fluid compositions on the emergency resuscitation for patients with traumatic shock. Sixty patients were enrolled and divided into two groups, Group A and Group B. The patients in Group A were treated with resuscitation fluid, with 2:1 ratio of crystal (0.9% sodium chloride injection) and colloid (hydroxyethyl starch 40 injection). The patients in Group B were treated with hypertonic sodium chloride hydroxyethyl starch 40 injection (HSH40). Both vital signs and fluid dosage were monitored and recorded. At the beginning of resuscitation (T₀) and 30 min (T₁), 60 min (T₂) and 120 min (T₃) after resuscitation, indicator parameters including hemoglobin (HB), hematocrit (HCT), prothrombin time (PT), arterial blood lactate (LA) and C-reactive protein (CRP) were monitored and recorded. Tissue oxygenation and hemodynamic profile were also analyzed. At T₁, T₂ and T₃ after fluid resuscitation, the heart rates of the patients in Group B were lower than those in Group A, whereas the average arterial pressure in Group B was significantly higher than that in Group A. Notably, significant decreases of HB and HCT were detected at T₁, T₂ and T₃ compared with T₀ in Group A. In contrast, no significant difference was shown in detected HCT at T₂ and T₃ compared with T₀ in Group B, while the detected HB value was smaller. A statistically significant decrease of LA was detected at T₁, T₂ and T₃ in Group A and Group B compared with that at T₀. At T₂ and T₃ in Group A and Group B, a statistically significant increase of PT was detected compared with the beginning of resuscitation. At T₂ and T₃ after resuscitation, CRP in both Group A and Group B was significantly increased compared with that upon admission to hospital, and was lower in Group B than in Group A.
LETTER TO THE EDITOR

EFFECT OF NEW-PATTERN OBSTETRICAL NURSING IN REDUCING CESAREAN DELIVERY RATE

Y. JIANG and XW. LIU

Department of Obstetrics, Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing, China

Received June 15, 2015 – Accepted September 7, 2015

Spontaneous labor is the preferred delivery way ensuring health of fetus. However, recently, more and more puerperae tend to choose cesarean. However, cesarean delivery is likely to induce various short-term and long-term potential complications, severely threatening maternal and child health. To discuss the clinical effects of new-pattern obstetrical nursing in reducing cesarean delivery rate, 680 primiparas who delivered between December 2011 and December 2013 were selected from Beijing Obstetrics and Gynecology Hospital, Capital Medical University, China as research subjects. They were randomly divided into an observation group (n=340) and a control group (n=340). Primiparas in the observation group were taken care of by new-pattern nursing measures during pregnancy and the puerperal period, while primiparas in the control group received traditional nursing measures. Cesarean delivery rate was compared between two groups. Cesarean delivery rate was statistically significant between the observation group and the control group (21.8% vs 32.9%) (P<0.05). Also, it was found that, the incidence rate of perioperative complications of the observation group was much lower than the control group, and the difference was statistically significant (P<0.05). The findings suggest that new-pattern obstetrical nursing is effective in reducing the cesarean delivery rate, therefore is worth promoting and applying in clinical practice.
Glioma is a serious life-threatening disease, the pathogenesis of which remains to be investigated. The objective of the present investigation was to explore the expression and clinical significance of tumor suppressor gene (P53), O6-methylguanine-DNA methyltransferase (MGMT) and epidermal growth factor receptor (EGFR) in glioma. Immunohistochemical staining was applied to study the clinical characteristics of 40 samples from glioma patients, detect the expression of and analyse the relationship between P53, MGMT and EGFR and glioma. The results demonstrated that the positive expression rate of P53 was 47.5% in 40 cases of glioma samples, of which the expression of P53 in the high grade glioma was higher than that of the low grade samples ($P < 0.05$); the positive expression rate of MGMT was 37.5%, but there was no significant significance of MGMT expression between the high grade glioma and the low grade glioma ($P > 0.05$); the positive expression rate of EGFR was 55%, of which the expression of EGFR of the high grade glioma was higher than that of the low grade glioma ($P < 0.05$). There was no significant difference in the expressions of P53, MGMT and EGFR in the glioma patients of different ages, gender and with different tumor sizes. The expressions of P53 and MGMT were negatively correlated ($P < 0.05$). The expressions of P53 and EGFR were positively correlated ($P < 0.05$). In conclusion, P53, EGFR and MGMT could play a role in the occurrence, development and deterioration of glioma.
LETTER TO THE EDITOR

UNEXPECTEDLY HIGH OCCURRENCE OF ESCHERICHIA COLI AND STAPHYLOCOCCUS AUREUS ISOLATES FROM RAW MILK IN ILAM, WESTERN IRAN

M. TAHERIKALANI¹, S. HEMATI², K. HEIDARZADI², Z. MAHDAVI², F. GHANBARI¹, M. MOHAMADI², S. GHAFOURIAN², A.M. VARZI¹, F. AZIZI JALILIAN⁴, L. BOGDANOVIC⁵ and K. SAKI⁶

¹Razi Herbal Medicines Research Center and Department of Microbiology, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran; ²Clinical Microbiology Research Center, Ilam University of Medical Sciences, Ilam, Iran; ³Department of Immunology, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran; ⁴Department of Microbiology, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran; ⁵Department of Public Health, University of Naples Federico II, Naples, Italy, ⁶Department of Psychiatry, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Received July 19, 2015 – Accepted September 16, 2015

Raw milk contains diverse nutritional components that provide a suitable medium for spoilage and the growth of potentially pathogenic microorganisms. Unpasteurized milk consumption by a large number of people can threaten health and increase public concerns. In this study, sixty-two raw cow’s milk samples were collected from the dairy farms of Ilam, Western Iran. All samples were collected in sterilized containers and were transferred via ice boxes to the laboratory. Isolates were then identified by standard methods. Totally, 88.7% (n=55) of samples were contaminated. Our study also showed that Escherichia coli had a high prevalence among isolates (43: 69.4%), while Klebsiella pneumoniae and Klebsiella planticola showed the lowest prevalence (1: 1.6%). Staphylococcus aureus was also detected in 17.7% (n=11) of samples. The raw milk microbial contamination is complex. Some of the microorganisms threaten public health via different traits, therefore it is recommended that raw milk consumption should be avoided.
LETTER TO THE EDITOR

