Abstract

Chitosan is one of the low toxic and natural polysaccharides which is obtained from deacetylation of chitin. Chitosan-based nanoparticles have good biodegradation and bio-distribution in the biological milieu, which have made it as one of the most attractive nanocarriers for delivering different therapeutic agents to the tumour cells especially ovarian cancer cell lines. Chitosan can covalently and non-covalently be modified and attached to different polymers and targeting moieties through its free amine groups and reach to the tumour site through passive and active targeting strategies. Ovarian cancer is one of the most common and resistant cancers with poor prognosis among women, which scientists are trying to prepare new methods for improving their treatments outcomes in past decades. In this article, we tried to take an overview on the recent developments in different modifications of chitosan-based nanoformulations, which are utilised for ovarian cancer therapy.
Title: The Angel catheter for the prevention of pulmonary embolism: combining an IVC filter and a triple-lumen central venous catheter

Author: Kira Achaibar, Carl Waldmann & Fabio Silvio Taccone

Journal: Expert Review of Medical Devices

Volume: Accepted author version posted online: 14 Feb 2019

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Abstract

Introduction: Pulmonary embolism is common in critical care patients and carries significant morbidity and mortality. Concurrent risk of severe bleeding in this population may prohibit anticoagulation.

Areas covered: The Angel Catheter device is a central venous catheter combined with an inferior vena cava filter inserted at the bedside for pulmonary embolism prevention. Our review examines the role of this device, safety, efficacy and the limitations it presents.

Expert opinion: We conclude the Angel catheter should be considered in critical care patients with significant risk of pulmonary embolus as bridging therapy until anticoagulation can be safely resumed.

Database

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Abstract

Aim: To propose a system for convenience in using CAPTCHA by the Visually Impaired person.

Method: To make this access secure CAPTCHA (“Completely Automated Public Turing test to tell Computers and Humans Apart”) was invented. This form of CAPTCHA requires that the user type the letters of a distorted image, sometimes with the addition of an obscured sequence of letters or digits that appears on the screen. This traditional method receives many criticism from the disable people. Hence a finger print based CAPTCHA is introduced.

Result: A CAPTCHA MONSTER, a convenient system of breaking CAPTCHA for the Visually Impaired is Proposed.

Conclusion: Thus in this proposed system, it is possible to access the web services on websites for various day to day applications by effective authentication procedure.

Database

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Abstract

**Background:** The burden of mental illness (MI) is exacerbated when adolescents with MI are confronted with stigma and social exclusion. Adolescents face the difficult decision whether or not to disclose their MI. Focus groups (FGs) were conducted with parents of adolescents with MI as well as with teachers, mental health professionals (MHPs) and adolescents without MI.

**Aim:** To collect information from relevant stakeholders on secrecy versus disclosure of MI among adolescents.

**Methods:** Thirteen FG sessions with 87 participants were recorded, transcribed and analyzed using qualitative content analysis to identify major themes.

**Results:** Selective disclosure and social media as a potential way of disclosure emerged as dominant themes. Negative aspects of disclosure on social media were discussed. Stigma and labeling were seen as disadvantages of disclosure. Social support was perceived as one advantage of disclosure. Distinctive features of adolescence, such as self-discovery, appeared as specific problems. Parents, teachers, MHPs and adolescents without MI were considered important for disclosure. Participants discussed how to help adolescents with their dilemma between disclosure and secrecy.

**Conclusions:** The findings suggest that disclosure decisions are personal and influenced by the individual’s environment. Implications for interventions that aim to support adolescents with MI in this regard are discussed.
Title: 4β-Hydroxycholesterol as an Endogenous Biomarker for CYP3A Activity: Literature Review and Critical Evaluation

Author: Scott R. Penzak PharmD Carlos Rojas-Fernandez PharmD

Journal: The Journal of Clinical Pharmacology

Volume: Version of Record online: 12 February 2019

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Abstract

A number of cytochrome P450 (CYP)3A phenotyping probes have been used to characterize the drug interaction potential of new molecular entities; of these, midazolam has emerged as the gold standard. Recently, plasma 4β-hydroxycholesterol (4β-OHC), the metabolite of CYP3A-mediated cholesterol metabolism, has been championed as an endogenous biomarker for CYP3A, particularly during chronic conditions where CYP3A activity is altered by disease and in long-term treatment studies where midazolam administration is not optimal. Multiple studies in humans have shown that 4β-OHC can qualitatively differentiate among weak, moderate, and potent CYP3A induction when an inducer, typically rifampin, is administered for up to 2 weeks. Conversely, longer durations of CYP3A inhibitor administration (≥1 month) appear to be necessary to differentiate among weak, moderate, and potent CYP3A inhibitors. A number of studies have reported statistically significant linear relationships between 4β-OHC plasma concentrations (and 4β-OHC:cholesterol ratios) and midazolam clearance. However, sufficiently powered studies assessing the ability of 4β-OHC or 4β-OHC:cholesterol ratios to measure CYP3A activity (ie, predictive performance) have not been conducted to date. Additional limitations associated with 4β-OHC phenotyping include inability to detect acute changes in CYP3A activity, uncertainty with regard to its intestinal formation, ambiguity surrounding the role of CYP3A5 in its metabolism, and lack of clarity regarding the role of transporters in its disposition. As such, the data do not support the use of 4β-OHC or 4β-OHC:cholesterol ratios as an endogenous biomarker for CYP3A activity.

