

Hot Articles

“July|2017”

Health Science



Title: [Osteogenic commitment and differentiation of human mesenchymal stem cells by low-intensity pulsed ultrasound stimulation](#)

Author: Viviana Costa, Valeria Carina, Simona Fontana, Angela De Luca, Francesca Monteleone, Stefania Pagani, Maria Sartori, Stefania Setti, Cesare Faldini, Riccardo Alessandro, Milena Fini and Gianluca Giavaresi

Journal: Journal of Cellular Physiology

Volume: Version of Record online: 11 JUL 2017

Doi: 10.1002/jcp.26058

Abstract

Low-intensity pulsed ultrasound (LIPUS) as an adjuvant therapy in in vitro and in vivo bone engineering has proven to be extremely useful. The present study aimed at investigating the effect of 30 mW/cm² LIPUS stimulation on commercially available human mesenchymal stem cells (hMSCs) cultured in basal or osteogenic medium at different experimental time points (7, 14, 21 days). The hypothesis was that LIPUS would improve the osteogenic differentiation of hMSC and guarantying the maintenance of osteogenic committed fraction, as demonstrated by cell vitality and proteomic analysis. LIPUS stimulation (a) regulated the balance between osteoblast commitment and differentiation by specific networks (activations of RhoA/ROCK signaling and upregulation of Ribosome constituent/Protein metabolic process, Glycolysis/Gluconeogenesis, RNA metabolic process/Splicing and Tubulins); (b) allowed the maintenance of a few percentage of osteoblast precursors (21 days CD73+/CD90+: 6%; OCT-3/4+/NANOG+/SOX2+: 10%); (c) induced the activation of osteogenic specific pathways shown by gene expression (early: ALPL, COL1A1, late: RUNX2, BGLAP, MAPK1/6) and related protein release (COL1a1, OPN, OC), in particular in the presence of osteogenic soluble factors able to mimic bone microenvironment. To summarize, LIPUS might be able to improve the osteogenic commitment of hMSCs in vitro, and, at the same time, enhance their osteogenic differentiation.

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Title: [A Cross-Study Analysis Evaluating the Effects of Food on the Pharmacokinetics of Rivaroxaban in Clinical Studies](#)
Author: Liping Zhang, Gary Peters, Lloyd Haskell, Purve Patel, Partha Nandy, Kenneth Todd Moore
Journal: The Journal of Clinical Pharmacology
Volume: First Published: 5 July 2017
Doi: 10.1002/jcph.958

Abstract

US prescribing guidelines recommend that 15- and 20-mg doses of rivaroxaban be administered with food for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and for reduction in the risk of recurrence of DVT and PE. In addition, the US prescribing guidelines recommend these doses be administered with an evening meal to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (AF). The purpose of this model-based cross-study comparison was to examine the impact of food, with regard to both meal timing and content, on the pharmacokinetics (PK) of rivaroxaban, using data collected during its clinical development. Results of this analysis showed that a PK model built from pooled data in the AF population (for whom rivaroxaban was administered with an evening meal) and in the DVT population (for whom rivaroxaban was administered with a morning meal) can describe both data sets well. Furthermore, the PK model built from data in the AF population alone can adequately predict the PK profile of the DVT population and vice versa. This cross-study analysis also confirmed the findings from previous clinical pharmacology studies, which showed that meal content does not have a clinically relevant impact on the PK of rivaroxaban at 20 mg. Therefore, although the administration of rivaroxaban with food is necessary for maintaining high bioavailability, neither meal timing nor meal content appears to affect the PK of rivaroxaban.

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Title: [Heartwood extract from Dalbergia sissoo promotes fracture healing and its application in ovariectomy-induced osteoporotic rats](#)

Author: Anirudha Karvande, Vikram Khedgikar, Priyanka Kushwaha, Naseer Ahmad, Priyanka Kothari, Ashwni Verma, Padam Kumar, Geet Kumar Nagar, Prabhat Ranjan Mishra, Rakesh Maurya and Ritu Trivedi

Journal: Journal of Pharmacy and Pharmacology

Volume: Version of Record online: 30 JUN 2017

Doi: 10.1111/jphp.12764

Abstract

Objectives: This study was undertaken to investigate the effects of a heartwood ethanolic extract (HEE) made from the Dalbergia sissoo on fracture healing and in the prevention of pathological bone loss resulting from estrogen deficiency in ovariectomized (Ovx) rats.

