PP033—EFFECTS OF PREGABALIN ON DRIVING

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Introduction: Pregabalin, an agent in treating partial epilepsy and peripheral neuropathic and central pain, was studied for its effect on driving performance in healthy volunteers. The study was approved by the ethical committee of Ehime University Hospital. Written informed consent was obtained from the volunteers before participation in the study, which was performed in accordance with the principles of the Declaration of Helsinki.  
Patients (or Materials) and Methods: Sixteen regularly driving, healthy male volunteers were enrolled for a double-blind placebo control study of pregabalin on driving performance. Driving simulator was used to test the simple and complicated braking reaction time, simple and complicated steering wheel techniques. Pregabalin was also evaluated for the effect of training on driving tests.  
Results: The mean (SD) age of pregabalin and placebo groups were 26.0 (2.9) and 28.6 (3.5) years, respectively. The body weight, plasma creatinine level, and eGFR of pregabalin group were 69.0 (4.7) kg, 0.8 (0.04) mg/dL, and 94.1 (5.7) mL/min, respectively. The body weight, plasma creatinine level, and eGFR of placebo group were 62.16 (4.6) kg, 0.8 (0.05) mg/dL, and 96.7 (6.5) mL/min, respectively. Six members of the pregabalin group and 2 members of placebo group reported sleepiness. The other 2 members of the pregabalin group presented somnolence during driving. All the subjects showed no serious adverse effects. There were no significant differences of both simple and complicated braking reaction time between pregabalin and placebo groups. The simple and complicated wheel techniques also showed no differences between pregabalin and placebo groups. In comparing the effect of training on the driving performance, the placebo group showed the improvement in the test of simple steering wheel technique. The number of errors in handling wheel detected 1 hour and 2 hours from the baseline showed significantly reduction compared with the baseline data. However, the pregabalin group showed no improvement in handling wheels with the training. Both pregabalin and placebo groups had no changes in both simple and complicated braking reaction time, and complicated handling wheel tests.  
Conclusion: In our study using driving simulator, pregabalin exhibited no serious central nervous system side effects in engaging driving, but caused mild effects to decrease the training of driving.  
Disclosure of Interest: None declared.

PP036—HEPATOTOXICITY IN ACUTE AND REPEATED SUPRATHERAPEUTIC PARACETAMOL INGESTION IN CHILDREN AND ADOLESCENTS. RETROSPECTIVE COHORT STUDY CONDUCTED BETWEEN 2005 AND 2010  
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Introduction: To calculate the incidence, describe the suspected cases of paracetamol poisoning, and determine the differences between the patterns of acute versus chronic ingestion in patients <18 years of age who were treated at a tertiary hospital.  
Patients (or Materials) and Methods: Retrospective cohort study of patients <18 years of age who were treated in the emergency department (pediatric and general) of the La Paz University Hospital for suspected paracetamol intoxication and for whom paracetamol serum level tests were requested.  
Results: Ninety-two (92) patients with suspected paracetamol poisoning were identified between 2005 and 2010. The incidence for 2007 was 1.53 cases (95% CI Poisson, 0.24–5.57) per 10,000 patients treated at the pediatric emergency department. The most common cause of poisoning was attempted suicide (47.8%), with a median age of 15 years, followed by accidental poisoning (42.2%), with a median age of 2.63 years. Following the assessment of causality, we found that 1 patient with acute poisoning showed a hepatic disorder secondary to paracetamol, while 7 of the 11 patients with chronic poisoning showed liver enzyme disorders secondary to paracetamol poisoning. The time required to find medical care was 6.83 hours for acute poisoning and 52.3 hours for chronic poisoning (P < 0.001).  
Conclusion: Chronic paracetamol poisoning is a potential risk factor for hepatotoxicity and ALF; delays in seeking medical help may be a contributing factor. The parents/guardians should therefore be notified of this fact, and the ED physicians’ clinical suspicion increased.  
Disclosure of Interest: None declared.

