BRANCHES OF PHARMACOLOGY

1. Decide in which branch of pharmacology texts belong.

2. Explain what the text is about and summarize what is the branch of pharmacology studying.

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Original Research Article

Cardiology department hospitalization costs in patients with acute heart failure vary according to the etiology of the acute heart failure: Data from the AHEAD Core registry 2005–2009

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Background: To assess the distribution of costs associated with Cardiology Unit hospitalization due to acute heart failure (AHF) and evaluate, from the perspective of the healthcare payer, the heterogeneity of resources use according to AHF etiology in patients from 2005 to 2009.
Methods: The type and etiology of AHF was determined upon hospital admission. The cost of in-patient care was based on the individual hospital account of each patient (1759 patients in total; 58.7% male; mean age 71 years).
Results: The median hospital stay was 7 days and the mean total cost of in-patient care was €3364. A Coronary Care Unit (CCU) stay was recorded in 67.4% patients (median 3 days). Significantly higher costs were found in de-novo AHF patients (mean €3678) with a greater need for CCU care, a longer stay in the CCU and a greater need for intervention (particularly that of percutaneous coronary intervention (PCI)), than in patients with acute decompensation of chronic heart failure (mean cost €2878; $p<0.001$). Acute coronary syndrome was a major precipitating factor, with the highest costs (€4429) resulting from having received PCI (63.3% of patients) and CCU admission (91.7% of patients). Variations in length of stay according to AHF etiology were minor (median, 6–8 days). In-hospital mortality was 15.0%.

https://www.sciencedirect.com/science/article/pii/S0010865012001154?via%3Dihub

[Prescription to elderly patients: reducing underuse and adverse drug reactions and improving adherence].

(PMID:17969547)

Legrain S

Bulletin de L'Academie Nationale de Medecine [01 Feb 2007, 191(2):259-69; discussion 269-70]

Type: Comparative Study, English Abstract, Journal Article (lang: fre)

Abstract

Many elderly people take multiple medications, usually for multiple health disorders. This "polymedication" increases the risk of iatrogenic disorders, may affect adherence to treatment, and represents an economic burden for society. It is therefore essential to optimize drug prescription to the elderly. The general practitioner is most involved in treating the elderly, who tend not to consult specialists as frequently as younger adults do. Most elderly subjects with comorbidities and polymedication are excluded from clinical trials, and geriatrics is not considered a priority during medical training. Three suboptimal prescription modalities have been described in the elderly population : "overuse", "misuse", and "underuse". Adverse drug reactions are frequent in the elderly and have a major economic cost. They are behind about 10 % of hospital admissions over the age of 65, and 20 % over 80. Yet most advers drug reactions are preventable. The public health consequences of non adherence to drug therapy are poorly documented. Elderly people may have several risk factors for non adherence, and a combination of measures may be necessary to improve the situation.

Effect of Endocannabinoid Oleamide on Rat and Human Liver Cytochrome P450 Enzymes in In Vitro and In Vivo Models

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ABSTRACT

The endocannabinoid system is important for many physiologic and pathologic processes, but its role in the regulation of liver cytochromes P450 (P450s) remains unknown. We studied the influence of the endocannabinoid oleamide on rat and human liver P450s. Oleamide was administered intraperitoneally to rats at doses of 0.1, 1, and 10 mg/kg per day for 7 days. The content and activity of key P450s were evaluated in rat liver microsomes. Moreover, interactions with nuclear receptors regulating P450 genes and serum levels of their ligands (prolactin, corticosterone, and free triiodothyronine) were tested in in vitro P450 inhibition assays. Decreased protein levels and metabolic activities of CYP1A2, CYP2B, and CYP2C11, along with a drop in metabolic activity of CYP2D2, were observed in animals treated with oleamide (10 mg/kg per day). The activities of CYP2C6, CYP2A, and CYP3A and the levels of hormones were not altered. In vitro, oleamide exhibited a weak inhibition of rat CYP1A2, CYP2D2, and CYP2C6. The activities of rat CYP2A, CYP2B, CYP2C11, and CYP3A and human CYP1A2, CYP2B6, CYP2C9, and CYP3A4 were not altered. Oleamide did not interact with human pregnane X, constitutive androstane, or aryl hydrocarbon receptors in reporter gene experiments and did not regulate their target P450 genes in primary human hepatocytes. Our results indicate that oleamide caused the downregulation of some rat liver P450s, and hormones are not mediators of this effect. In vitro oleamide inhibits mainly rat CYP2C6 and is neither an agonist nor antagonist of major human nuclear receptors involved in the regulation of xenobiotic metabolism.

http://dmd.aspetjournals.org/content/dmd/46/6/913.full.pdf

ClinicalEvidence

Paracetamol (acetaminophen) poisoning

Search date October 2014

B. Kevin Park, James W. Dear, and Daniel J. Antoine

Paracetamol is the most common drug used for self-poisoning in the UK. [1] It is also a common means of self-poisoning in the rest of Europe, North America, and Australasia. In the UK, around 98,000 patients attend emergency departments each year with paracetamol poisoning and around 49,000 are admitted for treatment. [2] Overdoses from paracetamol alone directly result in an estimated 150 to 200 deaths and 15 to 20 liver transplants each year in England and Wales (data from routinely collected health and coronial statistics). [3] [4] Pack-size restrictions instituted in the UK in 1998 resulted in modest reductions in large overdoses, liver transplants, and deaths in England and Wales. In Scotland, the reduction in admissions and mortality from paracetamol overdose was short lived. [3] [4]