Methods: Heartwood ethanolic extract (250, 500 and 1000 mg/kg per day) was administered orally immediately next day after drill-hole injury and continued for 2 weeks. Oxv rats received HEE at same doses for 12 weeks and compared with 17- β estradiol (E2; 100 μ g/kg for 5 days/week subcutaneously) group. Confocal imaging for fracture healing, micro-architecture of long bones, biomechanical strength, formation of mineralized nodule by bone marrow osteoprogenitor cells, bone turnover markers and gene expression were studied. One-way ANOVA was used to test significance.

Key findings: Heartwood ethanolic extract treatment promoted fracture healing, formation of new bone at the drill-hole site and stimulated osteogenic genes at callus region. HEE administration to the Oxv rats exhibited better micro-architectural parameters at various anatomical positions, better bone biomechanical strength and more osteoprogenitor cells in the bone marrow compared with Oxv + vehicle group. HEE exhibited no uterine estrogenicity.

Conclusions: Oral administration of HEE was found to promote fracture healing and exhibited osteoprotective effect by possibly stimulation of osteoblast function.

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Title: [Perceived stress, disturbed sleep, and cognitive impairments in patients with work-related stress complaints: a longitudinal study](#)

Author: Anita Eskildsen, Hanne Nørr Fentz, Lars Peter Andersen , Anders Degn Pedersen, Simon Bang Kristensen & Johan Hviid Andersen

Journal: Stress

Volume: Published online: 29 Jun 2017

Doi: 10.1080/10253890.2017.1341484

Abstract

Patients on sick leave due to work-related stress often present with cognitive impairments as well as sleep disturbances. The aim of this longitudinal study was to examine the role of perceived stress and sleep disturbances in the longitudinal development in cognitive impairments in a group of patients with prolonged work-related stress (N = 60) during a period of 12 months following initial professional care-seeking. Objective cognitive impairments (neuropsychological tests) were measured on two occasions – at initial professional care-seeking and at 12-month follow-up. Questionnaires on perceived stress, sleep disturbances, and cognitive complaints were completed seven times during the 12 months which facilitated multilevel analysis with segregation of within-person (change) and between-person (baseline level) components of the time-varying predictors (perceived stress and sleep disturbances). Change in perceived stress was associated with concurrent and subsequent change in self-reported cognitive complaints over the period of 12 months and to a lesser extent the change in performance on neuropsychological tests of processing speed from baseline to 12-month follow-up. Change in sleep disturbances was also associated with concurrent and subsequent change in self-reported cognitive complaints over the 12 months but not with change on neuropsychological test performance. Although the mechanism behind the improvement in cognitive impairments in patients with work-related stress should be further explored in future studies, the results could suggest that improvement in cognitive impairments is partly mediated by decreasing levels of perceived stress and, to a lesser extent, decreasing levels of sleep disturbances.

Database

Taylor & Francis Online Journals

Title: [Neratinib for the treatment of HER2-positive early stage breast cancer](#)
Author: Isabel Echavarría, Sara López-Tarruella, Iván Márquez-Rodas, Yolanda Jerez & Miguel Martín
Journal: Expert Review of Anticancer Therapy
Volume: Published online: 26 Jun 2017
Doi: 10.1080/14737140.2017.1338954

Abstract

Introduction: Despite the advances in the treatment of HER2-positive breast cancer, resistance to actual chemotherapeutic regimens eventually occurs. Neratinib, an orally available pan-inhibitor of the ERBB family, represents an interesting new option for early-stage HER2-positive breast cancer.

Areas covered: In this article, the development of neratinib, with a special focus on its potential value in the treatment of early-stage HER2-positive breast cancer, has been reviewed. For this purpose, a literature search was conducted, including preclinical studies, early-phase trials in advanced cancer with neratinib in monotherapy and in combination, and phase II and large phase III trials in the early setting. Management of neratinib-induced toxicity, future perspectives for the drug, and ongoing trials are also discussed in this review.

Expert commentary: Neratinib is emerging as a promising oral drug for the treatment of HER2-positive breast cancer. Although FDA and EMA approval is derived from the extended adjuvant treatment, this setting may not be the ideal scenario to obtain the beneficial effects of neratinib. Confirmatory data in the neoadjuvant setting and subgroup analysis from the ExTENET trial might bring some light into the best setting for neratinib therapy. Data from confirmatory trials in the metastatic setting are also required.