PP037—INJECTION OF PHARMACEUTICAL TABLETS OF BUPRENORPHINE: DIFFERENCES BETWEEN SUBUTEX® AND ITS GENERICS  
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Introduction: Mises de buprenorphine concern –30% of patients treated for drug detoxification in cases of opioid abuse. Injecting pills that are not intended for intravenous (IV) administration may have harmful consequences, particularly because of particles. The main difference between Subutex® and its generics concern the insoluble
PP038—SOY DIET CAUSES HISTOLOGICAL CHANGES ON THE REPRODUCTIVE ORGANS OF ADULT MALE RATS
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Introduction: Soy products are used in human diet and in food additives because of their beneficial effects in menopause and their potential protective effects in cancer and other diseases. Nevertheless, genistein and other phytoestrogens contained in soy may disrupt the endocrine system by modulating the hypothalamic-pituitary-gonadal axis, and thus they may influence spermatogenesis and reproduction. The objective of this study was to investigate the adverse effects of chronic soy diet on the histologic characteristics of the reproductive organs in adult male rats.

Patients (or Materials) and Methods: Two groups of adult male albino Wistar rats, 6 months old, were used: the study group and the control group. The study group received ad libidum food enriched in soy protein for 3 months. The control group received ad libidum the standard food for 3 months. Both groups were grown under the same conditions and according to the rules of Good Laboratory Practice. The study was approved by the local Ethics Committee. The animals of both groups were sacrificed, and specimens of the reproductive organs were prepared and stained for microscopic examination. The preparations were observed by 2 different persons, blinded to the source of the specimen. Statistical analysis was performed with the statistical package SPSS.

Results: The seminiferous epithelium of the testes was found lower and contained fewer layers of spermatocytes in the study group compared with the control group. Similar changes were observed in the epididymal epithelium and the epithelium of the vas deferens and the seminal vesicles of the study group. The number of spermatozoa in the seminiferous tubules of the testes, in epididymis, and in the vas deferens was much lower in rats fed with soy diet compared with the rats fed with standard food.

Conclusion: Chronic soy diet causes histologic changes in the reproductive organs and influences the number of spermatozoa in the testes of the adult rats. Diet containing phytoestrogens may influence male fertility and should probably be avoided in a chronic basis when pregnancy is desired.

Disclosure of Interest: None declared.

PP039—DIFFICULTIES IN PHARMACOVIGILANCE PRACTICES IN EUROPEAN NON-EU COUNTRIES AND THEIR DIFFERENCES FROM EU REQUIREMENTS
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Introduction: Enforcement of new EU Pharmacovigilance (PV) Regulation 1235/2010 and Directive 2010/84/EU, in July 2012, caused differences from local PV regulations of some European non-EU countries. Consequently, disturbances of PV practices have been caused at local affiliates of international pharmaceutical companies who based their operational procedures on local law aligned with EU Legislation.

Patients (or Materials) and Methods: The review and comparison of EU PV Legislation and Local PV Regulation of Serbia 64/2011 were done. Main differences are listed and their impact on local PV practice is presented. Local PV regulation of Serbia was chosen because: (1) authors are from Serbia; and (2) the local regulation is more complex than others in the region.

Challenges in local PV practices are presented based on experience of Janssen local safety unit (LSU).

Results: Main differences: (1) Pharmacovigilance System Master File (PSMF) and Summary of Pharmacovigilance System (SPS) vs. Detailed Description of Pharmacovigilance System (DDPS); (2) Periodicity and timelines for Periodic Safety Update Reports (PSUR) submission; (3) European Risk Management Plan (EU RMP) vs. RMP (4) Safety reports for renewals: Addendum Clinical Overview (ACO) vs. Summary Bridge Report (SBR) and Addendum report (AR); (1) According to EU legislation, SPS has to be submitted to European Medicines Agency and PSMF only in case of explicit requirement. According to local requirements, global and local DDPS are needed. SPS is not enough. PSMF accepted, but could not be requested. Appropriate global document is milestone to be compliant and to obtain approval/renewal license.

(2) Locally, periodicity, and timeline for PSUR submission are still “old.” However, Local Health Authority (LHA) accepts European Union Referens Dates (EURD) list for “centralized products” (CP) and for non-CP with renewals. Unevenness requires enhanced monitoring of PSUR periodicity and timelines and make compliance difficult.

(3) Locally, EU RMP is accepted. However, implementation is delayed since LHA based approval on EMA approval.

(4) Locally, SBR and AR is accepted for renewals. LHA tends to accept ACO, but currently, only as additional document. Consequences are additional effort and cost for Company to prepare SBR and AR, and ACO, in addition.

Overall, LHA has not had access to EudraVigilance database, and worldwide individual case safety reports have to be submitted to LHA by LSU, which is time-consuming.