NEGLECTED GIANT SPINOCELLULAR CARCINOMA OF THE LOWER LIP

I. BAKARDZHIEV¹, A.A. CHOKOEVA², G.K. MAXIMOV³, U. WOLLINA⁴,
T. LOTTI⁵,⁶, S. GIANFALDONI⁷ and G. TCHERNEV⁸

¹Medical College, Medical University of Varna, Bulgaria; ²“Onkoderma” Policlinic for
Dermatology and Dermatologic Surgery, Sofia, Bulgaria; ³Department “Medicines Use Control”,
Sofia, Bulgaria; ⁴Department of Dermatology and Allergology, Academic Teaching Hospital
Dresden-Friedrichstadt, Dresden, Germany; ⁵University of Rome “G. Marconi”, Rome, Italy;
⁶Department of Biotechnology, Delft University of Technology, Delft, The Netherlands; ⁷Division of
Dermatology, Department of Critical and Experimental Medicine, University of Pisa, Pisa, Italy;
⁸Policlinic for Dermatology and Venereology, Saint Kliment Ohridski University, Medical Faculty,
University Hospital Lozenetz, Sofia, Bulgaria

Received August 21, 2015 – Accepted October 5, 2015

Although squamous cell carcinoma (SCC) is the most common type of lip cancer worldwide, its giant
form is extremely rare, due to its easy detection and early diagnosis. The survival rate is good if early
eradication is performed, as 5-year survival accounts for approximately 80-90%. We present a rare
variant of giant form of SCC on the lower lip in a 70-year-old patient, which had been neglected for many
years, due to social disadvantages and absence of any resources for adequate medical help, until the
tumor caused total inability of administration of food and drink. The recent diagnostic and therapeutic
options are considered. Despite well-known etiologic factors regarding squamous cell carcinoma and the
newest prognostic factors on tumor differentiation, such as β-catenin abnormal expression, the negative
influence of the demographic characteristics of the patient were also in focus. Certain outcast ways
of living should be considered as potential risk factors for the development of giant forms of SCC. In
addition, an improvement of the quality of life of these patients results as being critical for the prevention
of various of risk factors, as well as improving the survival rate in general.
LETTER TO THE EDITOR

EXPRESSION OF mTOR AND ITS INHIBITORY EFFECT ON CELL PROLIFERATION AND APOPTOSIS OF BREAST CANCER CELLS

XF. CHENG1, Q. LIU2, XF. ZHANG1, HD. ZHAO1, W. WANG1 and AJ. CHU1

1Surgery Department of Galactophore, The First Affiliated Hospital of Henan University of TCM, Zhengzhou City, Henan Province, China; 2Scientific Bureau, Henan University of TCM, Zhengzhou City, China; 3Department of Traditional Chinese Medicine and Western Medicine, Henan Cancer Hospital, Zhengzhou City, Henan Province, China

Received May 21, 2015 – Accepted September 23, 2015

The first two authors contributed equally to this work

The aim of this study is to investigate the expression of mTOR in breast cancer and observe the effect of CCI-779 on proliferation and apoptosis of MDA-MB-231 cells. Immunohistochemical staining was used to detect the expression of mTOR protein in breast cancer tissues and MDA-MB-231 cells. MTT assay was used to assess the effect of CCI-779 on proliferation of MDA-MB-231 cells. AnnexinV-FITC/PI assay was utilized to evaluate the effect of CCI-779 on apoptosis of MDA-MB-231 cells. Among the 71 cases of breast cancer tissues, 54.9% were mTOR-positive that exhibited significantly higher expression than the 32 cases of normal tissues (21.9%); mTOR protein was also found to be expressed in MDA-MB-231 cells. The mTOR inhibitor CCI-779 significantly inhibited the proliferation of MDA-MB-231 cells that was dose- and time-dependent. However, CCI-779 was unable to induce apoptosis of MDA-MB-231 cells as demonstrated with AnnexinV-FITC/PI assay. mTOR plays a key role in the initiation and development of breast cancer, and its inhibitor CCI-779 exerts a strong suppressive activity against MDA-MB-231 cells, suggesting its therapeutic potential to treat breast cancer.
LETTER TO THE EDITOR

EXPRESSION AND DIAGNOSIS OF TRANSIENT RECEPTOR POTENTIAL VANILLOID1 IN UROTHELION OF PATIENTS WITH OVERACTIVE BLADDER

H.Y. ZHANG¹, J.F. CHU¹, P. LI¹, N. LI¹ and Z.H. LV²

¹Department of Urology, Yantai Hill Hospital of Yantai City, Shandong, China; ²Department of Urology, First People’s Hospital of Jining, Shandong, China

Received January 29, 2015 – Accepted June 4, 2015

The first two authors contributed equally to this paper

This study was carried out to test expression of transient receptor potential vanilloid1 (TRPV1) in urothelium of female patients with overactive bladder (OAB) and explore clinical significance of TRPV1 in diagnosing female OAB. TRPV1 expression in urothelium of female OAB patients (n=21) and healthy females (n=9) was detected using Strept Avidin-Biotin Complex (SABC), an immunohistochemical method and image analysis system. Relative content of TRPV1 was expressed by average optical density (AOD) and was analyzed through data of urodynamics. Compared to TRPV1 expression in urothelium of healthy females (AOD 0.3658 ± 0.1009), TRPV1 expression in OAB patients was much higher (AOD 0.4834 ± 0.1252) and the difference was significant P<0.05. Observation and comparison in clinic of urodynamic parameters of female patients and healthy females revealed that the former had lower indexes with remarkable differences (P<0.05) such as Qmax, first desire volume (FDV), strong desire volume (SDV), maximum cyst capacity (MCC) and bladder compliance (BC). Thus high expression of TRPV1 in urothelium of female OAB patients is closely correlated to OAB occurrence, showing great importance of improved bladder sensitivity in female OAB occurrence mechanism.
LETTET TO THE EDITOR