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Taylor & Francis Online Journals

Title: [Delivering information and brief advice on alcohol \(IBA\) in social work and social care settings: an exploratory study](#)
Author: Trish Hafford-Letchfield, Betsy Thom, Rachel Herring & Mariana Bayley
Journal: Drugs: Education, Prevention and Policy
Volume: Published online: 09 Jul 2017
Doi: 10.1080/09687637.2017.1344621

Abstract

Social workers and practitioners working in social care are potentially key players in the prevention of alcohol-related harm and harm reduction for people using services and their carers. This requires attention to workforce development alongside the selection of appropriate tools to support prevention strategies. We report findings from a UK exploratory study into the potential of using Identification and Brief Advice (IBA) as a tool for screening and prevention in social work and social care settings. Thirty-six social workers and social care practitioners attended one of two training workshops on IBA in the South East of England. Pre and post-workshop surveys (n = 35 and n = 20, respectively) and four post-workshop focus groups (n = 36) were conducted with participants to explore the application of IBA taking into account the paradigmatic shift towards prevention and holistic approaches indicated in recent UK legislation and policy. Four themes emerged from the findings: (1) perceptions of the social work/social care role in responding to alcohol problems, (2) ethical concerns, (3) time conflicts and problems of delivering IBA and (4) the role of training. Further studies are needed to evaluate the effectiveness of motivational techniques and tools that social workers can use to promote preventative practise for alcohol-related harm. Different strategies are required to engage and support those working in social care to increase proactive engagement with problematic alcohol use in everyday practise settings.

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Title: [Quantitative genetics of circulating Hyaluronic Acid \(HA\) and its correlation with hand osteoarthritis and obesity-related phenotypes in a community-based sample](#)

Author: Jai Prakash, Gulzhan Gabdulina, Svetlana Trofimov & Gregory Livshits

Journal: Annals of Human Biology

Volume: Published online: 09 Jul 2017

Doi: 10.1080/03014460.2017.1334822

Abstract

Background: One of the potential molecular biomarkers of osteoarthritis (OA) is hyaluronic acid (HA). HA levels may be related to the severity and progression of OA. However, little is known about the contribution of major risk factors for osteoarthritis, e.g. obesity-related phenotypes and genetics to HA variation.

Aim: To clarify the quantitative effect of these factors on HA.

Subjects and methods: An ethnically homogeneous sample of 911 apparently healthy European-derived individuals, assessed for radiographic hand osteoarthritis (RHOA), HA, leptin, adiponectin, and several anthropometrical measures of obesity-related phenotypes was studied. Model-based quantitative genetic analysis was used to reveal genetic and shared environmental factors affecting the variation of the study's phenotypes.

Results: The HA levels significantly correlated with the age, RHOA, adiponectin, obesity-related phenotypes, and the waist-to-hip ratio. The putative genetic effects contributed significantly to the variation of HA ($66.2 \pm 9.3\%$) and they were also significant factors in the variations of all the other studied phenotypes, with the heritability estimate ranging between $0.122 \pm 4.4\%$ (WHR) and $45.7 \pm 2.2\%$ (joint space narrowing).

Conclusions: This is the first study to report heritability estimates of HA variation and its correlation with obesity-related phenotypes, ADP and RHOA. However, the nature of genetic effects on HA and its correlation with other study phenotypes require further clarification.

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Title: [Impact of medical comorbidity in psychiatric inpatient length of stay](#)

Author: Nuno Rodrigues-Silva & Lúcia Ribeiro

Journal: Journal of Mental Health

Volume: Published online: 07 Jul 2017

Doi: 10.1080/09638237.2017.1340605

Abstract

Background: Medical comorbidity is associated with worse psychiatric outcomes, reduced functioning and higher services use, including inpatient psychiatric care.

Aim: We explored the relation between medical comorbidity and length of stay, adjusting for potential confounders.

Methods: We retrospectively analyzed an administrative database comprising all inpatient admissions between 2005 and 2014 at the Department of Psychiatry and Mental Health at Vila Nova de Gaia/Espinho Healthcare Center, Vila Nova de Gaia – Portugal. Psychiatric diagnosis and medical comorbidity were coded according to single-level and multi-level classification schemes, respectively, as proposed by the Clinical Classification Software.

