antagonists (49.41%), coumarins (45.88%) and statins (42.35%).

Comparing the differences and similarities of the therapy of DCM patients with NYHA class I to those with NYHA class IV, ACE-I use was relatively similar (37.14% to 39.1%), diuretics use increased (42.83% to 81.81%) and beta blockers use decreased (42.83% to 31.81%). The use of beta blockers was associated with an improvement of LVEF within 6 months from a median of 30% to 48%, in 27.37% of the patients.

Conclusion: Despite the lack of official guidelines, DCM patients received optimal treatment leading to the improvement of LVEF. Beta blockers, ACE-I and diuretics were the most frequently used drugs for the management of DCM patients, while cardiac glycosides angiotensin II receptor blockers and calcium channel blockers were less frequently used.

**CORRELATION BETWEEN DIABETIC CATARACT, HBA1C AND GURAKHU: A CLINICAL STUDY IN CHHATTISGARH STATE**

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**Introduction:** In diabetes mellitus, higher amounts of glycated hemoglobin, indicating poorer control of blood glucose levels, have been associated with cardiovascular disease, nephropathy, and retinopathy. Gurakhu’s basic components are nicotine and jaggery; jaggery is made up of sugarcane so can have a diabetogenic potential which is exacerbated in presence of nicotine. This work had done with the aim to find correlation between Diabetic cataract, HbA1c and Guraku.

**Material and Methods:** A cross sectional observational study of total 75 subjects had been performed. Data was collected from the prescriptions, medical history and self designed questionnaire. The subjects were enrolled according to the inclusion and exclusion criteria.

**Results:** In the study it was found that people consuming Guraku had a high level of HbA1c thus are more prone to the development of diabetic cataract. Male subjects (57%) are the more than female subjects (43%). Most of the subjects belong to the lower socioeconomical class and not very educated. Average blood glucose (29%), Subjects with high level of HbA1c (40%) and subjects with high level of Glucose tolerance value (30%) in diabetic cataract were observed.

**Conclusion:** It could be concluded that this type of study could be useful in identifying number of subjects suffering from diabetic cataract whose condition get worse by use of nicotine product like Guraku and preventive measure to be taken in prevention of this type of diabetic complication.

**Key words:** Diabetic cataract, HbA1c, Guraku, Diabetogenic potential

**PHARMACOKINETIC ISSUES IN OBSESE PATIENTS**

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**Introduction:** Obesity is associated with several pathophysiological changes that may interfere with pharmacokinetic properties of drugs including increased plasma volume, fatty liver disease, and changes in glomerular filtration rate (GFR). Drastic weight changes with bariatric surgery further complicate the issue. Correct drug dosing in obese patients, particularly following bariatric surgery, therefore appears a difficult task.

**Material and Methods:** We reviewed and summarized relevant literature and available information on drug-disease interaction and pharmacokinetic alterations associated with obesity and bariatric surgery.

**Results:** Adipose tissue accumulation, changes in regional blood flow, and changes in plasma protein binding capacities change the volume of distribution of drugs in obese patients. Additionally, cytochrome P450 enzyme activities may be changed, although not in a consistent manner. For example, CYP3A4 activity appears to be decreased in obesity, but 1 year after bariatric surgery, metabolism of CYP3A4-dependent drugs is enhanced despite the loss of intestinal CYP3A4 activity through surgery. GFR is transiently increased in early obesity and then tends to decline secondary to glomerular damage that develops with longstanding obesity. Several examples for dose adjustment suggestions were identified in the literature, many not based on solid evidence. Pharmacokinetic consequences of bariatric surgery and implications for drug therapy are divergent and individually influenced by type of surgery, drug properties and potential intestinal adaptions after surgery.

**Conclusions:** We identified a tremendous knowledge gap caused by the lack of appropriate studies regarding dose adjustments in obesity and after bariatric surgery. The lack of knowledge poses a safety concern in massively obese subjects, particularly for drugs with a small therapeutic window.

**PREDICTIVE ABILITY OF DIFFERENT ANALYTICAL PARAMETERS IN MYCOPHENOLATE PHARMACOKINETICS AND DOSING**

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**Background:** Mycophenolate (MPA), antimetabolite immunosuppressant of choice in solid organ transplant regimens, is available in two compounds (mofetil and sodium) and displays large between-subject pharmacokinetic (PK) variability. The aim of this study was to identify and model the different factors influencing MPA variability.

**Methods:** Patients treated with oral mycophenolate (mofetil or sodium) in our institution and having a record of drug serum levels were included in this observational, cross-over study over a period of six years (2004–2010). Both biodemographic (age, sex, weight, height, ethnicity) and analytical data (creatinine, total and direct bilirubin) were collected. Renal function was assessed by CKD-EPI formula. The influence of these variables on mycophenolate pharmacokinetics was evaluated following a multiple linear regression model.

**Results:** Data from 136 patients, treated with mycophenolate mofetil (64%) or sodium (36%), were included; mean age 53 years, 67% men. Dose values MPA/kg and minimum plasma drug concentration (Cmin), in addition to serum creatinine and bilirubin - total and direct - were [mean (SD)] 11 mg/kg (3.6), 2.43 mg/mL (1.61), 1.69 mg/dL (3.10), 0.61 mg/dL (0.28), 0.28 mg/dL (0.10), respectively. Mean renal function was 58.8 mL/min/1.73 m² (23.2), according CKD-EPI formula. The regression analysis showed that 19.4% of Cmin variation can be explained by the different drug formulation (P = 0.018) and the individual clearance pattern of each patient - renal (P = 0.001) and hepatic function (P = 0.033).

