Abstract

Objectives
To evaluate the analgesic effect of Glucantime (antimoniate N-methylglucamine) in Leishmania amazonensis infection and complete Freund's adjuvant (CFA), chronic paw inflammation model, in BALB/c mice.

Methods
Two models of chronic inflammatory pain in BALB/c mice paw were used: infection with L. amazonensis and CFA stimulation. Both animals models received daily treatment with Glucantime (10 mg/kg, i.p.) and during the treatment was measured the mechanical hyperalgesia with electronic version of von Frey filaments. After the treatment, the paw skin sample was collected for analysis of myeloperoxidase (MPO) and N-acetyl-β-glucosaminidase (NAG) activity, and IL-1β, TNF-α, IL-6, IFN-γ and IL-10 cytokines production by ELISA.

Key findings
Leishmania amazonensis-induced chronic inflammation with significant increase in mechanical hyperalgesia, MPO and NAG activity, and IL-1β, TNF-α and IL-6 production in the paw skin. Glucantime (10 mg/kg, i.p.) inhibited L. amazonensis-induced mechanical hyperalgesia and IL-1β and IL-6 cytokines productions. In chronic inflammatory model induced by CFA, Glucantime treatment during 7 days inhibited CFA-induced mechanical hyperalgesia, MPO and NAG activity, and IL-1β, TNF-α, IL-6 and IFN-γ production as well as increased IL-10 production.

Conclusions
Our data demonstrated that Glucantime reduced the chronic inflammatory pain induced by L. amazonensis and CFA stimuli by inhibiting the hyperalgesic cytokines production.

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Drug utilization evaluation among an elderly population: a retrospective cross-sectional study in a tertiary care hospital in Pakistan

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Abstract

Objectives
Aging and its associated physiological changes make elderly more prone to chronic diseases, ultimately leading to escalated drug use. The aim of this study was to execute retrospective drug utilization evaluation among elderly patients discharged from the hospital.

Methods
A descriptive, retrospective, cross-sectional study design was employed. Data were collected from the medical records of discharged elderly patients admitted between July 2016 and December 2016 in Bahawal Victoria Hospital, Bahawalpur, Punjab, Pakistan. Statistical Package for Social Sciences (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 21.0. Armonk, NY, USA: IBM Corp.) was used for analysing the data. Multiple linear regression analysis was used to find the independent factors associated with increased utilization of drugs. P-value < 0.05 was considered statistically significant.

Key findings
The average number of drugs per prescription was 4.74 (SD = 1.4). The most commonly prescribed drug classes were as follows: A – alimentary tract and metabolism (77.8%), J: anti-infectives for systemic use (68.5) and C: cardiovascular system (67.5%) respectively. The total drug consumption varied between 0.02 defined daily dose (DDD)/1000 patient days and 77.1 DDD/1000 patient days. The maximally consumed drug in all the medical wards was omeprazole. 48.3% patients were prescribed at least one potentially inappropriate medication independent of disease or condition. 10.2% patients were prescribed at least one inappropriate medication dependent on disease or condition. 61.8% prescriptions had drug interactions. The total number of drug interactions found in the prescriptions was 781, and among them, majority (74.2%) were moderate interactions.

Conclusions
Our study identified that drug use in elderly is not appropriate and special emphasis must be put on rationalizing the drug use in this population. The findings of this study may provoke the policymakers and healthcare professionals to formulate appropriate strategies for ensuring rational drug use.

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Abstract

Neuroglobin (NGB) is a relatively recent discovered monomeric heme-protein, which behave in neurons as a sensor of injuring stimuli including oxidative stress, hypoxia, and neurotoxicity. In addition, the anti-apoptotic activity of overexpressed NGB has been reported both in neurons and in cancer cell lines. We recently demonstrated that, NGB functions as a compensatory protein of the steroid hormone 17β-estradiol (E2) protecting cancer cells against the apoptotic death induced by oxidative stress. However, the E2-induced signaling pathways at the root of NGB over-expression and mitochondrial re-localization in breast cancer cells is still elusive. By using a kinase screening library, here, we report that: i) There is a strong positive correlation between NGB and ERα expression and activity in breast cancer cells; ii) The E2-activated phosphatidylinositol 3 kinase (PI3K)/protein kinase B (AKT) and protein kinase C (PKC) pathways are necessary to modulate the NGB protein levels; iii) The E2-induced persistent activation of AKT drive NGB to mitochondria; iv) Reactive oxygen species (ROS)-inducing compounds activating rapidly and transiently AKT does not affect the NGB mitochondrial level; and v) High level of NGB into mitochondria are necessary for the pro-survival and anti-apoptotic effect of this globin in cancer cells. As a whole, these results underline the E2 triggered pathways in E2-responsive breast cancer cells that involve NGB as a compensatory protein devoted to cancer cell survival.
Abstract