Results: We included a total of 4613 psychiatric inpatient admissions. The prevalence of medical comorbidity was 25.4% and it was associated with an average increase of 3.5 days ($p < 0.001$) in length of stay, comparing to patients without medical comorbidity. After adjusting for potential confounders, such as age, sex and year of discharge, medical comorbidity was associated with a 13% increase in length of stay.

Conclusions: Medical comorbidity has measurable effects in inpatient outcomes, such as the length of stay and should be a major focus for intervention, in ambulatory care but also during psychiatric hospitalization.

Database

Taylor & Francis Online Journals

Title: [Brief overview of nanoparticulate therapy in cancer](#)

Author: Rajesh R. Wakaskar

Journal: Journal of Drug Targeting

Volume: Published online: 04 Jul 2017

Doi: 10.1080/1061186X.2017.1347175

Abstract

Nanoparticles govern an all-important role, in this day and age, in determining the tissue distribution of either hydrophobic or hydrophilic anti-cancer drugs by encapsulating them or by covalent attachment. The whole purpose is to systematically improve upon the existing anti-tumour efficacy of these drugs. Selective delivery of these chemotherapeutic agents to the compromised or diseased tissue is the key to avoid any potential toxicity problems. Certain types of nanoparticles, through various mechanisms such as active targeting or reversing multi-drug resistance, display immense potential in adding to the existing anti-tumour efficacy profile. Determining the optimal composition of the polymers or size of the nanoparticles or appropriately tailoring the surface of these nanoparticles with molecular ligands are the key components in governing the successful biological fate of these nanoparticles.

Database

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Title: [Is Ultrasound Useful for Further Evaluation of Homogeneously Hyperattenuating Renal Lesions Detected on CT?](#)
Author: Mahadevaswamy Siddaiah, et al. | American Journal of Roentgenology
Journal: American Journal of Roentgenology
Volume: Jul 5, 2017 (Ahead of Print)
Doi: 10.2214/AJR.17.17814

Abstract

OBJECTIVE. The purpose of this study was to evaluate the ability of ultrasound (US) to characterize hyperattenuating cysts detected as indeterminate hyperattenuating renal lesions on unenhanced and single phase enhanced CT.

MATERIALS AND METHODS. A total of 107 consecutive homogeneously hyperattenuating renal lesions underwent gray-scale and Doppler US at our institution between 2010 and 2013. Two radiologists who were unaware of the final diagnosis retrospectively evaluated US images for visibility and diagnosis (simple cyst, intermediate complexity cyst, cystic or solid mass showing internal flow on Doppler US, or indeterminate). A third radiologist assessed lesion size, location, and distance to skin on CT and US. US visibility was compared using chi-square and independent t tests. Consensus US interpretation was compared with reference standard diagnoses, and accuracy for diagnosis of hyperattenuating cysts was tabulated.

RESULTS. Mean lesion size \pm SD was 20 ± 16 mm (range, 6–96 mm) and mean distance to skin on CT was 62 ± 25 mm (range, 18–125 mm). In all, 89.7% (96/107) of the lesions were visible on US, including all lesions that were 15 mm or larger. Nonvisible lesions were smaller than visible ones (10.0 ± 3.6 mm vs 20.7 ± 16.3 mm, $p = 0.03$) regardless of location ($p > 0.05$). CT overestimated lesion distance to skin compared with US (46.6 ± 18.6 mm, $p < 0.001$). Final diagnoses for US visible lesions ($n = 96$) were hyperattenuating cyst ($n = 66$), Bosniak IIF cyst ($n = 13$), and cystic or solid neoplasm ($n = 15$); two patients were lost to follow-up. Of the 66 hyperattenuating cysts, 54 (81.8%) appeared as simple cysts on US with sensitivity and specificity for diagnosis of hyperattenuating cyst of 81.8% (95% CI, 75.6–84.3%) and 92.9% (95% CI, 78.1–98.7%), respectively. The other 12 (18.2%) hyperattenuating cysts appeared complex. Two of the 13 Bosniak IIF lesions were incorrectly classified as simple cysts with US. Including the 11 (10%) nonvisible lesions reduced sensitivity and specificity for diagnosis of hyperattenuating cyst to 73.0% (95% CI, 66.9–75.9%) and 89.7% (95% CI, 74.2–97.2%), respectively.

CONCLUSION. US can further characterize hyperattenuating cysts presenting as indeterminate hyperattenuating renal lesions on CT in the majority of cases.

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