EFFECT AND MECHANISM OF DIHYDROARTEMISININ ON PROLIFERATION, METASTASIS AND APOPTOSIS OF HUMAN OSTEOSARCOMA CELLS

C. TANG¹, PY. AO², YQ. ZHAO¹, SZ. HUANG¹, Y. JIN¹, JJ. LIU¹, JP. LUO¹, J. ZHENG¹ and DP. SHI³

¹Department of Orthopedics, People’s Hospital of Zhengzhou University and Henan Province People’s Hospital, Zhengzhou, Henan, China; ²Department of Traditional Chinese Orthopedics and Physiotherapy, Traditional Chinese Medicine Hospital of Baoji, Baoji, Shaanxi, China; ³Department of Radiology, People’s Hospital of Zhengzhou University and Henan Province People’s Hospital, Zhengzhou, Henan, China

Received July 1, 2015 – Accepted September 22, 2015

Osteosarcoma represents an aggressive type of bone malignancy that poses a significant health threat. The objective of the current study was to analyze the effect and mechanism of dihydroartemisinin (DHA) on the proliferation, metastasis and apoptosis of human osteosarcoma cells. A gradient concentration of DHA (15, 25 and 35 µmol.L⁻¹) was used to stimulate the cells, along with control and Dimethyl sulfoxide (DMSO). The phenotypic outcomes were characterized using MTT assay, clone formation assay, Hoechst 33258 staining assay, luciferase reporter plasmid assay, Western blot and wound healing assay. In addition, IBM SPSS Statistics 18.0 software was applied for statistical analysis and all experimental data were expressed as mean ± s.d. Analysis of variance (ANOVA) was applied to compare the differences among multiple groups. Our results demonstrated that DHA inhibited the proliferation and metastasis of osteosarcoma cells and promoted the apoptosis in the cytomorphosis.
LETTER TO THE EDITOR

INFLUENCE OF COLORECTAL CANCER TUMOR SUPPRESSOR GENE CHD5 METHYLATION ON ITS CLINICAL AND PATHOLOGICAL CHARACTERISTICS

JB. LIU, QB. ZHOU, JZ. XU, GX. WANG and WT. YUAN

Colorectum surgery department of the First Affiliated Hospital of Zhengzhou University,
Zhengzhou, China

Received June 25, 2015 – Accepted September 25, 2015

Recently, abnormal tumor suppressor gene (TSG) methylation has become a hotspot in the research on colorectal cancer (CRC). This study aimed to explore the influence of CHD5 methylation of CRC TSG on its clinical and pathological characteristics. A total of 40 operation samples as well as corresponding tissue specimens were collected from CRC patients treated in the First Affiliated Hospital of Zhengzhou University from January to December in 2014. CHD5 gene methylation in tissue specimens was detected with methylation specific polymerase chain reaction (MSP); moreover, messenger ribose nucleic acid (mRNA) expression of CHD5 in each tissue was tested using reverse transcription-polymerase chain reaction (RT-PCR), and Western blot was applied to detect the expression of CHD5 protein in those tissues and to analyze the correlation between mRNA and protein of cancer tissue CHD5 as well as the relationship between CHD5 methylation and protein expression. Results revealed that the expression rate of CHD5 methylation in 40 normal mucosal tissues, para-carcinoma tissues, adenoma tissues and CRC tissues was 12.5% (5/40), 22.5% (9/40), 47.5% (19/40) and 72.5% (33/40), respectively. The mRNA expression of CHD5 in the above tissues was 0.225±0.276, 0.169±0.231, 0.147±0.159 and 0.013±0.011 and the protein expression of CHD5 was 0.438±0.205, 0.398±0.180, 0.156±0.1 and 0.024±0.311, respectively. Methylation rate of CHD5 was 87% (20/23) in 23 cases of CHD5 protein loss expression and 52.9% (9/17) in 17 cases of CHD5 protein expression. Results of chi-squared test indicated that there was a significant difference in methylation rate (P < 0.05), that is, the methylation rate of negatively expressed CHD5 protein was obviously higher than positively expressed protein. Thus, it can be concluded that the CHD5 methylation rate rises gradually in the evolution of CRC, which is related to the occurrence and development of CRC. Furthermore, CHD5 mRNA is positively correlated with protein expression and CHD5 gene methylation is associated with protein loss expression. Therefore, TSG CHD5 methylation of rectal cancer has a great effect in influencing its clinical and pathological features.
LETTER TO THE EDITOR

ANGIOGENESIS OF HEPATOCELLULAR CARCINOMA UNDER MULTISLICE SPIRAL CT PLAIN SCAN AND ENHANCED SCAN

A.D. MA\(^1\), Y. ZHANG\(^1\), Z. XUE\(^1\) and K. LI\(^2\)

\(^1\)Department of Radiology, Shandong Jining No.1 People’s Hospital, Jining, Shandong, China; \(^2\)Department of Gynaecology and Obstetrics, Affiliated Hospital of Shandong Academy of Medical Sciences, Shandong, China

Received May 11, 2015 – Accepted July 14, 2015

This study explores the value of 64-layer spinal computed tomography (CT) in diagnosing hepatocellular carcinoma (HCC) through performing dynamic contrast-enhanced scans. The study includes analysis of enhancement presentation of HCC in dynamic contrast-enhanced scan performed by multislice spinal CT (MSCT), comparison of detection rate and positive predictive value of neoplastic foci in subdivided arterial phases and portal venous phases, optimization of optimal scanning scheme for diagnosing HCC and discussion of the value of quantitative indexes such as T-D curve, maximum enhancement rate and clearance rate in diagnosing and identifying HCC. A total of 61 lesions were detected in 40 patients with HCC who were selected from the First People’s Hospital, Jining, Shandong, China. Density difference was observed with statistical significance between the solid part of tumor and normal liver in different periods after CT scan and enhanced scan (\(H = 45.208, P < 0.01\)), and difference in the late arterial phase was the most obvious; enhanced peak value mostly appeared in the late arterial phase. In terms of lesion detection rate, the difference of HCC detection rate was statistically significant in early, middle and late arterial phase and early and late portal vein phases (\(\chi^2 = 32.910, P = 0.001\)), and the rate was the highest in the late arterial phase (78.689%). Lesions were divided into 3 cm or less group (small HCC) and over 3 cm group based on the maximum parameter. Detection rate of the late arterial phase was the highest, 85% (3 cm or less) and 75.61% (over 3 cm), respectively. When lesions with high density in arterial phase and/or low density in portal venous phase were considered as positive, and moreover, those confirmed clinically or pathologically were as true positive, we found positive predictive value of the over 3 cm group reached 100% in all phases, but that of 3 cm or less group was the highest (100%) in early and late portal venous phases. Among four scanning schemes involving early, middle and late arterial phases, detection rate of the early and late arterial phases and three arterial phases were consistent, reaching the highest value (3 cm or less group: 90%; the 3 cm over group: 78.049%). This study confirmed that the late arterial phase was the best time to detect abundant blood supplied HCC. The scanning scheme involving double arterial phases (early and late), late portal venous phase and stable phase which can help improve detection rate and correct diagnosis rate of HCC, was thought to be the most effective. Using dynamic enhanced CT examination in the diagnosis of HCC is meaningful.
LETTER TO THE EDITOR
IDENTIFICATION OF BENIGN AND MALIGNANT ENDOMETRIAL CANCER WITH TRANSVAGINAL ULTRASONOGRAPHY COMBINED WITH ELASTOGRAPHY AND TISSUE HARDNESS ANALYSIS