Delafloxacin, a fluoroquinolone, has activity against Gram-positive organisms including methicillin-resistant S. aureus and fluoroquinolone-susceptible and -resistant Gram-negative organisms. The intravenous formulation of delafloxacin contains the excipient sulfobutylether-β-cyclodextrin (SBECD), which is eliminated by renal filtration. This study examined the pharmacokinetics and safety of SBECD after single intravenous (IV) infusions in subjects with renal impairment. The study was an open-label, parallel-group, crossover study in subjects with normal renal function or mild, moderate, or severe renal impairment, and those with end-stage renal disease undergoing hemodialysis. Subjects received 300 mg delafloxacin IV or placebo IV, containing 2400 mg SBECD, in 2 periods separated by ≥14-day washouts. SBECD total clearance decreased with decreasing renal function, with a corresponding increase in area under the concentration-time curve (AUC0-∞). After IV delafloxacin 300 mg administration, SBECD mean total clearance was 6.28 and 1.24 L/h, mean AUC0-∞ was 387 and 2130 h·μg/mL, and mean renal clearance was 5.36 and 1.14 L/h in normal and severe renal subjects, respectively. Similar values were obtained after IV placebo administration. In subjects with end-stage renal disease, delafloxacin 300 mg IV produced mean SBECD AUC0-48 values of 2715 and 7861 h·μg/mL when dosed before and after hemodialysis, respectively. Total SBECD clearance exhibited linear relationships to estimated glomerular filtration rate and creatinine clearance. Single doses of IV delafloxacin 300 mg and IV placebo were well tolerated in all groups. In conclusion, decreasing renal function causes reduced SBECD clearance and increased exposures, but SBECD continues to exhibit a good safety and tolerability profile in IV formulations.
Abstract

**Background:** African Americans are generally known to have lower heavy drinking prevalence than Whites despite often greater individual and community risk factors. While it is supposed that their protective resources explain this “paradox,” studies have not explicitly examined this.

**Objective:** Assess the contribution of protective resources to Black–White differences in heavy drinking, and (secondarily) whether protective resources operate by reducing heavy drinking and/or increasing abstinence.

**Methods:** Using data from the 2009–2010 U.S. National Alcohol Survey (N = 3,133 Whites and 1,040 Blacks ages 18+), we applied propensity score (PS) weighting to estimate racial differences in heavy drinking and abstinence under hypothetical conditions in which Whites are similar to Blacks in: (1) age and marital status; (2) socioeconomic position and unfair treatment; (3) neighborhood socioeconomic conditions and alcohol outlet density; and (4) protective resources (proscriptive religiosity, area-level religiosity, “drier” network drinking norms and patterns, and family social support).

**Results:** The Black–White gap in male and female drinkers' baseline heavy drinking increased after weighting adjustments for demographics. In women, this gap was reduced after weighting on disadvantage and eliminated after adjusting for protective resources. In men, adjustment for disadvantage increased the racial gap, and protective resources reduced it. Protective resources had a stronger effect on Black–White differences in men's abstinence than heavy drinking, but similar effects on these outcomes in women.

**Conclusion:** Protective resources help explain Black–White differences in men’s and particularly women’s heavy drinking. Future research is needed to elucidate mechanisms of action and additional factors underlying racial differences in men’s heavy drinking.
Title: A multifunctional nanoparticle constructed with a detachable albumin outer shell and a redox-sensitive inner core for efficient siRNA delivery to hepatocellular carcinoma cells

Author: Bohui Xu, Yan Xu, Gaoxing Su, Hongyan Zhu & Li Zong

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Abstract

Successful delivery of small interfering RNA (siRNA) into the cytoplasm of target cells relies on biocompatible and efficient vectors. In this study, a novel multifunctional core/shell nanoparticle [CS-SS-9R/BSA-c(RGDyK)] was developed to effectively deliver siVEGF to hepatocellular carcinoma cells (Bel-7402 cells). To improve the gene payload and transfection efficiency, a positively charged inner core (CS-SS-9R) was constructed by grafting nona-arginine (9R) onto chitosan (CS) using disulphide bonds. The negatively charged outer shell [BSA-c(RGDyK)] assembled on the surface of the inner core by electrostatic forces that shielded high cationic charges and provided improved targeting. The protein outer shell gradually detached from the inner core in the acidic lysosomal environment, leaving the cationic inner core exposed in order to escape from lysosomes. The nanoparticles were capable of delivering siVEGF into Bel-7402 cells via integrin receptor-mediated endocytosis. Successful lysosomal escape of the inner core and the rapid release of siVEGF into the cytoplasm resulted in a 78.9% decrease in VEGF expression and 81.2% inhibition of tumour cell proliferation. In conclusion, this nanoparticle is responsive to the intracellular environment and accurately delivered siRNA into the cytoplasm, providing a safe and highly efficient gene delivery strategy for cancer therapy.

