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In Vitro Screening Research on Detection of Sensibilization to Amoxicillin in Pregnant Women

KEYWORDS: pregnancy, ELISA (enzyme-linked immune sorbent assay), amoxicillin, medically related allergy prevention for newborns.

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ABSTRACT *Aim: To conduct an in vitro screening of pregnant women to detect sensibilization and develop ways of preventing pharmaceutically induced allergy in newborns affected by mother's sensibility to drugs.Materials and methods: The research' components included blood samples of pregnant women at different stages of gestational age (n=72).The antibodies' identification method was conducted through ELISA.Results: show that in 61 (84.7%) patient IgE levels belong to <0> EAST-class, in other words these pregnant women are not sensible to amoxicillin. In addition, 12.5 % of pregnant women are found to have low level to amoxicillin-related IgE and 2.8% of patients have been found to have a higher level. According to the concluded research, 15.3% [95% confidence interval, 7.8-25.7] of pregnant women have shown a higher level of sensitivity to amoxicillin, contrary to the fact that they had never experienced allergic reactions prior. Considering this fact, the possibility of the child receiving a portion of the allergy-sensible medicine is not excluded. Therefore, the child may be subjected to weakened immune system and allergy based illnesses. Conclusion:We consider development of electronic medication passport – a new perspective way of prognostication, prevention and decrease of allergic reaction risks appearing in pregnant women as well as in their babies. In our opinion the research results received prove the necessity of usage of electronic document suggested by us while developing branch programs on quality improve for rendering medical aid to the pregnant and the newborn in Ukraine.*

Introduction

Nearly 20% of all medically-induced fatal anaphylaxes in Europe and 75% in USA are the result of penicillin [4, 10] which corresponds to 500-1000 deaths per year [10]. The news of penicillin-based antibiotics causing allergic reactions is the most prevalent amongst all medical allergies, ranging from 5% to 10% amongst adults and children [11]. The United States accounts for a whole 19.3% of all emergency department admissions, due to the unfortunate side effects related to medical drugs [7]. According to the patients' electronically summarized reports, (patients who had previously attended the emergency department at least once), the prevalent number makes up 9%, while cephalosporin counts only for 1.3%. In contrast to men, women have shown to be under greater risk of side effects developing to all kinds of antibiotics, including penicillin. Throughout the duration of pregnancy and child birth anaphylaxis may cause catastrophic consequences to both mother and child. The triggers most commonly known to cause anaphylaxis during pregnancies are beta-lactam antibiotics. Today, nearly 10-25% of pregnant women are taking antibiotics. Data research has shown a doubtless connection between antibiotic usage during pregnancy and the development of child disease, in particular bronchial asthma [14]. It should be mentioned that over 25 years ago Barker (1989) had diagnosed the term as "fetal programming of diseases", meaning that the unfortunate development of events happening in early stages of a fetus' life will thereafter affect its quality of life in the future. It has been found that in case of existent allergies in mothers during pregnancy may have a direct effect on the development of the child's immune system as well as the child's allergy reactions [8]. Therefore, the world's medicinal community reiterates the importance of conducting future interdisciplinary research in learning allergies and anaphylaxis during the time of pregnancy [12].

Ukraine has a set of established protocol instructions as to conducting and screening of the population's allergy related illnesses, its diagnosis and immune system related treatments [2]. At the same time the research behind allergy prevention during period of pregnancy is lacking behind. Considering the modern technological tools, society's informed knowledge and new innovative ways of lab work; we have assigned our research a relevant strategy, a goal and a design pattern.

Materials and methods

The research' components included the pregnant women's' blood samples, at different stages of gestational age

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(n=72). The samples had been collected in Lviv throughout September 2013 – May 2014. All blood samples collected through inner vein injections were subject to written consent of the pregnant women participating. Descriptive statistics of patients' general characteristics is included in Table 1.