Database

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Abstract

Osteosarcoma, including spinal osteosarcoma, has properties of high degree of malignancy, high rate of recurrence, and high incidence of metastasis. microRNAs can exert oncogenic or tumor suppressive roles in cancer cells. This study explored the effects of microRNA-493-5p (miR-493-5p) on osteosarcoma cell viability, migration, invasion, and apoptosis, as well as the underlying possible mechanism. First, the expression of miR-493-5p in osteosarcoma tissues and cells was detected using quantitative reverse transcription polymerase chain reaction (qRT-PCR). Then, the effects of miR-493-5p overexpression (or suppression) on osteosarcoma cell viability, migration, invasion, and apoptosis, as well as Kruppel-like factor 5 (KLF5) expression, were assessed using the Cell Counting Kit-8 assay, two-chamber transwell assay, Annexin V-FITC/PI apoptosis detection kit, qRT-PCR, and western blotting, respectively. Finally, the roles of KLF5 in miR-493-5p suppression-induced U2OS cell viability, migration, and invasion enhancement, as well as the PI3K/AKT pathway activation, were evaluated. We found that miR-493-5p had lower expression in tumor tissues of spinal osteosarcoma and osteosarcoma cells. Overexpression of miR-493-5p inhibited osteosarcoma U2OS cell viability, migration, and invasion, but induced cell apoptosis. On the contrary, suppression of miR-493-5p promoted U2OS cell viability, migration, and invasion. KLF5 was a direct target gene of miR-493-5p, which participated in the effects of miR-493-5p on U2OS cell viability, migration, invasion, and apoptosis. Furthermore, suppression of the miR-493-5p activated PI3K/AKT pathway in U2OS cells by upregulating KLF5. In conclusion, we revealed that miR-493-5p exerted tumor suppressive roles in spinal osteosarcoma and osteosarcoma cells. Overexpression of miR-493-5p inhibited proliferation and metastasis of osteosarcoma cells by downregulating KLF5 and inactivating the PI3K/AKT signaling pathway.
Abstract

Objectives: Our main aim was to investigate the short-term therapeutic effects, safety/tolerability and potential side effects of the cannabis galenical preparation (Bedrocan) in patients with a range of chronic conditions unresponsive to other treatments.

Methods: In this retrospective, ‘compassionate use’, observational, open-label study, 20 patients (age 18–80 years) who had appealed to our ‘Second Opinion Medical Consulting Network’ (Modena, Italy), were instructed to take sublingually the galenical oil twice a day for 3 months of treatment. The usual starting dose was low (0.5 ml/day) and gradually titrated upward to the highest recommended dose (1 ml/day). Tolerability and adverse effects were assessed at baseline and monthly thereafter during the treatment period through direct contact (email or telephone) or visit if required. Patients’ quality of life was evaluated at baseline and 3 months using the medical outcome short-form health survey questionnaire (SF-36).

Key findings: From baseline to 6 months post-treatment, SF-36 scores showed: reductions in total pain (P < 0.03); improvements in the physical component (P < 0.02); vitality (P < 0.03); social role functioning (P < 0.02); and general health state (P < 0.02). No changes in role limitations (P = 0.02) due to emotional state (e.g. panic, depression, mood alteration) were reported. Monthly reports of psychoactive adverse effects showed significant insomnia reduction (P < 0.03) and improvement in mood (P < 0.03) and concentration (P < 0.01).

Conclusions: These data suggest that a cannabis galenical preparation may be therapeutically effective and safe for the symptomatic treatment of some chronic diseases. Further studies on the efficacy of cannabis as well as cannabinoid system involvement in the pathophysiology are warranted.
Abstract

Objectives: Biopharmaceutical innovation is highly dependent on a period of exclusive marketing after approval, to cover the costs of research and development programs. Longer R&D programs are not, however, associated with longer periods of exclusive marketing. Instead exclusivity dwindles with each additional month of pre-commercialization research — an innovation paradox.

Methods: Drawing on the length of premarket programs from 1984 to 2016 using a dataset of regulatory milestones made public through FDA’s implementation of the patent term restoration provisions of the 1984 Hatch-Waxman statute, this article explores the impact of the innovation paradox on drug research and development decisions.