Database

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**Abstract**

**Introduction:** The prognosis of recurrent/metastatic (R/M) squamous cell carcinoma of the head and neck (HNSCC) after failure of first line chemotherapy is dismal. Until the publication of the results of CheckMate 141, not a single agent provided any survival benefit as a second line treatment for R/M HNSCC.

**Areas covered:** A comprehensive review of the literature was conducted on the role of nivolumab in HNSCC.

**Expert commentary:** Nivolumab is approved by the Food and Drug Administration for the treatment of patients based on the results of CheckMate 141 showing an overall survival benefit as compared to standard care (single agent docetaxel, methotrexate, or cetuximab). Of particular interest are immune-related adverse events which should be managed according to published guidelines.

**Database**

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Fitting the right non-vitamin K antagonist oral anticoagulant to the right patient with non-valvular atrial fibrillation: An evidence-based choice

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Annals of Medicine

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Abstract

Atrial fibrillation (AF) is the most prevalent arrhythmia and is associated with an increased risk of ischemic stroke (IS) and systemic embolism (SE). Stroke prevention is a key element for the overall management of AF patients. The non-vitamin K antagonist oral anticoagulants (NOACs), such as dabigatran, rivaroxaban, apixaban and edoxaban, are at least as effective as warfarin in reducing IS/SE with a lower rate of major bleeding. Various analyses from the large Phase III randomised trials demonstrated different efficacy and safety of NOACs in specific subgroups of patients. The randomised trials are supplemented by effectiveness and safety data from real world observational cohorts following the availability of these drugs for use in everyday clinical practice. Given the clinical heterogeneity of AF patients, the available data from trials and real-world studies allow us to fit the right NOAC to the particular patient’s characteristics, with the aim of optimising outcomes for individual patient. This review article aims to provide a summary of the evidence on the performance of NOACs in AF patients with specific clinical characteristics. Evidence-based suggestions are presented to provide a simple and viable strategy for clinicians for the choice of a particular NOAC.

Database

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Abstract

OBJECTIVE. The purpose of this study is to evaluate the diagnostic accuracy of a process incorporating computer-aided detection (CAD) for the detection and prevention of retained surgical instruments using a novel nondeformable radiopaque μTag.

MATERIALS AND METHODS. A high-specificity CAD system was developed iteratively from a training set (n = 540 radiographs) and a validation set (n = 560 radiographs). A novel test set composed of 700 thoracoabdominal radiographs (410 with a randomly placed μTag and 290 without a μTag) was obtained from 10 cadavers embedded with confounding iatrogenic objects. Data were analyzed first by the blinded CAD system; radiographs coded as negative (n = 373) were then independently reviewed by five blinded radiologists. The reference standard was the presence of a μTag. Sensitivity and specificity were calculated. Interrater agreement was assessed with Cohen kappa values. Mean (± SD) image analysis times were calculated.

RESULTS. The high-specificity CAD system had one false-positive (sensitivity, 79.5% [326/410]; specificity, 99.7% [289/290]). A combination of the CAD system and one failsafe radiologist had superior sensitivity (98.5% [404/410] to 100% [410/410]) and specificity (99.0% [287/290] to 99.7% [289/290]), with 327 (47%) radiographs not requiring immediate radiologist review. Interrater agreement was almost perfect for all radiologist pairwise comparisons (κ = 0.921–0.992). Cumulative mean image analysis time was less than one minute (CAD, 29 ± 2 seconds; radiologists, 26 ± 16 seconds).

CONCLUSION. The combination of a high-specificity CAD system with a failsafe radiologist had excellent diagnostic accuracy in the rapid detection of a nondeformable radiopaque μTag.
Abstract

OBJECTIVE. The purpose of this article is to provide radiologists with an introduction to the imaging appearances of various types of penile prostheses and discuss imaging pitfalls.

CONCLUSION. Two major types of penile prostheses currently are in use: malleable penile prostheses and inflatable penile prostheses. Sonography is useful in the assessment of the pelvic reservoir and scrotal pump. MRI helps in the complete evaluation of all the prosthetic components, making it a “one-stop shop” imaging technique.

Database

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