Y. ZHANG¹, L. LUO² and Q. LUO¹

¹Department of Radiology, Shandong JiNing No.1 People’s Hospital, Jining, Shandong, China; ²Department of Gynaecology and Obstetrics, Shandong JiNing No.1 People’s Hospital, Jining, Shandong, China

Received May 15, 2015 – Accepted July 20, 2015

This study was designed to explore tissue hardness and distinguish benign and malignant endometrial cancer with the use of transvaginal ultrasonography combined with elastography. Color Doppler ultrasonic diasonograph was used to carry out transvaginal ultrasonography and elastography. Once the nidus was observed, features of the 2D image were analyzed. Then features of elasticity of the uterine cavity in different states were analyzed by elastography, and strain rate ratio was measured. Finally, elasticity scoring (0–5 points) was made. Receiver operating characteristic (ROC) curve was drawn based on elasticity score and strain rate ratio. The area under the elasticity score curve and strain rate ratio curve was 0.761 and 0.852, respectively, and there was no statistically significant difference between them ($c²= 4.663, P>0.05$). Then 2.98 was confirmed as the diagnostic cut-off value of benign and malignant lesions, based on strain rate ratio. Ultrasonic elastography as an effective assistance for transvaginal ultrasonography provides more valuable information for confirmation of lesions and offers more accurate evidence for diagnosis of disease in the uterine cavity.

With the constant development of society and increase of diseases, an increasing number of people are concerned for their health and more females pay attention to physical examination. Endometrial cancer has become one of the frequently seen malignant tumors in the female reproductive system, and the number of young people diagnosed with this disease is increasing (1). Though its incidence is lower than cervical cancer in China, endometrial cancer is observed with an incidence rate higher than carcinoma of uterine cervix in some European countries and ranks first of all the gynecologic malignant tumors (2, 3). Ultrasonic testing is a routine gynecological screening program and plays an important function in screening uterine cavity diseases. Transvaginal ultrasonography is able to clearly demonstrate the state, size and blood flow of the uterus in different states. Transvaginal ultrasonography has been widely applied in clinical use as a non-invasive, effective and rapid method of examination (4). However, its feasibility in diagnosing the space occupying lesions in the uterine cavity has not yet been confirmed. During exploration, many authors held that it is of great importance to find...
LETTER TO THE EDITOR

EFFECT OF MYO-INOSITOL AND ALPHA-LIPOIC ACID ON OOCYTE QUALITY IN POLYCYSTIC OVARY SYNDROME NON-OBESE WOMEN UNDERGOING IN VITRO FERTILIZATION: A PILOT STUDY

R. RAGO¹, I. MARCUCCI², G. LETO³, L. CAPONECCHIA², P. SALACONE², P. BONANNI², C. FIORI², G. SORRENTI² and A. SEBASTIANELLI²

¹Department of Materno Infantile, Unit of Pathophysiology of Reproduction, Sandro Pertini Hospital, Rome Italy; ²Department of Specialist Medicine, Unit of Andrology and Pathophysiology of Reproduction, S.M Goretti Hospital, Latina, Italy; ³Department of Experimental Medicine, Sapienza University of Rome, Polo Pontino, Latina, Italy

Received March 30, 2015 – Accepted September 2, 2015

The aim of the present study was to evaluate the effectiveness of the combined administration of myo-inositol and α-lipoic acid in polycystic ovary syndrome (PCOS) patients with normal body mass index (BMI), who had previously undergone intracytoplasmic sperm injection (ICSI) and received myo-inositol alone. Thirty-six of 65 normal-weight patients affected by PCOS who did not achieve pregnancy and one patient who had a spontaneous abortion were re-enrolled and given a cycle of treatment with myo-inositol and α-lipoic acid. For all female partners of the treated couples, the endocrine-metabolic and ultrasound parameters, ovarian volume, oocyte and embryo quality, and pregnancy rates were assessed before and after three months of treatment and compared with those of previous in vitro fertilization (IVF) cycle(s). After supplementation of myo-inositol with α-lipoic acid, insulin levels, BMI and ovarian volume were significantly reduced compared with myo-inositol alone. No differences were found in the fertilization and cleavage rate or in the mean number of transferred embryos between the two different treatments, whereas the number of grade 1 embryos was significantly increased, with a significant reduction in the number of grade 2 embryos treated with myo-inositol plus α-lipoic acid. Clinical pregnancy was not significantly different with a trend for a higher percentage for myo-inositol and α-lipoic acid compared to the myo-inositol alone group. Our preliminary data suggest that the supplementation of myo-inositol and α-lipoic acid in PCOS patients undergoing an IVF cycle can help to improve their reproductive outcome and also their metabolic profiles, opening potential for their use in long-term prevention of PCOS.
LETTER TO THE EDITOR

SERUM 25-HYDROXYVITAMIN D LEVELS IN CHILDREN WITH RECURRENT TONSILLITIS LIVING IN MILAN

S. TORRETTA\(^1\), P. MARCHISIO\(^2\), E. IOFRIDA\(^1\), P. CAPACCIO\(^1\) and L. PIGNATARO\(^1\)

\(^1\)Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Otorhinolaryngological Clinic, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; \(^2\)Pediatric Clinic, Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Pediatric Highly Intensive Care Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Received May 13, 2015 – Accepted September 28, 2015

