Hospital in London. Dosing protocols of rituximab were two 750 mg/m² intravenous infusions or four weekly 375 mg/m² infusions. Serum concentrations of rituximab were not measured. CD19+ lymphocyte counts were taken before and after rituximab treatment. A turnover mechanism described the life cycle of CD19+ lymphocytes with rituximab increasing the death rate of CD19+ lymphocytes; a negative feedback was added on the production rate to examine the rebound effect. Rituximab was assumed to decay by first-order kinetics. Results 258 measurements of CD19+ lymphocyte counts were collected from 39 children with 8 autoimmune diseases. The dose-response model well described the time course of CD19+ lymphocytes following rituximab administration. The elimination half-lives of rituximab and CD19+ lymphocytes were estimated to be 19 and 35 days, respectively, consistent with findings from other studies [1–5]. The rebound increase in CD19+ lymphocytes was found negligible. Methotrexate and cyclophosphamide increased the maximum death rate by 66% and 38% respectively. Age and gender were not significant covariates.

Simulations from the model suggested that a single infusion of rituximab of 375 mg/m² can provide similar six-month suppression of CD19+ lymphocytes to the higher doses currently used. Methotrexate or cyclophosphamide added minimal suppression effect on CD19+ lymphocytes when taken concurrently with rituximab.

Conclusions Our results could be used in future to assess the effect of rituximab biosimilars and to inform biosimilar dosing in paediatric populations.

REFERENCES

Disclosure(s) Nothing to disclose

P76 THE EFFECT OF THE PREGNANCY AND LACTATION LABELING RULE ON PRESCRIBING INFORMATION OF FDA-APPROVED DRUGS

Background The U.S. Food and Drug Administration implemented the new Pregnancy and Lactation Labeling Rule (PLLR) in June 2015. Under PLLR, all new drug applications were to present a narrative risk assessment (as opposed to letter category), while drug approvals after June 2001, were required to phase in by June 2020. The purpose of this study was to assess the quality of presented pregnancy and lactation data in the drug labeling and degree of adherence to the PLLR.

Design/Methods We reviewed the labeling data of all new molecular entities (NMEs) approved from 1999–2017. The pregnancy and lactation information was classified as: 1. Harmful to use 2. Safe to use 3. Consideration of safety and efficacy. For drugs approvals after June 2001, presence of pregnancy letter category system was noted.

Results Of the 456 NMEs, 131 (29%) were classified as harmful to use in pregnancy and 207 (45%) as harmful to use during lactation. This number did not follow any specific pattern over the course of 19 years. Less than 1% of drugs were deemed to be safe during pregnancy or lactation. Human data was the source of pregnancy or lactation information for only 2% of drugs. Up to 70% of drugs belonged to each implementation schedule has yet to meet the PLLR compliance requirement.

Conclusion(s) Pregnant and lactating women are mostly advised against use of medications that might be needed for their health and health of their infants based on very limited data. Pharmaceutical companies lagged behind the required adherence rule for labeling updates on pregnancy and lactation information.

Disclosure(s) Nothing to disclose

P75 RELATION BETWEEN POLYMORPHISM OF FOLIC ACID CYCLE GENES AND EFFECTIVENESS OF METHOTREXATE IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background Methotrexate (MTX) is the basic treatment of patient with Juvenile Idiopathic Arthritis (JIA), but effectiveness of this therapy is different. We aimed to study effectiveness of MTX in children with JIA with different genotypes of folic acid cycle genes.

Methods The study included 8 patients with JIA. For determination of MTX effectiveness the American College of Rheumatology pediatric criteria (ACR-pedi) was used. Patients were divided into 2 groups according the effectiveness of MTX treatment. Group I included 4 patients, who were non-responders because ACR-pedi was less than 10%. Second group contained 4 patients, who had ACR-pedi more than 10%. The megerment of genotypes of genes of folate cycle, such as 5-methyltetrahydrofolate-homocysteine methyltransferase (MTR), 5-methyltetrahydrofolate-homocysteine methyltransferase reductase (MTRR), 5,10methylene tetrahydrofolate reductase C677T and A1298C variants (MTHFR-677 and MTHFR129) by polymerase chain reaction (PCR) was performed for all patients.

Results In II group effectiveness of therapy according ACR-pedi was from 30% to 70% in 75% of children and more then 70% - in 25% of patients. In general, MTR gene indicated AA-genotype in 50% of patients, AG and GG-genotypes - in 25%; MTRR gene was performed with AA-genotype in 25%, AC-genotype in 12.5% and CC-genotype in 62.5%. MTHFR1298 gene was presented in 50% of patients with AA-alleles, in 25% - with AC and CC-genotypes. 50% of children had CC-genotype of MTHFR677 gene and other 50% - AC-genotype of MTHFR677 gene. CC-genotype of MTHFR1298 gene more frequently was determined in II group (p< 0.01). In group of non-responders AA-genotype of MTR gene was found more frequent in comparison with patients from group II (p< 0.01).

Conclusion Response to standard therapy in patients with JIA depends on time of prescription of MTX and genotype of MTHFR1298 and MTR genes.

Disclosure(s) Nothing to disclose