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4610347/pdf/2015-2101.pdf

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4. Ustekinumab

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The psoriasis immunopathogenesis has provided new therapeutic options in recent years [7]. Among recent breakthroughs, ustekinumab (Stelara, Janssen Pharmaceutica, Beerse, Belgium) is a fully human monoclonal antibody of the IgG1 class. It is directed to the shared p40 subunit of both IL-12 and IL-23 [41–43]. Thus, the drug neutralizes the bioactivities of both cytokines by blocking interaction with the IL-12R β1 cell surface receptor. The pharmacological characteristics and both the clinical efficacy and tolerability of ustekinumab are clearly proven in patients with chronic moderate to severe plaque psoriasis, including subjects with psoriatic onychopathy and psoriatic arthritis [8, 43–46].

IL-23 expression is significantly increased in the psoriatic epidermis [5, 38]. IL-23 messenger RNA expression is significantly higher in lesional skin of psoriatic patients as compared with healthy skin in the same patients [5, 38]. IL-23 secretion by monocytes and mature dendritic cells derived from patients with psoriasis is unusually high [38]. This cytokine promotes survival and proliferation of Th17 cells [47–51]. As a result, Th17 cytokines, such as IL-17, stimulate keratinocyte proliferation enabling further stimulation of keratinocyte proliferation in psoriatic lesions [6, 29].

The therapeutic efficacy of ustekinumab is obtained after IL-12 and IL-23 inhibition leading to the abated expression of cell surface markers associated with skin homing (CLA), activation of anti-inflammatory cytokines including IL-5, and inhibition of the secretion of the proinflammatory cytokines IFNγ, IL-2, IL-8, IL-10, IL-17A, and TNFα. A reduction in CD4+ Th cells and NK cells was reported after a single dose of ustekinumab. However, changes varied across time and did not appear to be dose dependent. Ustekinumab pharmacokinetics is notably affected by body weight. This aspect is particularly important to consider in case of metabolic syndrome comorbidity.

J Biomed Biotechnol

Current recommended vancomycin dosing regimens in pediatric patients (40-60 mg/kg/day), result frequently in subtherapeutic concentrations.[33] Febrile neutropenia, a significant risk factor for augmented renal clearance in this subpopulation, indirectly influenced vancomycin clearance (Clvan) due to increased glomerular filtration rate (GFR). Increasing the initial dose is, therefore, required for achieving optimal therapeutic concentrations in pediatric patients with febrile neutropenia.[34] The probability of achieving an AUC/MIC >400 using only one trough serum concentration and one minimum inhibitory concentration (MIC) in patients receiving 15 mg/kg every 6 hours is variable according to the method used to calculate AUC. In children, an AUC/MIC of 400 correlates with a Ctrough of 11 mg/L using a trapezoidal method to calculate AUC.[35]

For pediatric patients, monitoring of vancomycin Ctroughs is a recommendation stated in the summary of product characteristics and by several professional societies.[3] During a study where vancomycin TDM was performed and 7935 vancomycin concentrations were obtained, the median Ctrough increased from 10.9 to 13.7 mg/L,[36] which agrees with the recommendations published by the Infectious Disease Society of America.[2] These data suggest that vancomycin TDM is commonly performed in pediatric patients, and the majority of abnormal Ctroughs are associated with appropriate modifications of the dosing regimen.[36] Nevertheless, vancomycin TDM practices are reported to be highly variable in children admitted to pediatric hospitals.[37] The frequency with which serum vancomycin concentrations were monitored in children increased after the publication of the adult guidelines. This fact made some authors claim that the development of pediatric consensus guidelines is needed to optimize patient care and resource utilization.[37]

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6113434/

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Completed suicides of citalopram users-the role of CYP genotypes and adverse drug interactions.

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Abstract

Depression is known to be a risk factor for suicide. Currently, the most used antidepressants are selective serotonin reuptake inhibitors (SSRIs). Not all users, however, benefit from them. In such cases, treatment failure can be explained in part by genetic differences. In this study, we investigated the role of pharmacogenetic factors in citalopram-positive completed suicides (n = 349). Since citalopram is metabolized by CYP2C19 and CYP2D6 enzymes, the study population was genotyped for clinically relevant CYP2C19 and CYP2D6 polymorphisms and CYP2D6 copy number variation. To assess genetic differences between suicide cases and Finns in general, Finnish population samples (n = 855) were used as controls. Also, the role of drug interactions among suicide cases was evaluated. We found enrichment of a combined group of genetically predicted poor and ultrarapid metabolizer phenotypes (gMPs) of CYP2C19 among suicide victims compared to controls 0.356 [0.31-0.41] vs. 0.265 [0.24-0.30] (p = 0.0065). In CYP2D6 gMPs, there was no difference between cases and controls when the study population was analyzed as a whole. However, there were significantly more poor metabolizers among females who committed suicide by poisoning compared to female controls. In 8% of all drug poisoning deaths, lifetime drug-drug interaction was evaluated having a contribution to the fatal outcome. From clinical perspective, pharmacogenetic testing prior to initiation of SSRI drug could be beneficial. It may also be useful in medico-legal settings as it may elucidate obscure poisoning cases. Also, the possibility of unintentional drug interactions should be taken into account in drug poisoning deaths.

KEYWORDS: CYP2C19; CYP2D6; Citalopram; Drug interactions; Postmortem; Suicide

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