Involvement of 25-hydroxyvitamin D in the etiopathogenesis of tonsillar disease in children is still debated; this study assesses possible differences in serum 25-hydroxyvitamin D levels between 309 Caucasian children (58.1% males; mean age 55.7±31.0 months) living in Milan with a history of recurrent tonsillitis (RT) and healthy controls. Mean serum 25(OH)D levels were significantly reduced in the children with a history of RT (22.0±8.7 ng/mL vs 24.6±7.8 ng/mL; p=0.03), and the proportion of children with insufficient or deficient serum 25(OH)D levels was higher in the RT group (81.5% and 6.5% respectively) than in the control group (75.1% and 3.5%) (not significant). The multivariable model created to test the independent association between serum 25(OH)D levels and a history of RT after adjusting for age and season showed that the association was not significant. Our study failed to find any significant reduction in serum 25(OH)D levels after adjustment for age and season in a case series of children with RT in comparison with healthy controls, which suggests that vitamin D does not play a relevant role in the etiology of pediatric tonsillar infections.
LETTER TO THE EDITOR

TREATMENT WITH TERIPARATIDE MIGHT BE ASSOCIATED WITH CARDIOMETABOLIC CHANGES IN POSTMENOPAUSAL SEVERE OSTEOPOROTIC WOMEN

E. PASSERI¹, E. DOZIO², M. MENDOLA¹, E. COSTA³, F. BANDERA⁴, M.M. CORSI ROMANELLI²,⁵ and S. CORBETTA¹,²

¹Endocrinology Unit, IRCCS Policlinico San Donato, San Donato M.se, Milan, Italy; ²Department of Biomedical Sciences for Health, University of Milan, Milan, Italy; ³Clinical Chemistry Laboratory, IRCCS Policlinico San Donato, San Donato M.se, Milan, Italy; ⁴Heart Failure Unit, IRCCS Policlinico San Donato, San Donato M.se, Milan, Italy; ⁵UOC SMEL-1 Clinical Pathology, IRCCS Policlinico San Donato, San Donato M.se, Milan, Italy

Received March 16, 2015 – Accepted September 22, 2015

Parathormone (PTH) has been suggested to affect the cardiovascular system. Teriparatide (TPT), the hormonally active 1-34 fragment of PTH, provides an anabolic treatment for osteoporosis. The aim of the present study was to evaluate the cardiometabolic effects of 18-month treatment with 20 μg/die teriparatide subcutaneously. Fourteen women with postmenopausal severe osteoporosis treated with once-daily sc 20 μg TPT (aged 67.6±2.5 years; BMI 27.7±1.0 kg/m²) and 24 age- and BMI-matched severe osteoporotic women treated with iv yearly 5 mg zoledronate (ZLN) were evaluated at baseline and at 12-18 months of treatment for anthropometric measures, calcium, glucose and lipid metabolic parameters, and assessment of cardiac geometry by conventional echocardiography. TPT was effective in increasing mean lumbar spine bone mineral density with no clinically relevant changes in calcium metabolism parameters. TPT patients experienced an increase of BMI (27.7±1.0 at baseline vs 29.0±1.0 kg/m² at last evaluation, P=0.005) and mean whole body fat percentage (37.0±2.1 vs 40.3±1.9%, P=0.05), associated with increased serum leptin levels (17.3±2.1 vs 22.9±3.0 ng/ml; P=0.049). Glucose and lipid parameters were not affected by TPT as well as by ZLN treatment. Furthermore, TPT was associated with a decrease in systolic blood pressure; a decrease in the fractional shortening (41.2±2.3 vs 36.9±1.2; P=0.05) and an increase in the relative wall thickness (0.39±0.01 vs 0.48±0.01 mm; P=0.002), suggestive for concentric cardiac remodeling, was detected by echocardiographic monitoring. These changes could not be detected in bone active drug-free age- and metabolic-matched controls. In conclusion, long-term TPT therapy might affect cardiometabolic and cardiac geometry parameters in severe osteoporotic women, though changes are not clinically relevant.
ALLERGIC RHINITIS IS CONSIDERED A STRONG RISK FACTOR FOR THE ONSET OF ASTHMA. HOWEVER, FEW STUDIES HAVE ADDRESSED THIS ISSUE FROM A FUNCTIONAL POINT OF VIEW. IN THIS WORK THE CLOSE LINK BETWEEN UPPER AND LOWER AIRWAYS IS HIGHLIGHTED, SUGGESTING THAT SPIROMETRY SHOULD BE PRECOCIOUSLY PERFORMED ON PATIENTS WITH ALLERGIC RHINITIS.
Persistent shoulder pain is a highly prevalent problem, due to different pathologies, that is frequently associated with limited range of motion and decreased function. The correct diagnosis can lead to the best treatment for each pathology. In this study we tried to understand what could be the role of hyaluronic acid and its effective benefit in patients affected by mild-to-moderate glenohumeral osteoarthritis. From January 2013 to June 2014, we prospectively followed-up 61 consecutive patients with shoulder osteoarthritis degrees I, II, and III. We divided the patients into 2 homogeneous groups: 31 patients in the first group treated with 5 intra-articular injections of Hyalgan 20mg/2ml and a specific physiotherapy program, and 30 patients in the second group treated only with physical therapy. The mean follow-up examination was carried out 5.2 months after the beginning of the therapy for both groups. The statistical analysis revealed a significant difference (P<0.05) between the two groups in terms of pain reduction and improvement in the activities of daily living. The present study demonstrates the greater and long-lasting efficacy of a five-injection treatment with hyaluronic acid (Hyalgan 20mg/2ml) combined with a physical therapy program in comparison with physical therapy only in patients affected by glenohumeral osteoarthritis degree I, II or III.
PERISURGICAL AND INTRA-REHABILITATIVE SALIVARY STEROID HORMONE PROFILES IN BICOMPARTMENTAL ARTHROPLASTY

S. PEREGO¹, D. GRASSO¹, B.D. BODINI², F. CAVAIANI², C. DE SANTIS², N. URSINO³, C. PELOSI², G. BANFI¹,⁴ and G. LOMBARDI¹

¹Laboratory of Experimental Biochemistry and Molecular Biology, I.R.C.C.S. Istituto Ortopedico Galeazzi, Milan, Italy; ²O.U. Rehabilitation, ¹st Division – Clinical Orthopaedic Rehabilitation, I.R.C.C.S. Istituto Ortopedico Galeazzi, Milan, Italy; ³O.U. Reconstructive Joint Surgery and Orthopaedic Surgery (C.A.S.C.O.), I.R.C.C.S. Istituto Ortopedico Galeazzi, Milan, Italy; ⁴Vita-Salute San Raffaele University, Milan, Italy

