Conclusions This preliminary analysis suggests that CYP1A2 and CYP2C19 polymorphisms may be associated with toxicity in patients with RCC treated with sunitinib. Polymorphisms associated with toxicity and survival in this preliminary analysis are being validated in an independent cohort of 95 RCC patients treated with sunitinib.

No conflict of interest.

PHC-019 PHARMACOGENETICS OF ANTIPLATELET AGENTS: TOWARDS PERSONALISED TREATMENT?

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Background Clopidogrel antiplatelet effects differ according to genotypes ABCB1 and CYP2C19, establishing normal, intermediate and slow metabolizers. The intermediate and slow metabolizers and poor transporters are responsible for the poor response to the antiplatelet drug.
Purpose To determine the prevalence of CYP2C19 and ABCB1 genetic polymorphism in the normal Andalusian population (control) and compare it with other populations as a step to implement this determination in clinical practise.
Materials and Methods We genotyped 100 controls from the Andalusian DNA bank for CYP2C19 * 2 (rs4244285), CYP2C19 * 3 (rs4986893) and ABCB1 (rs1045642) using TaqMan probes and allelic discrimination technique. Statistical analysis for allelic and genotypic distributions was calculated by chi-squared test or Fisher's exact test, when necessary, using the Statcalc software packages.
Results Genotype frequencies CYP2C19 (*2) in the Andalusian population: *1/*1: 73%, *1/*2: 25%, *2/*2: 2%, and CYP2C19 * 3: none; the same results as in HapMap (NW European ancestry) population. ABCB1: Andalusian population: CC 36%, CT 44%, TT 20%; HapMap population CC 27%, CT 50%, TT 23%. Allelic frequencies: NW European ancestry HapMap CYP2C19 * 2: G is 85% and A is 15%, the same as our Andalusian control results. ABCB1: HapMap C allele frequency is 45% and the T is 55%, and our frequencies are 57% C and 43% T. Having made the genotype study, 59% of the controls were sensitive to clopidogrel and 41% resistant to it.
Conclusions

- Frequencies for CYP2C19 * 2 and * 3 were similar to those reported in other studies. The frequencies for ABCB1 differed slightly
- It is necessary to perform this type of study in patients with acute coronary syndrome undergoing a percutaneous coronary intervention, to ensure effective treatment as it is documented that clopidogrel is not an effective drug in polymorphisms with allele CYP2C19 * 2 (*1/*2 and *2/*2) and/or ABCB1 TT.

No conflict of interest.

PHC-020 PHARMACOKINETICALLY GUIDED DOSE ADJUSTMENT OF 5-FLUOROURACIL (5-FU) IN GASTROINTESTINAL CANCER PATIENTS

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Background Appropriate dosing of chemotherapeutic drugs is critical to reducing mortality and increasing progression-free survival. 5-fluorouracil (5-FU) is a widely used chemotherapeutic drug in gastrointestinal cancer. The standard approach to dosing 5-FU is based on body surface area (BSA). However, BSA does not account for many of the factors that are responsible for 5-FU clearance such as age, gender, genotype, disease state, drug-drug interactions, organ dysfunction and co-morbidities. Clinical evidence indicates a strong correlation between both toxicity and therapeutic efficacy and total 5-FU exposure expressed as area under the curve (AUC) concentration. This evidence make 5-FU a good candidate for pharmacokinetic (PK)-guided dosing.
Purpose To evaluate the role of therapeutic drug monitoring (TDM) of 5-FU in daily clinical oncology practise.
Materials and Methods Prospective study of adult patients diagnosed with gastrointestinal cancer treated with infusion schedule regimes based on high doses of 5-FU (2.5–3.2 g/m^2 in 24–46 h infusion) in a university hospital. All patients were included regardless of disease state or general clinical status. Individual pharmacokinetic parameters were calculated based on anthropometrics and history of 5-FU administration using the Bayesian software programme (USC*Pack). In the first cycle the dose was calculated using the BSA, and subsequent doses were adjusted to an optimal target AUC of 30–35 mg·h/L.
Results Fifty-four patients were included in the study. Male/female ratio was 31/23, and average age and weight were 60.9 ± 12.8 years and 72.2 ± 16.9 Kg. Mean estimated pharmacokinetic parameters for volume of distribution and 5-FU clearance were 0.49 ± 0.08 L/Kg and 203 ± 68.6 L/h, respectively. To achieve the target AUC of 30–35 mg·h/L, the dose had to be increased in 33 (86.8%) patients and adjusted downward in 5 (13%). No adjustment was needed in 16 patients (29.6%).When the estimate was based on BSA, 30 patients (55.6%) had AUC < 25 mg·h/L.
Conclusions BSA-based 5-FU dosing approaches are limited when it comes to achieving optimal plasma levels in most patients. Pharmacokinetically guided dosing represents a better strategy to improve the efficacy and safety of 5-FU.

