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in severely obese diabetic patients having BS versus conventional/ intensive anti-diabetic therapy.\(^1\)\(^2\) Respectively, in these trials: patient numbers were 60 and 130, primary end points were 2-year HbA1C level ≤6.5% (with fasting glucose <100 mg/dL and no anti-DI pharmacotherapy) and 1-year HbA1C levels ≤6%, and surgical interventions were gastric bypass and biliopancreatic diversion and gastric bypass and sleeve gastrectomy. As previously described,\(^3\) we calculated respective unadjusted RC (akin to relative risk), NNT, and 95% CI values.

Results: The patients in these trials did not suffer any serious complications from their BS. Respective RC, NNT, and corresponding (CI) values were 8.5 (2.0–36.4) and 1.33 (1.08–1.74) and 3.2 (1.2–8.4) and 3.68 (2.42–7.68).

Conclusion: In the short-term (1–2 years), BS was a highly effective means of eliminating DM in these patients. The perceived success rate depended on the precise criteria used to define diabetes and the type of BS, but due to small sample sizes apparent statistical significance cannot be discerned with confidence.

Disclosure of Interest: None declared.

References

PP173—CYTISIN AMIDOPHOSPHATE SHOWS HEPATOPROTECTIVE EFFECT

T. Nurgozhin\(^1\); A. Gulyaev\(^2\); and A. Gazaliyev\(^3\)
\(^1\)Translational Medicine, Longevity and Global Health, Center for Life Sciences, Astana; and \(^2\)Chemistry, Karaganda State Technical University, Karaganda, Kazakhstan

Introduction: The problem of effective and rational treatment of no viral hepatitis is still actual. During several last years, the screening of the bioactivity of the list of semi-synthetic derivatives of alkaloid cytisine was held in our laboratories. The result was the synthesis of O,O dimethyl-N-cytinizylphosphate (cytisin amidophosphate). Hepatoprotective properties were noted on the several models of acute and chronic hepatitis. Purpose: to study the efficacy and safety of cytisin amidophosphate under the name of Cytaphat in patients with toxic hepatopathy.

Patients (or Materials) and Methods: A total of 142 patients (age, 16–56) with the verified (by history, objective status, ultrasound, and according to biochemical tests) diagnosis of acute toxic hepatitis (poisoning with ethyl alcohol – 49; alcohol surrogates – 89; paracetamol – 3; reserpine – 1), who took treatment in the toxicologic department were included in the clinical research. The patients were randomly divided into 3 groups: 34 patients were taking Essentiale (200 mL of 5% glucose + 10 mL of Essentiale) IV once per day for 3 days; 94 patients were taking Cytaphat (10 mg/kg + 200 mL of 5% glucose) IV once per day for 3 days; 14 patients were taking placebo (200 mL of 5% glucose) IV once per day for 3 days. The method of clinical trials was double-blind.

Results: Three days after the implementation of Essentiale or Cytaphat, all patients reported a significant (subjective opinion) recovery: reduction of the discomfort, epigastric pain and the pain in the right upper quadrant; normalizing of the appetite; patients become active and vigorous. Patients who received placebo, subje-

Disclosure of Interest: None declared.

PP175—EVIDENCE OF DRUG–DRUG INTERACTIONS THROUGH UPTAKE AND EFFLUX TRANSPORT SYSTEMS IN RAT HEPATOCYTES: IMPLICATIONS FOR CELLULAR CONCENTRATIONS OF COMPETING DRUGS

Y. Daali\(^1\); P. Millot\(^2\); P. Dayer\(^3\); and C. Pastor\(^4\)
\(^1\)Clinical Pharmacology and Toxicology, Geneva University And Geneva University Hospitals; \(^2\)Unité de Neurophysiologie, Geneva University Hospitals; and \(^3\)Laboratoire de Physiopathologie Hépatique et Imagerie, Geneva University And Geneva University Hospitals, Geneva, Switzerland

Introduction: The interplay between uptake and efflux transporters determines hepatic concentrations of drugs. Gd-BOPTA is a contrast agent used in liver magnetic resonance (MR) imaging that enters into human hepatocytes through OATP and exit unchanged into bile through MRP2. Rifampicin (RIF) is transported by the same membrane proteins and may compete with Gd-BOPTA for hepatic uptake. The aim of the study was then to elucidate the acute cellular interactions between Gd-BOPTA and RIF in perfused rat liver preparations.

Patients (or Materials) and Methods: Normal and rats lacking the canicular transporter Mrp2 were used to prepare the perfused rat livers. We perfused livers with 133Gd-DTPA and 133Gd-BOPTA and hepatic concentrations were measured using a gamma scintillation probe. After RIF perfusion, hepatic concentrations and bile excretion rates were measured using high-performance liquid chromatography.

