chotic (11.4%) drugs were the most common groups taken by the patients, followed by opioids (10.0%) and other analgetics and antipyretics (9.0%). The need for information about possible drug adverse effects was the reason for contacting the service in 62.6% of all enquiries concerning drugs for the nervous system. 42.6% of the patients asked about possible drug interactions and 20.9% of the enquirers wanted information about the therapy of a particular disease. Questions about drugs for the nervous system are a very common reason for contacting the drug information service for patients. The advisory service can provide patients with detailed information about their medication, possible side effects and interactions. Hence, the treatment can be improved, and the follow-up medical problems can be minimized.

29 Non-Adherence – The Underestimated Problem: New Options Utilizing a Database with Claims Data

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Non-Adherence to drug therapies especially for chronic illnesses is common. Many patients experience difficulty in following treatment recommendations. Reasons therefore are magnitude. For this purpose, epidemiologic and pharmacy practice research is needed to evaluate persistence (refill compliance) as a prerequisite of adherence in ambulatory care. The German Institute for Drug Use Evaluation (Deutsches Arzneiprüfungsinstitut; DAPI) is active in the area of pharmacoeconomic and pharmacoepidemiological analyses (www.dapi.de). The objective is to further the aims of science and research and to contribute to improved drug safety. This is realized by establishing, maintaining and managing a pharmaceutical institute engaged in scientific processing of matters regarding data analyses for pharmaceuticals. Therefore, the DAPI supports organizations and institutions in the healthcare sector in matters regarding drug use evaluations (DUE). Since January 2000, the institute receives prescription data (GKV) as a completely anonymized copy of claims data from currently 5 major data processing centers covering >80% of German community pharmacies. Monthly, approximately 50 million claims data are uploaded to the data warehouse (DHW). The DWH can provide individual evaluations to cover special queries. These include not only aggregated data, but also analyses based on case-related data. This allows follow-up of drug therapy of individual, anonymized patients over an extended period, and to provide answers to detailed pharmacoepidemiological and pharmacoeconomic questions as well as to questions relevant to DUE, drug utilization review (DUR), and pharmaceutical care (e.g. persistence, adherence). One of the most interesting options is to use these data for persistence research. In cooperation with the Institute of Pharmacology of the Goethe-University in Frankfurt, two PhD projects started recently to evaluate persistence in patients treated with antihypertensives and antidepressants, respectively. Results of these data analyzes will be compared with self-report data collected from patients in German community pharmacies. Other projects of the DAPI are exploring persistence with antihypertensive comedication in insulin-treated diabetics, persistence with antidementives, prevalence of potential drug/drug-interactions, distribution of high value products (costs of ≥ 8.00 – 10.00 € per pill), and prescription of COX-2 inhibitors in Germany after safety warnings and market withdrawals, to name a few. Much more data is needed in the area of persistence/adherence in daily ambulatory practice or primary care, and the DAPI can and will contribute to this piece of research.

30 Relationship between Serum Aripiprazole, Dehydroaripiprazole, Prolactin and Testosterone Concentrations and Clinical Response to Aripiprazole in Male Schizophrenic Patients

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Aripiprazole is an atypical antipsychotic with partial agonist activity at dopamine D2 receptors. Antipsychotics generally have the potential to induce sexual dysfunction through blockade of D2 receptors in the tuberoinfundibular pathway, leading to elevated prolactin levels. However, aripiprazole is documented as a prolactin-sparing antipsychotic. We studied the association between aripiprazole dosage, serum drug levels, serum prolactin and sex hormones levels and clinical response. A total of 30 male schizophrenic patients (15 treated and 15 un-treated) of reproductive age were recruited. Aripiprazole dosage ranged from 5 to 20 mg per day. Drug monitoring of serum aripiprazole and its major metabolite dihydroaripiprazole levels by HPLC and measurement of prolactin and sex hormones (testosterone, oestrogen, progesterone, SHBG and DHEAS) using ELECSYS were performed at baseline and at the end of each week. Patients were followed up to end of 8th week medication. The clinical status of the patients was assessed every week using PANSS and CGI. Aripiprazole dosage had effect on serum testosterone levels at the end of week 3 ($F = 13.43$; $p = 0.035$). Prolactin levels reduced significantly after the first ($T = 3.005$; $p = 0.006$), the third ($T = 2.527$; $p = 0.02$) and the fifth week ($T = 3.314$; $p = 0.005$). Basal prolactin levels and prolactin change after aripiprazole treatment showed correlations with PANSS-negative score change ($R = 0.782$; $p = 0.001$), PANSS-global score change ($R = 0.78$; $p = 0.001$) and CGI change ($R = 0.831$, $p = 0.041$) after the treatment. Smoking ($F = 7.72$; $p = 0.021$) and number of cigarettes consumed per day ($F = 6.004$, $p = 0.037$) showed significant effect on change of prolactin levels. The results indicated that aripiprazole treatment can normalise the high basal prolactin level and thus indirectly induce positive effect on testosterone sparing in male schizophrenic patients. However, this prolactin sparing effect showed no significant effect on the clinical response.

31 Pharmacogenetic-Based Dose Adjustments in Psychopharmacology

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For many psychotropic drugs, pharmacogenetic polymorphisms are known to affect biotransformation and clinical outcome. In antidepressant drug treatment, most drugs are metabolized via the polymorphic cytochrome P450 enzymes CYP2D6 and CYP2C19. Huge differences in pharmacokinetic parameters have been consistently shown for many tricyclics, some SSRIs, and other antidepressant drugs. However, the effects on therapeutic drug efficacy and adverse events have been described controversially. Pharmacokinetic differences caused by genetic polymorphisms can be overcome by adapting the drug dosages and dosing intervals. Similar to bioequivalence studies, the aim to achieve similar plasma concentration time courses of antidepressants might help to reduce side effects and therapeutic failure. In the field of antipsychotic drug treatment, genetic polymorphisms in drug metabolizing enzymes as well influence pharmacokinetic parameters to a large part. In these kinds of drug therapy, a clearer dose dependency of side effects such as extrapyramidal side effects exists, and the consideration of genetic polymorphisms might be more beneficial. Recent studies showed a relationship between the occurrence of adverse antipsychotic drug effects and CYP2D6 genotype. A prospective evaluation of the cost-benefit of genotyping in this field would be very helpful for the aim of introducing pharmacogenetic diagnostic into drug therapy. For candidates in pharmacodynamic pathways, many clinical studies on polymorphisms in logical candidate genes report an association between neurotransmitter receptor and transporter genotypes and therapy response or adverse drug reactions. In other studies these findings could not be replicated. For this reason, it is not yet possible to fully translate pharmacogenetic parameters into therapeutic recommendations. At present, antidepressant and antipsychotic drug responses can best be explained as the combinatorial outcome of complex systems that interact at multiple levels. In spite of these limitations, combinations of polymorphisms in pharmacokinetic and pharmacodynamic pathways of relevance might