Table 1: Descriptive statistics of patients' general characteristics

Characteristics	Value
Participant quantity, N	72
Patients' age, min-max, years	21-43
Patients average age, years ± SD*	30.5±5.7
Gestational age min-max, month	3-22
Gestational average age, month ± SD	11.6±5.4

*SD – Standard Deviation

The antibodies' identification method was conducted through ELISA, its form based on specific binding of both antigens and antibodies, one of the components being conjugated and fermented. As a result of its appropriate reaction to substrate formation, a colored product is being formed, its quantity being determined through ELISA photometric measurement device "Immunochem 2100", (High Technology, Inc. USA). An automated tablet was used for the preparation "Immunochem 2600" (High Technology, Inc. USA) as well as thermoshaker "Immunochem 2200" (High Technology, Inc. USA). The research was conducted according to RIDASCREEN/Specific IgE ELISA protocol, used for the quantitative determination of specific IgE antibodies in human serum. The validation tests included five (5) different serums (concentration levels of 0.35; 0.70; 3.50; 17.50 and 50.0 ml) as well as the standard collection of reagents as by the "R-Biopharm AG" (Germany). Simple linear regression method was used to evaluate IgE blood levels. All Patient sera, standard sera, negative and positive controls were tested in duplicates. The system analysis, bibliographical, analytical and comparative, ELISA analysis, standardization, statistical analysis, prognosis and modeling methods have been applied.

Results

Rectilinear dependence between optical density and amoxicillin specific IgE samples were observed to have ranged from 0.35 to 3.5 MO/ml. Regression analysis was used to determine the coefficient's correlation using the least square regression method [(1)]. Thereafter, we examined the optical density and estimated Amoxicillin specific IgE concentrate in 72 blood plasma samples (Table 2).

Table 2: Analyzed Blood Samples and Amoxicillin-specific IgE Content ratings

Concentration mcg/mL	EAST class	Sample rating Amoxicillin based samples	Number of Cases:	
			Abs.	%
0.00-0.34	0	IgE absent or unable to detect	61	84.7
0.35-0.69	1	Lower level	9	12.5
0.70-3.49	2	Somewhat higher	2	2.8
3.50-17.49	3	Substantially higher	0	0
17.50-49.99	4	High	0	0
50.000-99.99	5	Very High	0	0
≥100.00	6	Extremely High	0	0
Total			72	100

Using the standardized Allergen specific IgE RIDASCREEN ELISA [(6)] protocol each concentration value was rated and classified into assigned EAST-group. In determining sensitizations 61 (84.7%) of patients are classified into the EAST class (enzyme allergo-sorbent test). In other words, those pregnant women are not sensitized to amoxicillin. In addition, 12.5% of pregnant women are showing to have higher levels of IgE. Remarkably, those with a higher IgE level towards amoxicillin throughout allergy testing.

Considering this fact it is safe to state that the usage of amoxicillin during pregnancy may lead to hypersensitivity, or an immune-mediated reaction to the drug. Accompanied by the release of a number of mediators including histamine, leukotriene, prostaglandins, and therefore shows an obvious appearance of clinical manifestations.

Discussion

The results of the study indicate that 15.3% [95% confidence interval, 7.8-25.7] of pregnant women have shown a greater amount of sensitivity towards amoxicillin, despite the prior absence of these symptoms. It is known that throughout the duration of the pregnancy the child bears all of its mother's nutrients and immunity based cells. Therefore, the possibility of allergen based IgE occurring in the child's development cannot be excluded. Thus, at child birth the child may already be more susceptible to the allergens, characterized by potentially life threatening causations such as anaphylactic shock, Stevens-Johnson syndrome, and Lyell's syndrome. Taking into account all the facts mentioned above, a safe treatment of pregnant women during the gestational stages of pregnancy, should be prioritized. It is important to develop a preventative treatment method as to protect the child from pharmacotherapeutical mishaps, born to mothers whose IgE levels are above normal.

The information needed to prevent such occurrences must include the mother's medical history as well as allergy-triggering medications prior to the pregnancy. The prototype of such document is widely spread abroad, known as "medical passport" book [(3, 13, 15)]. The latter are used mainly as a means of athletes' doping/steroid control; the passport is prepared individually and validated electronically. In our case, we are talking about an electronically generated medical book for the new born that may be potentially used to determine medical sensitivities and provide necessary treatment options throughout his/her life.

Conclusion

We consider development of electronic medication passport – a new perspective way of prognostication, prevention and decrease of allergic reaction risks appearing in pregnant women as well as in their babies. In our opinion the research results received prove the necessity of usage of electronic document suggested by us while developing branch programs on quality improve for rendering medical aid to the pregnant and the newborn in Ukraine. A significant advantage of our research results apply is considered to be their prospects on improving pharmacotherapy safety by means of adverse reactions medicine prevention before they have been introduced.

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