No conflict of interest.

PHC-021 PHARMACOKINETICS OF PIPERACILLIN AND CIPROFLOXACIN IN CRITICALLY ILL PATIENTS UNDERGOING CONTINUOUS VENOVENOUS HAEMODIALYSIS (CVVHD) OR CONTINUOUS VENOVENOUS HAEMODIAFILTRATION (CVVHDF)

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Background Critically ill patients on intensive care units are often suffering from sepsis and multiorgan failure causing a high mortality rate. In the presence of acute renal failure (ARF) survival can be improved by continuous renal replacement therapy (CRRT). However these procedures are known to be associated with underdosing of the antibiotic agents.
Purpose To investigate the efficacy and safety of antibiotic treatment, especially piperacillin/tazobactam and ciprofloxacin in patients undergoing CRRT.
Materials and Methods A total of 24 patients with ARF treated with CRRT were enrolled in the clinical trial. Plasma and dialysate concentrations of piperacillin/tazobactam and ciprofloxacin were measured in the steady state treatment phase. Serum concentrations of piperacillin and ciprofloxacin were analysed by a validated HPLC method. Optimum exposure to piperacillin is to be expected when serum concentrations are maintained 4–5 times higher than the minimal inhibitory concentration (MIC), i.e. above 64 mg/l. Optimum exposure to ciprofloxacin is given when the ratio (AUIC) of the area under the curve (AUC) and MIC is ≥125 h. In addition the Cmax/MIC ratio should amount to ≥10.
Results For 10 of 21 patients treated with piperacillin/tazobactam 4/0.5g three times a day plasma concentrations lower than 64 mg/l

were measured. According to a Clopper-Pearson interval 26–70% of the patients were underdosed and the exposure to piperacillin was too low. Only in 9 of 20 patients treated with ciprofloxacin 200 mg twice per day the calculated AUIC averaged ≥125 h and the Cmax/MIC ratio ≥10. Thereby 29–76% of patients treated with ciprofloxacin were underdosed. With regard to the total body clearance 29% of piperacillin and 16% of ciprofloxacin were eliminated by CRRT. Despite the moderate rate of ClCRRT the exposure of the patients to piperacillin and ciprofloxacin was revealed to be inadequate.

Conclusions In critically ill patients undergoing CRRT for piperacillin/tazobactam increased doses of 4/0.5g four times per day and for ciprofloxacin doses of 400 mg twice per day are recommended.

No conflict of interest.

PHC-022 PRACTICAL USE OF THERAPEUTIC DRUG MONITORING OF TEICOPLANIN

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Background The trough concentration of teicoplanin should be >10 mg/L for successful treatment, although it needs to be >20 mg/L for more severe staphylococcal infections, such as endocarditis and osteomyelitis.

Purpose To analyse the trough serum concentrations for teicoplanin by therapeutic drug monitoring (TDM) in current clinical practise in our hospital.

Materials and Methods Descriptive, analytical, observational study involving the first determination of trough serum concentration of teicoplanin, intravenously administered, from 2010 to 2012.

Results Trough serum concentrations of teicoplanin from 48 inpatients (56.3% female) were analysed. The mean age was 59.8 years (CI95%: 55.7–63.9). 58.3% of the inpatients received one single loading dose of 800 mg, the other 37.5% received 400 mg twice daily for the first day, one patient (2.1%) 400 mg twice daily for two days and another patient (2.1%) 400 mg each day. 70.8% of inpatients continued with 400 mg twice daily, 25% with 400 mg once daily and the rest with 200 mg once daily. The mean dose was 6.9 mg/kg/day (CI95%: 5.4–8.5 mg/kg/day). The number of doses received until the first determination was 4.7 (CI95%: 4.1–5.3 doses)

It was observed that the 37.5% of inpatients had a trough serum concentration of teicoplanin lower than 10 mg/L, 58.3% between 10–25 mg/L and 4.2% greater than 25 mg/L. 64.3% of the patients received 400 mg once daily and 26.5% had doses of 400 mg twice daily and had concentrations lower than 10 mg/L.