Key Findings: Lengthy clinical testing periods can lead to shortened effective patent life.

Conclusions: If the length of the pre-market process correlates with particular drug types, disease targets, or studied outcomes, we may be offering an inadequate incentive in entire areas of medicine where we have a critical need for new treatments.
Title: Overstated Harms of Breast Cancer Screening? A Large Outcomes Analysis of Complications Associated With 9-Gauge Stereotactic Vacuum-Assisted Breast Biopsy

Author: Leng Leng Young Lin, et al.

Journal: American Journal of Roentgenology

Volume: Ahead of Print: Feb 11, 2019

Doi: https://doi.org/10.2214/AJR.18.20421

Abstract

OBJECTIVE. The purpose of this study was to assess the rate, type, and severity of complications related to 9-gauge stereotactic vacuum-assisted breast biopsy (SVAB) and to delineate associated factors that may contribute to a higher rate of complications.

MATERIALS AND METHODS. This retrospective study included 4776 patients who underwent SVAB between 2003 and 2016. A total of 319 patients with documented postbiopsy complications were identified. Complications were subcategorized as bleeding, pain, lightheadedness, bruising, and other complications, and their severity was classified as minor, moderate, or severe. Hematoma volumes were correlated with biopsy location and complication severity. A group of control subjects who underwent SVAB but had no complications was compared with the group of study patients with regard to age, biopsy location, lesion type, and pathologic findings. Postbiopsy screening adherence was assessed. Statistical analyses were performed using the Fisher exact, Mann-Whitney, Kruskal-Wallis, and Spearman rank correlation tests.

RESULTS. Of the 319 patients with complications who were identified (representing 6.7% of the 4776 patients who underwent SVAB), 307 (96.2%) had mild complications, 12 (3.8%) had moderate complications, and no patients had severe complications. The most common complication was bleeding or hematoma (89.3% of patients [285/319]), followed by pain (6.9% [22/319]), lightheadedness (0.9% [3/319]), bruising (0.9% [3/319]), and other complications (1.9% [6/319]). No significant differences were noted between the study group and the control group in terms of age (p = 0.474), biopsy location (p = 0.065), histologic findings (p = 0.056), or lesion type (p = 0.568). Hematoma volume (median, 7.5 cm³) did not correspond to the severity of complications. Larger hematoma volumes were associated with a posterior biopsy location (p = 0.008). The rate of return to annual screening after biopsy was not adversely affected by the presence of biopsy complications.

CONCLUSION. Clinically significant complications associated with SVAB were exceedingly rare (0.3%) in this large study spanning 13 years.

Database

American Roentgen Ray Society,
Thymic size is increased by infancy, but not pregnancy, nutritional supplementation in rural Gambian children: a randomized clinical trial

Sophie E. Moore, Anthony J. C. Fulford, Fatou Sosseh, Patrick Nshe, Momodou K. Darboe and Andrew M. Prentice

BMC Medicine

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Abstract

Background: Thymic size in early infancy predicts subsequent survival in low-income settings. The human thymus develops from early gestation, is most active in early life and is highly sensitive to malnutrition. Our objective was to test whether thymic size in infancy could be increased by maternal and/or infant nutritional supplementation.

Methods: The Early Nutrition and Immune Development (ENID) Trial was a randomized 2 × 2 × 2 factorial, partially blinded trial of nutritional supplementation conducted in rural Gambia, West Africa. Pregnant women (N = 875) were randomized to four intervention groups (iron-folate (standard care), multiple micronutrients, protein energy or protein energy + multiple micronutrients at ‘booking’ (mean gestational age at enrolment = 13.6 weeks, range 8–20 weeks) until delivery. The iron-folate and multiple micronutrient arms were administered in tablet form and the protein energy arms as a lipid-based nutritional supplement. All intervention arms contained 60 mg iron and 400 μg folic acid per daily dose. From 24 to 52 weeks of age, infants from all groups were randomized to receive a daily lipid-based nutritional supplement, with or without additional micronutrients. Thymic size was assessed by ultrasonography at 1, 8, 24 and 52 weeks of infant age, and a volume-related thymic index calculated. Detailed data on infant growth, feeding status and morbidity were collected.

Results: A total of 724 (82.7%) mother-infant pairs completed the trial to infant age 52 weeks. Thymic size in infancy was not significantly associated with maternal supplement group at any post-natal time point. Infants who received the daily LNS with additional micronutrients had a significantly larger thymic index at 52 weeks of age (equivalent to an 8.0% increase in thymic index [95% CI 2.89, 13.4], \( P = 0.002 \)). No interaction was observed between maternal and infant supplement groups.

Conclusions: A micronutrient-fortified lipid-based supplement given in the latter half of infancy increased thymic size, a key mediator of immune function. Improving the micronutrient status of infants from populations with marginal micronutrient status may improve immune development and survival.

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