**Conclusions:** MPA formulation, as well as renal (CKD-EPI) and hepatic function (total bilirubin), were the covariates identified as influencing MPA Cmin. Therefore, individualisation of MPA treatment using a forecasting model to assess target concentration that contemplates these factors must be considered in preference to giving a standard dose.

**COMPARATIVE SAFETY PROFILE OF AMOXICILLIN ALONE AND IN ASSOCIATION WITH CLAVULANIC ACID IN PEDIATRICS: DATA FROM SPONTANEOUS REPORTING IN ITALY**

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**Introduction:** Amoxicillin (A) and amoxicillin-clavulanic acid (A/C) are commonly used in the treatment of a wide range of infections in pediatric patients, with the latter drug being available in various dosage forms.

**Objectives:** The objective of this study was to evaluate the safety profile of A and A/C in pediatric patients, based on data reported through the Italian spontaneous reporting system.

**Methods:** A retrospective analysis of spontaneous reports received by the Italian Pharmacovigilance Centre (CIP) from January 2004 to December 2011 was conducted. Reports involving A and A/C were included.

**Results:** A total of 407 reports were analyzed, of which 203 were for A and 204 for A/C. The most commonly reported adverse events were allergic reactions (19%), gastrointestinal symptoms (16%), and hepatic disorders (14%). A/C was associated with a slightly higher incidence of allergic reactions and abdominal pain compared to A.

**Conclusions:** The safety profile of A and A/C in pediatric patients was generally acceptable. However, close monitoring is recommended for patients at risk of allergy, particularly those with a history of penicillin allergy.

**Acknowledgments:** This study was supported by the Italian Pharmacovigilance Centre (CIP).
Background or Introduction: Amoxicillin alone and with clavulanic acid are among the most prescribing antibacterial agents in Italy. These drugs are generally well tolerated and usually prescribed by paediatrics, although published studies indicate that they are frequently associated with adverse drug reactions (ADRs), in particular cutaneous and gastrointestinal ones. We analyzed the Italian database of spontaneous reporting of suspected ADRs in order to compare the safety profile of amoxicillin and amoxicillin/clavulanic acid (amoxiclav) in pediatrics.

Material and Methods: Reports of suspected ADRs due to amoxicillin and amoxi-clav in pediatric patients, until 1 September 2014, were extracted. ADRs were coded using MedDRA terminology. To evaluate the correlation between drug use and occurrence of ADRs a disproportionality analysis through Reporting Odds Ratio (ROR) was performed.

Results: We collected 3,345 reports associated with amoxicillin and amoxicillin/clavulanic acid, 1.188 (35.5%) related to amoxicillin and 2.157 (64.5%) to amoxicillin with clavulanic acid. The percentages of serious ADRs were 12% for amoxicillin and 16% for amoxiclav. The percentage of skin reactions was higher for amoxicillin (75%) than for amoxicillin/clavulanic acid (67%) and for gastrointestinal reactions was higher for amoxicillin/clavulanic acid (16%) than for amoxicillin (10%). For amoxicillin, significant disproportionality was observed only for cutaneous ADR like dermatitis (ROR, 2.35; 95% CI, 1.26–4.25), rash (1.30; 1.08–1.57), erythematous rash (1.70; 1.18–2.45). For amoxicillin/clavulanic acid was observed only for gastrointestinal ADR: diarrhoea (1.56; 1.15–2.12), abdominal pain (2.11; 1.14–3.93) and sickness (1.69; 1.20–2.38).

Conclusions: Our analysis shows a different safety profile for amoxicillin and amoxi-clav in pediatrics: the first is associated with a higher risk of skin reactions while the amoxi-clav with gastrointestinal ADR. We found a disproportionality analysis through step analysis of how participants per group went through the 6Step route, visualized by a matrix method and yielded various step-patterns.

CARDIOPROTECTIVE PROPERTIES OF POLYPHENOL CONCENTRATE IN RAT MODEL OF DOXORUBICIN-INDUCED CARDIOMYOPATHY

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Purpose: Present study aimed to investigate possible cardioprotective properties of polyphenol concentrates obtained from Cabernet Sauvignon type of Kazakhstani grapes using rat model doxorubicin-induced cardiomyopathy.

Methods: Study was conducted on 20 white outbred female rats weighing 160±20 g. that were divided into three groups: two groups with cardiomyopathy (14 rats) and one intact group (6 rats).

Cardiomyopathy was obtained by i.p. administration of doxorubicin (8.0 mg/kg). The experimental group (7 rats) was receiving intragastrically 0.5 ml of polyphenols concentrate during the next 7 days after injection of doxorubicin. The control group of animals with cardiomyopathy (7 rats) was not treated. Activity of aspartate aminotransferase (AST) was determined in plasma. An oxidative status in rats’ blood plasma was analyzed with 4 FRAS (Evolve srl, Italy) using d-ROMs Test, which indicates the amount of free radicals, and PAT Test, which characterizes total antioxidant activity of blood plasma.

Results: The AST content, a measure of cytolysis, was higher for 22% in animals with doxorubicin cardiomyopathy than in the intact animals. Administration of polyphenols restored the AST content degree to normal values. The d-ROMs test showed an activation of oxidative stress in control group compared to the intact animals by 24%, whereas the administration of polyphenols decreases oxidative stress activity by 12%. In comparison with intact animals, rats with cardiomyopathy had a decrease in antioxidant potential by 28% according to the PAT Test. However, the treated with polyphenols group had 9% higher total antioxidant activity than the control group.

Conclusion: A concentrate of polyphenols obtained from Cabernet Sauvignon prevents reduction of the total antioxidant activity of plasma, limits the development of oxidative stress, and prevents cytolytic processes in rats with doxorubicin cardiomyopathy.