INTENSIVE MONITORING PROGRAM OF TERATOGEN AND NON-TERATOGEN RISK OF DRUGS DURING PREGNANCY: THE STORK PROJECT

1)Tuccori M.. 2)Convertino I.. 3)Galiulo M.. 4)Capogrosso sansone A.. 5)Mantarro S.. 6)Marino A.. 7)Vannacci A.. 8)Parrilli M.. 9)Corona T.. 10)Blandizzi C..

University Hospital of Pisa

Exposure to drugs during pregnancy has the potential of harming offspring. Therefore, ethical issues limit the enrolment of pregnant women in randomized clinical trials (Frew, Saint-Victor et al. 2014). Although animal studies have limited power to predict the drug teratogenic potential, pre-clinical evidence is currently largely used to allocate drugs in specific pregnancy risk categories (e.g. US FDA Pregnancy Category, Micromedex Pregnancy Category and Australian Pregnancy Category). Post-marketing observational studies are important tools to investigate on the putative risk for neonates associated with drug exposure during pregnancy in humans (Hameen-Anttila, Jyrkka et al. 2013, Lupattelli, Spigset et al. 2014, Schaefer, Peters et al. 2015). Unfortunately, the design of these studies is particularly tricky and subjected to methodological shortcomings. Therefore, their results must be often taken with caution. In the scenario of uncertainty, women and clinicians are often concerned about whether using or not drugs during pregnancy. The STORK project was aimed at: a) providing information to clinicians and women living in Tuscany on drug exposure during pregnancy; b) identifying the most concerning drugs for pregnancy use in the Tuscan population; c) evaluating the occurrence of adverse drug events in neonates after accidental or voluntary exposure during pregnancy. This project was carried out from 1st January 2012 to 31st December 2016, with the activation of a Teratologic Counselling Centre (TCC) at the University of Pisa. The activity was dedicated to Tuscan clinicians and citizens, requesting a formal or informal counselling, respectively. A data collection form (including demographic details, background information, call motivations) was used to record phone requests. Answers can be provided during the phone call based on a priority flow-chart. When a formal counselling was requested by healthcare professionals, a detailed report was provided within maximum 3 working days. If the motivation of a contact was an actual exposure to drugs during pregnancy, the customer was offered to enter into a program of telephone follow-up and a formal informed consent was requested to the pregnant woman. A total of 94 informal and 1 formal counselling were recorded throughout the study period. In most cases, counselling was on over-the-counter medications, taken for seasonal diseases or pregnancy related complications. Inadequate information (62.11%), second opinion (18.95%), conflicting information (13.68%), worrying symptoms (4.21%) and information overload (1.05%) were the calling motivations. The most frequent enquires were on: metoclopramide, amoxicillin, acyclovir, ibuprofen, paracetamol, dexchlorpheniramine, loratadine, dextromethorphan and antacids containing aluminium, magnesium and calcium carbonate. In the first trimester of pregnancy, 43 calls, concerning inadequate information, were recorded and the anatomical therapeutic chemical classifications (ATCs) of the involved drugs were: NO2B (other analgesics and antipyretics), R06A (antihistamines for systemic use), R05D (cough suppressants excluding expectorant combinations), M01A (anti-inflammatory and anti-rheumatic products, non-steroids), A02A (antacids). In the second

trimester, 37 informal counselling, for inadequate information and second opinion, were recorded on the following ATCs: NO2B, R06A, J01C (penicillin), J05A (direct-acting antivirals). In addition, 14 calls, related to the third trimester and post-delivery, for inadequate information and conflicting information, involved: R06A, A02A, N02B. In 71 cases, a drug was actually taken and pregnant women were requested to be included in a monitoring programme. The 12% of these women (n=9) did not consent to be followed up. The remained women 87% (n=62) accepted to be followed up after delivery, but only 14% (n=10) answered to the follow-up questionnaire. All these 10 followed-up women delivered healthy neonates. Only one formal counselling was requested by a clinician at the University Hospital of Pisa. This counselling request was about the possible role of several drugs taken by a woman during pregnancy (acyclovir, beclomethasone, ambroxol, miconazole, betamethasone, rubella vaccine) and the death due to respiratory distress of the newborn, occurred soon after delivery. Notably, the final report did not correlate the newborn respiratory distress and death with any drugs exposure. In conclusion, this analysis of real world data highlights the need of the population for information about the use of drugs during pregnancy. Routine consultations could address physicians and patients to a safer and more aware approach to drug use during pregnancy.

Analysis of real world, pregnancy-related questions from

consumers demonstrates that women are concerned about

the safety of drug use in pregnancy

REFERENCES

Frew, P. M., D. S. Saint-Victor, M. B. Isaacs, S. Kim, G. K. Swamy, J. S. Sheffield, K. M. Edwards, T. Villafana, O. Kamagate and K. Ault (2014). "Recruitment and retention of pregnant women into clinical research trials: an overview of challenges, facilitators, and best practices." Clin Infect Dis 59 Suppl 7: S400-407.

Hameen-Anttila, K., J. Jyrkka, H. Enlund, H. Nordeng, A. Lupattelli and E. Kokki (2013). "Medicines information needs during pregnancy: a multinational comparison." BMJ Open 3(4).

Lupattelli, A., O. Spigset, M. J. Twigg, K. Zagorodnikova, A. C. Mardby, M. E. Moretti, M. Drozd, A. Panchaud, K. Hameen-Anttila, A. Rieutord, R. Gjergja Juraski, M. Odalovic, D. Kennedy, G. Rudolf, H. Juch, A. Passier, I. Bjornsdottir and H. Nordeng (2014). "Medication use in pregnancy: a cross-sectional, multinational web-based study." BMJ Open 4(2): e004365.

Schaefer, C., P. W. J. Peters and R. K. Miller (2015). "Drugs During Pregnancyand Lactation: Treatment Options and Risk Assessment." Amsterdam: Academic Press: 1-918.