Received June 29, 2015 – Accepted October 7, 2015

The first two authors contributed equally to the work

Sex hormones play a role in pain perception, a key variable in evaluating the progression and treatment of osteoarthritis. The aim of this study was to determine the relationship between salivary concentrations of four steroid hormones and functional/clinical outcomes after hip and knee arthroplasty. Saliva samples were collected from 24 otherwise healthy patients with osteoarthritis before surgery, on admission to rehabilitation, and at hospital discharge. Salivary concentrations of testosterone, 17β-estradiol, dehydroepiandrosterone (DHEA), and cortisol were immunoassayed. Changes in hormone levels were compared with clinical outcomes, as assessed by functional independence measure (FIM®), Barthel Index (BI), and visual analog scale for pain (VAS) scores. Changes in testosterone levels were significantly inversely correlated with VAS (r= -0.53, p=0.043) and FIM® and BI scores in all patients (r= -0.30, p= 0.043, and r= -0.35, p=0.031, respectively). The testosterone to cortisol ratio was inversely correlated with BI scores in all patients (r= -0.30, p=0.040), and in the men (r= -0.55, p=0.005) and the women (r= -0.28, p=0.042) when analyzed separately. Changes in salivary testosterone concentrations closely correlated with clinical outcome measurements for total hip and knee arthroplasty. Clinical outcome after arthroplasty was generally better among the men.
Tooth replantation, as a treatment concept, has been subject to controversies regarding the mechanism as well as the various parameters underlying this process. This work aimed to study time-related changes in the pulp of replanted mature human premolars through the changes in the levels of certain factors involved in the underlying mechanisms of pulpal tissue healing after replantation. Eleven experimental mature teeth were extracted, immediately replanted in the original socket and left without any other intervention for 1, 2, 3 and 12 weeks before re-extraction. Three premolars served as control. All specimens were subject to histological analysis and the levels of MMP-2, MMP-9, Annexin V, iNOS and BCL-2 (anti-apoptotic family) were analyzed employing immunohistochemistry. The results showed degradation of the extracellular matrix (ECM), inflammatory cell infiltrate, loss in pulpodentine interface and loss of odontoblasts in the dental pulp tissue. This was accompanied by increase over time of MMP-9, Annexin V, iNOS and a decrease of BCL-2 and MMP-2, suggesting that apoptosis increased throughout the experimental period.

DENTAL PULP IN MATURE REPLANTED HUMAN TEETH: MORPHOLOGICAL ALTERATIONS AND METALLOPROTEINESES-2 AND -9, ANNEXIN-5, BCL-2 AND iNOS MODULATION

A. LEONE1,2, A. ANGELOVA VOLPONI2, ML. UZZO1, GF. SPATOLA1, A. JURJUS3 and V. VANDEVSKA–RADUNOVIC4

1Department of Experimental Biomedicine and Clinical Neurosciences, Section of Histology, University of Palermo, Palermo, Italy; 2Department of Craniofacial Development and Stem Cell Biology, King’s College, London, UK; 3Department of Anatomy, Cell Biology and Physiology, American University of Beirut, Beirut Lebanon; 4Department of Orthodontics, Institute of Clinical Dentistry, University of Oslo, Oslo, Norway

Received June 24, 2015 – Accepted October 5, 2015

All authors share the same authorship
LETTER TO THE EDITOR

AIRBORNE NITRIC OXIDE AND NASAL CYTOLOGY IN PATIENTS WITH CHRONIC RHINOSINUSITIS AND NASAL POLYPS

S. TORRETTA, M. CAPPADONA, D. CAIROLI and L. PIGNATARO

Department of Clinical Sciences and Community Health, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Università degli Studi di Milano, Milan, Italy

Received July 21, 2015 – Accepted October 14, 2015

Nitric oxide (NO) is involved in eosinophilic inflammation. The fraction of exhaled nitric oxide (FENO) is increased in chronic rhinosinusitis with nasal polyps (CRSwNP), whereas nasal NO (nNO) is reduced in chronic rhinosinusitis. Nasal cytology can detect eosinophilic inflammation in CRSwNP. We aimed to describe the baseline rhinocytological characteristics and NO (FENO and nNO) levels in patients with CRSwNP, and assess their possible correlations. This longitudinal study involved 37 consecutive adult outpatients with CRSwNP and 36 healthy controls. They underwent a complete clinical otolaryngological assessment, measurement of FENO and nNO levels, and nasal scraping in order to collect material for nasal cytology. Disease severity was evaluated by means of endoscopic and Lund-Mackay radiological scores. Median FENO level was higher (p <0.001) in CRSwNP (28.3 ppb, 95%CI 13.0-33.6 ppb) than in the controls (7.5 ppb, 95%CI 6.1-8.9 ppb). Median nNO levels were lower (255.7, 95%CI 199.7-311.6 vs 385.5, 95%CI 345.0-425.9 ppb; p <0.001), and were lower in the patients with severe endoscopic obstruction (p=0.05). Lund-Mackay scores positively correlated with median FENO levels (R=0.11; p=0.05), and inversely with median nNO levels (R=−0.31; p=0.04). Metachromatic nasal cytotypes were more prevalent among CRSwNP patients who had previously undergone surgery (p=0.05). The number of metachromatic elements in the patients with CRSwNP positively correlated with their median FENO levels (R=0.24; p=0.002). Our results confirm the dynamic interplay between the upper and lower airways in patients with CRSwNP. FENO/nNO and nasal cytology can be useful for detecting and monitoring nasal inflammation in CRSwNP.
LETTER TO THE EDITOR

MICROBIOLOGICAL INVESTIGATION OF MEDICATION-RELATED OSTEONECROSIS OF THE JAW: PRELIMINARY RESULTS

V. CRINCOLI1, A. BALLINI2, M. DI COMITE2, L. TETTAMANTI3, M.F. COSCIA2, F. MASTRANGELO4 and D. DE VITO2

1Department of Interdisciplinary Medicine, University of Bari Aldo Moro, Bari, Italy
2Department of Base Medical Sciences, Neurosciences and Sense Organs, University of Bari Aldo Moro, Bari, Italy; 3Department of Oral Science, Insubria University of Varese, Varese, Italy; 4Unit of Dentistry, IRCCS San Raffaele Scientific Institute, Vita e Salute San Raffaele University, Milano, Italy