Results: RIF perfusion greatly decreased bile flow. RIF vascular clear-

Conclusion: Drug–drug interactions through transporters deter-

Disclosure of Interest: None declared.

PP176—COMPARISON OF INHIBITORY DURATION OF GRAPEFRUIT JUICE ON ORGANIC ANION- TRANSPORTING POLYPEPTIDE AND CYP3A4

S. Tanaka\(^1\); S. Uchida\(^1\); S. Miyakawa\(^2\); N. Inui\(^2\); K. Takeuchi\(^2\); H. Watanabe\(^2\); and N. Namiki\(^1\)

References
Introduction: Grapefruit juice (GFJ) is known to decrease the plasma concentrations of several drugs by inhibiting organic anion-transporting polypeptide (OATP) 2B1. We aimed to determine the duration of the inhibitory effect of GFJ on OATP by comparison with the duration of the GEJ-mediated effects on cytochrome P450 (CYP) 3A4 activity.

Patients (or Materials) and Methods: Seven Japanese healthy subjects were enrolled and administered ciprofloxin (Cel) and midazolam (Mdz), which are substrates of OATP2B1 and CYP3A4, respectively, on days 1, 3, and 7 (0, 48, and 144 hours after the ingestion of GEJ). On the control day, Cel (100 mg) and Mdz (15 μg/kg) were orally administered with water. Three days later, all subjects drank GFJ (200 mL 3 times a day) for 3 days. On day 1, the same doses of the drugs were administered with GFJ. On days 3 and 7, the subjects were administered the same doses of the drugs with water. Pharmacokinetics and hemodynamic parameters of both drugs were evaluated on each day. The plasma concentrations of Cel and Mdz were determined by LC-MS/MS. The study protocol was approved by the ethics committee of Hamamatsu University School of Medicine and University of Shizuoka, and all participants provided written informed consent before the study was initiated.

Results: Plasma concentrations of Cel were lower on day 1 than on the control day. AUC0–8 and Cmax of Cel were significantly decreased on day 1, and the mean ratios of these values and the corresponding control-day values were 0.21 and 0.13, respectively. The Cmax and AUC0–8 returned to the control level on days 3 and 7. In contrast, AUC0–8 of Mdz was higher on days 1 and 3 than on the control day, with the mean ratios of the corresponding values and control-day value being 2.00 and 1.42, respectively. The AUC0–8 returned to the control level on day 7. Systolic and diastolic blood pressure or heart rate at 1 and 3 hours after administration of drugs did not changed by the intake of GEJ.

Conclusion: GFJ greatly reduced Cmax and AUC0–8 of Cel suggesting that it strongly inhibited OATP2B1. However, the OATP2B1 inhibition caused by GFJ dissipated faster than the GFJ-mediated alterations in CYP3A4 activity, which were sustained for at least 48 hours. Our results are clinically relevant because many patients take OATP substrates daily, and knowing the duration of inhibition would help patient interactions.

Disclosure of Interest: None declared.

**PP178—ANTIEPILEPTIC DRUGS: PRESCRIBING PATTERNS AND INTERACTION RISK IN GENERAL PRACTICE**

D. Italiano1*; R. Ferrara1; G. Trifiro1; S. Gagliostro1; G. Starvaggi1; C. Pagliaro1; I. Lombardi2; M. Tari1; A. Capuano1; E. Spina1; and V. Arcoraci1

1Department of Clinical and Experimental Medicine, University of Messina, Messina; 2Caserta Local Health Unit, Caserta; and 3Dept. of Experimental Medicine, Pharmacology Section, Second University of Napoli, Napoli, Italy

Introduction: In the last years, a growing trend in antiepileptic drug (AED) use was observed, but few data concerning indication of use and drug interaction risk are available in general practice. The aims of this study were: to analyze the prevalence, incidence of use, and the risk of drugs interactions was calculated as overlapping days of this study were: to analyze the prevalence, incidence of use, and the risk of drugs interactions was calculated as overlapping days of prescription during 2005–2011 were identified. The use of newer and older AEDs was calculated as 1-year prevalence and incidence; AEDs consumption was evaluated as defined daily dose (DDD)/10,000 inhabitants/d. Clinically relevant interacting drugs were identified and the risk of drugs interactions was calculated as overlapping days between the exposition days of AEDs and interacting drugs.

Results: Prevalence of old AED use slightly increased from 10.7/1000 inhabitants in 2005 to 13.0/1000 in 2011, while a strong increase of newer AED use was observed from 14.7/1000 to 22.3 until 2006, followed by a deep fall to 16.2/1000 in 2011. Among older AEDs, phenobarbital and valproate were the most widely used in 2011.