All patients with concentrations lower than 10 mg/L were readjusted in their dose and frequency to reach serum trough concentrations greater than 10 mg/L, in steady-state.

Conclusions We found out one problem in our setting. The current TDM of teicoplanin can help to solve it, diminishing the risk of treatment failure or micobiological resistance to teicoplanin.

No conflict of interest.

PHC-023 RATIONAL USE OF MEDICINE IN SWEDISH COMMITTEE FOR AFGHANISTAN HEALTH FACILITIES

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Background Medicine and medical commodities constitute essential and important inputs to health service delivery in all health systems. Irrational use of medicines is a multi-dimensional issue and requires interventions at several levels including Health Systems, Organization, Doctors, Dispensers, Patients and Community and it still remains a challenge in health facilities (HF) all over the country, including those managed by the Swedish Committee for Afghanistan (SCA).

Purpose To identify the factors that influence prescribers' behaviour and decision-making (Personal, Interpersonal, Workplace and Informational) while managing medicines and medical supplies.

To provide detailed information for improving the Rational Use of Medicine in SCA health facilities.

Materials and Methods Along with my teams I assessed 4 SCA projects through register books, stock cards, prescriptions, structured questioners and medical records. 28 were selected randomly from 123 HFs with a sampling interval of 5 (every 4th HF). This constituted 10 Comprehensive Health Centres, 9 Basic Health Centres, 5 Sub Centres, 2 District Hospitals and 2 Provincial Hospitals.

Results The average number of medicines per encounter was 2.1, ranging between 1.76 in Saripul and 2.49 in Wardak.

Prescription of antibiotics in health facilities visited averaged at 53.4%. It ranged from 48%.in Saripul and 60% in Samangan. In Wardak it was 56% and it was 49% in Laghman.

The average percentage of injectables prescribed was 7.8 percent. Laghman prescribed 10%, Saripul 6.22%, Samangan 8% and Wardak 7%.

Conclusions Irrational use of medicines is a complex issue and calls for multi-dimensional interventions.

RUM training for professional staff and health education and awareness programmes for people who are living in rural areas as well as distribution of standard treatment guidelines will play a significant role in promoting the rational use of medicine.

Abstract PHC-023 Table 1

Indicator	Wardak	Laghman	Samangan	Saripul	Total Average
Average number of medicines prescribed per encounter	2.49	1.94	2.24	1.76	**2.11**
Percentage of antibiotics prescribed per encounter	56%	49%	60%	48%	**53.4%**
Percentage of injectable prescribed per encounter	7%	10%	8%	6.22%	**7.8%**

No conflict of interest.

PHC-024 RENAL FUNCTION ESTIMATION BY DIFFERENT METHODS (CKD-EPI,COCKCROFT-GAULT AND MDRD4-IDMS) AND ITS EFFECT ON THE DOSE OF IV DEXKETOPROFEN

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Background The different methods that currently exist to estimate renal function take into account different parameters, which may affect the dose of some drugs, such as dexketoprofen.

The recommended dose of IV dexketoprofen is 50 mg every 8 hours if eGFR is >80 mL/min/1.73 m^2, 25 mg every 12 hours if eGFR is between 50–80 mL/min/1.73 m^2 and it is contraindicated if eGFR is <50 mL/min/1.73 m^2 – according to the summary of product characteristics.

Purpose To determine the differences in the estimates of renal function, using CKD-EPI, MDRD4-IDMS and Cockcroft-Gault (CG) to estimate the glomerular filtration rate (eGFR) and to assess their effect on the functional characterization of patients and the dose of IV dexketoprofen.

Materials and Methods Retrospective observational study performed in adults admitted to surgical units – general, trauma and obstetric – treated with dexketoprofen IV in a tertiary hospital from January to September 2011 (9 months).