Received September 7, 2015 – Accepted October 28, 2015

Medication-related osteonecrosis of the jaw (MRONJ) is a well-recognized severe complication of bisphosphonate (BPs) treatment in patients with osteoporosis or metastatic cancer. Microbiological infection has been hypothesized as a contributing factor to bisphosphonate related osteonecrosis of the jaw (BRONJ). Despite infection being present in BRONJ patients, there is no clear data as to whether infection plays a role in the pathophysiology. Moreover, microbial cultures have not been helpful in directing therapy because specific pathogens have not been identified. The objective of this study was to determine the bacterial colonization of jawbone and identify the bacterial phylotypes associated with BRONJ. Twenty oncologic patients, aged 48-87 years (average age 70.65±8.86 years) with BRONJ were enrolled in this study and underwent three different microbiological samplings. Overall, 60 samples were obtained from oral mucosa, necrotic bone fragments and fistula drainage. The same procedure was performed for the laboratory culture of all these specimens. No significant differences regarding either gram+ and gram– species (Chi-squared= 0.1642; p = 0.6854) or aerobes and anaerobes bacteria (Chi-squared= 3.084; p = 0.0791) were found. Compared to other sampling techniques, the oral swab allowed to obtain valuable microbial data in order to recognize pathogens responsible for the infection and to outline a focused antimicrobial therapy.
Osteoarthritis is being increasingly characterised as an inflammatory incoming and recurrent disease, with the specific symptoms of inflammation at every stage of the disease. With regard to the pathogenesis over time, the degenerative and inflammatory components are combined and lead to osteocartilaginous degeneration. Such deterioration involves other joint tissues as well as the subchondral bone tissue, the suffering of which is the key event of the beginning and progression of OA; its involvement concerns the same pathogenetic mechanisms and the same chemical mediators of the chondropathy. The increase in joint inflammatory events leads to suspect the onset or the worsening of the osteometabolic disorder, which is documented by the MR as “bone edema” or as algodystrophic syndrome. The pain appears both while moving and resting and with signs of inflammation. The treatment of OA requires drugs, such as paracetamol, selective and nonselective NSAIDs and opiates, for pain control. Treatment should ensure the pharmacological control of the pain related to the osteometabolic juxta-articular alteration, through bisphosphonates, favouring those which can control bone loss, inflammation and pain.
LETTER TO THE EDITOR

BEHAVIOUR OF DENTAL PULP STEM CELLS ON DIFFERENT TYPES OF INNOVATIVE MESOPOROUS AND NANOPOROUS SILICON SCAFFOLDS WITH DIFFERENT FUNCTIONALIZATIONS OF THE SURFACES

M. MARRELLI1,2,3, G. FALISI4*, A. APICELLA5*, D. APICELLA1,2, M. AMANTEA1,3, A. CIELO6, L. BONANOME6, F. PALMIERF, L. SANTACROCE7*, S. GIANNINI6, E. DI FABRIZIO9,10, C. RASTELLI*, M. GARGARI11*, G. CUDA11*, F. PADUANO2* and M. TATULLO1,2,4*

1Unit of Maxillofacial Surgery, Calabrodental, Crotone, Italy; 2Tecnologica Research Institute, Biomedical Section, Crotone, Italy; 3Marrelli Hospital, Cancer Surgery Unit, Crotone, Italy; 4Department of Life, Health and Environmental Sciences, School of Dentistry, University of L’Aquila, L’Aquila, Italy; 5Department of Architecture and Industrial Design, Second University of Naples, Italy; 6Private practice in Rome; 7Department JSGEM, University of Bari - Section of Taranto, Italy; 8Department of Clinical Sciences and Translational Medicine, University of Rome “Tor Vergata”, Rome, Italy; 9BioNEM Laboratory, Department of Experimental and Clinical Medicine, Magna Grecia University of Catanzaro, Salvatore Venuta Campus, Catanzaro, Italy; 10Physical Science & Engineering Division, King Abdullah University of Science and Technology (KAUST), Thuwal, Kingdom of Saudi Arabia; 11Department of Experimental and Clinical Medicine, Magna Grecia University of Catanzaro, Salvatore Venuta Campus, Catanzaro, Italy

Received September 3, 2015 – Accepted October 22, 2015

* These Authors equally contributed to this research

Dental pulp stem cells (DPSCs) are stem cells found in the dental pulp. The ability of DPSCs to differentiate towards odontoblastic and osteoblastic phenotype was reported first in the literature, then in the following years, numerous studies on odontogenesis were carried out, starting from mesenchymal stem cells isolated from tissues of dental and oral origin. The aim of this research was to evaluate the behaviour of DPSCs grown on silicon nanoporous and mesoporous matrices and differentiated towards the osteogenic phenotype, but also to investigate the use of DPSCs in pilot studies focused on the biological compatibility of innovative dental biomaterials. Twenty-eight silicon samples were created with standardized procedures. These scaffolds were divided into samples made of silicon bulk, nanoporous silicon, mesoporous silicon, nanoporous silicon functionalized with (3-Aminopropyl) Trimethoxysilane (APTMS) and methanol (MeOH), nanoporous silicon functionalized with (3-Aminopropyl) Trimethoxysilane (APTMS)/toluene, mesoporous silicon functionalized with (3-Aminopropyl) Trimethoxysilane (APTMS) and methanol (MeOH) andmesoporous silicon functionalized with (3-Aminopropyl) Trimethoxysilane (APTMS)/toluene. DPSC proliferation on the tested silicon scaffolds was analyzed at 3 and 5 days. The assay showed that DPSCs proliferated better on mesoporous scaffolds functionalized with APTMS/toluene compared to a silicon one. These results show that the functionalization of silicon scaffold with APTMS/toluene supports the growth of DPSCs and could be used for future applications in tissue engineering.
LETTER TO THE EDITOR

HYALURONIC ACID-BASED MEDICAL DEVICE AND ORAL DISORDERS: CAN IT BE USED IN PAEDIATRIC DENTISTRY?

S. D’ERCOLE¹, A. NANUSSI², M. TIERI¹, D.F. BARATTINI³ and D. TRIPIDI¹

¹Unit of Paediatric Dentistry, Medical, Oral and Biotechnological Sciences, University “G. D’Annunzio” Chieti-Pescara, Italy; ²Gnato-posturology and cranio-facial pain therapy, Hospital “San Gerardo di Monza”, University Milan-Bicocca, Italy; ³Opera Consulting Srl, Timisoara, Romania

Received May 27, 2015 – Accepted October 22, 2015

Due to its physical and biological characteristics and safety profile, hyaluronic acid is very widely used in numerous clinical conditions, ranging from its best-known use in cosmetic surgery (as a filler and for its ability to promote tissue regeneration and therefore minimise scarring) to lesser-known fields such as ophthalmic surgery, major abdominal surgery (where it is used to prevent the complication of adhesion bands) and intra-articular use. Studies were recently published in which this type of device was also used in paediatric patients for the management of inflammatory disorders of the oral cavity and teething symptoms. As this is a highly topical field for dentists, we felt it would be useful to review the efficacy and safety of the device in the paediatric population treated, and analyse any discrepancies with the results obtained in the adult population. The preparations of hyaluronic acid used in pediatric dentistry, thanks to their anti-inflammatory and angiogenic properties, proved to be very effective in therapy of oral diseases in children. Further clinical research is needed to confirm the effectiveness of these products to dispel doubts about any side effects.
LETTER TO THE EDITOR

MEDICAL TREATMENT OF JOINT PROSTHESIS: INDICATION, OPPORTUNITIES AND LIABILITY PROFILES

L. MOLFETTA¹, C. TROMPETTO² and E. SILVESTRI³

¹Research Center on Osteoporosis and Osteoarticular Diseases, School of Medical and Pharmaceutical Sciences, University of Genoa, Italy; ²Neurosciences Department, School of Medical and Pharmaceutical Sciences, University of Genoa, Italy; ³Department of Radiology and Interventional Ultrasound, Evangelical Hospital International, Genoa, Italy

Received March 12, 2015 – Accepted November 11, 2015

Orthopaedic specialists should completely and sequentially manage osteoarthritis, from the onset to the prosthesis, with no attitude of resignation, complying with national and international Guidelines (GLs) and abiding by the criteria of appropriateness of drugs, rehabilitation and orthopaedic device prescription, in line with the ethics of the medical profession. The GLs are a paper that rationalises the quantity of existing information for a disease, without abusing the decision of the doctor; a large volume of scientific knowledge is concentrated in a format that is easily accessible to doctors when carrying out their work. The use of drugs has taken on a connotation of a rational and multifactorial choice, rather than an accidental and incremental choice - inspired only by safety, rather than efficacy criteria. The Notes compiled by the Italian Medicines Agency - a legal instrument to define the reimbursability of medicines and, therefore, an instrument for managing pharmaceutical expenditure – are, in reality, a means to guarantee the appropriateness of the use of medicines, orienting the therapeutic choices according to established Guidelines. In the specific case of osteoarthritis, the knowledge of the GLs is the most appropriate and complete approach towards the disease, in the context of its pathogenetic complexity in its natural history. Moreover, pharmacological treatment of the subchondral osteometabolic damage becomes necessary when documented by magnetic resonance or a scintigraphy; the bone-related pain cannot be challenged through symptomatic analgesic treatment alone.
LETTER TO THE EDITOR

BIOPHYSICAL STIMULATION AND THE PERIPROSTHETIC BONE: IS THERE A RATIONALE IN THE USE OF PULSED ELECTROMAGNETIC FIELDS AFTER A HIP OR KNEE IMPLANT?

L. MASSARI¹, R. OSTI¹, V. LORUSSO¹, S. SETTI² and G. CARUSO¹

¹Orthopaedic Institute of University, Ferrara, Italy; ²IGEA Spa, R&D Department, Carpi(MO), Italy

Received March 4, 2015 - Accepted November 17, 2015

The biophysical stimulation of bone and cartilage, using Pulsed ElectroMagnetic Fields (PEMF), covers many different aspects of bone formation and/or cartilage repair, such as healing of delayed or non-union of fracture, bone necrosis, osteocartilaginous defects. To date there are no specific data on the effects of PEMFs in osteointegration of prosthetic implants but there are some papers that denote clinical advantages, in terms of early recovery, in patients treated with these procedures. Considering these clinical applications, PEMF stimulation around hip or knee joint implants could be useful to reduce the bone oedema, pain and to reduce excessive bone reabsorption around the femoral stems.
LETTER TO THE EDITOR

ALKALINE PHOSPHATASE LEVEL IN GINGIVAL CREVICULAR FLUID DURING TREATMENT WITH QUAD-HELIX

A. DELLI MAURI¹, M. PETRINI², D. VITALE², S. TECCO², F. FESTA², E. BARBATO¹ and G. SPOTO²

¹Department of Head and Neck Pathology, University Sapienza, Rome, Italy;
²Department of Medical, Oral and Biotechnological Sciences, University G. d’Annunzio, Chieti-Pescara, Italy

Received April 1, 2015 – Accepted October 21, 2015

The aim of this work is to assess the level of the human alkaline phosphatase enzyme (ALP) during palatal expansion with Quad-Helix (QH) appliance. A total of twenty-two orthodontic patients characterized by contraction of the upper jaw, that needed application of a QH in order to treat their condition, were included in this study. Gingival crevicular fluid (GCF) was collected at four different times: before cementation (T0), after two weeks (T1), after four weeks (T2) and after one year (T3) from application of QH. In each patient maxillary first molars, right (UM-right) and left (UM-left), which were connected with bands to QH, were used for testing; first lower molars were used as Controls (LM-right, LM-left). Data show that ALP level in tension sites was proportional to the average increase of the inter-molar distance; on the contrary, the enzymatic level in compression sites was characterized by an inverse trend. The only exception to this phenomenon was recorded after one year (T3), when the increase of ALP level in both sites of tension and compression was ascribed to a mild inflammation due to bacterial plaque accumulation. The level of ALP in control sites was constant for the whole period of observation. The described ALP fluctuations in accordance with the inter-molar distance increment, shows that the main action of QH on bone remodelling was exerted during the fourth week (T2); for this reason, the monitoring of this enzyme could be used as a marker of effective function of the QH appliance.