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PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.1019545>Available online at: <http://www.iajps.com>**Research Article****PHYSICIANS' PREFERENCES FOR ALLERGIC RHINITIS  
TREATMENT IN PREGNANT WOMEN: COMPARISON  
WITHIN THE RUSSIAN FEDERATION****Natalia A. Chukhareva<sup>1\*</sup>, Roman A. Bontsevich<sup>2</sup>, Kristina V. Shchurovskaya<sup>2</sup>, Sergei B. Nikolaev<sup>2</sup>, Galina A. Lazareva<sup>3</sup>, Alexander A. Stepchenko<sup>3</sup>, Sergey V. Povetkin<sup>3</sup>, Vladimir I. Shutov<sup>4</sup>**<sup>1</sup> FSBI 'Kulikov Research Center for Obstetrics, Gynecology and Perinatology', Moscow, Russia<sup>2</sup> Belgorod State University, 85, Pobedy St., Belgorod, 308015, Russia<sup>3</sup> Kursk State Medical University, 3, K. Marx St., Kursk, 305041, Russia<sup>4</sup> Belgorod Regional Clinical Hospital of St. Joseph, 8/9, Nekrasov, Belgorod, 308007, Russia**Abstract:**

*The article is devoted to the essential problem of allergic diseases treatment in pregnant women, in particular, allergic rhinitis. The obstetrician-gynecologists (OGs) and general practitioners' (GPs) pregnancy follow-up tactics was analyzed during the research in Belgorod region. We compared the obtained results with the results of the All-Russian Pharmacoepidemiological Study, 2d stage- 'The Epidemiology of Drugs Use in Pregnant Women' (February-April, 2015).*

**Key words:** *pregnancy, allergic rhinitis, glucocorticosteroids, antihistamines.*

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**INTRODUCTION:**

One of the pressing issues of modern health care and economy is allergic diseases. Changes in the environment, eating behavior and the expansion of chemical industry led to a significant increase in the spread of allergies. According to the latest data from 30 to 40% of the population is diagnosed with one or more allergic disease [1].

A major concern of developing allergies represented by the main risk groups - the elderly, children, people with low immune function and pregnant women [2]. Up to 30% of pregnant and childbearing age women suffer from such allergic diseases as asthma, rhinitis, food and drug allergies, insect venom allergies, urticaria, eczema and angioedema. The bronchial asthma and allergic rhinitis are leading the list (up to 20% of pregnant women) [3,4].

It is noted that a third of the pregnancy has symptoms of impaired nasal airflow [3]. The change in the endocrine profile during the gestational period has a direct and indirect effect on the nasal blood flow and the nasal mucosa. This is a so-called hormonal rhinitis which is associated with an increased level of progesterone in the body. The treatment is needless in that case as all symptoms are gone after the pregnancy termination [4].

Drug and drug-free treatment is prescribed for patients who have attended respiratory organs pathology (seasonal allergic rhinitis, bronchial asthma) [5]. Pregnant women with the mentioned pathologies significantly suffer and could tolerate serious complications such as maternal and fetal hypoxia.

Allergic rhinitis is most often manifested in the form of nasal stuffiness, sneezing, watery discharge (rhinorrhea), lachrymation, itching and runny nose. These symptoms are seasonal, hereditarily tainted, likely to be accompanied by allergic conjunctivitis or eczema and terminated by treatment or by themselves [6,7].

Allergic rhinitis treatment is carried out in the following areas: non-drug therapy (patient education, mechanical removal of the allergen), pharmacotherapy and specific therapy (immunotherapy with allergens).

The high incidence of allergic rhinitis in pregnant women and the variety of pregnancy follow-up tactics raise an essential issue to consider in a pharmacoepidemiological study. The physicians' preferences in antiallergic treatment in women during pregnancy are also of great interest in the research.

The search for innovative molecules [8, 9] is an important task of pharmacology. In this case, their study should be carried out on pharmacological targets [10,11], in vivo models [12,13], pharmacokinetic parameters [14] and clinical studies [15,16].

The aim of study is (1) to determine the preferences of Belgorod and Belgorod region OGs and GPs in pollenosis treatment in pregnant women and (2) to compare the obtained data with the results of the all-Russian research conducted in February – April, 2015 in four federal districts - Central, Volga, Urals and Far East [17].

**MATERIALS AND METHODS:**

The anonymous questioning was held through the second stage of the all-Russian pharmacoepidemiological study called 'The Epidemiology of Drugs Use in Pregnant Women'. During the study 1066 questionnaires were analyzed including 734 questionnaires of OGs and 332 of GPs.

Ninety-four physicians participated in the survey in the Belgorod region (28.7% - of the inpatient facility and 69.1% of the polyclinic division,  $p < 0.001$ ), including 77 OGs (81.9%) and 17 GPs (18.1%) ( $p < 0.001$ ). According to work experience the physicians were divided into 4 groups: 24.4% - up to 5 years of work experience, 26.7% - from 5 to 10, 22.2% - from 10 to 20 and 26.7% - more than 20 years of work experience. We conducted the questioning on the basis of seven maternity welfare centers, city polyclinics, Belgorod maternity hospital and the Central District Hospital.

The information obtained in the survey was collected and processed in Microsoft Excel. Four-field tables were analyzed using nonparametric statistical criteria.

**MAIN PART**

In order to determine the physicians' preferences in treatment of allergic rhinitis, the most commonly used drugs list was presented in the questionnaire: intranasal glucocorticosteroids (GCS), cromoglicic acid, 1<sup>st</sup> gen H1histamine antagonists (HIHA) - chloropyramine ('Suprastin'), clemastine ('Tavegil'), promethazine ('Pipolphen'), mebhydroline ('Diazolin'), 2<sup>nd</sup> gen HIHA - loratadine ('Claritin'), cetirizine ('Zirtek'), desloratadine ('Erius'). We also provided the following answer option - 'Do not treat and redirect to another specialist'.

According to the results of the questionnaire, practicing physicians prescribe 1<sup>st</sup> and 2<sup>nd</sup> gen HIHA for seasonal allergic rhinitis treatment during pregnancy. For instance, chloropyramine ('Suprastin') was chosen as the most suitable drug by 28.7% of polled physicians in Belgorod region (31.2% of gynecologists and 17.7% of GPs,  $p > 0.05$ ). All-Russian questioning revealed a 'Suprastin'-prescription-preference among 19.9% of physicians (24.4% of obstetrician-gynecologists and 10.2% of GPs,  $p < 0.0001$ ). Mebhydroline ('Diazolin') is preferred by 14.9% of respondents in Belgorod region (16.9% of OGs, 5.9% of GPs,  $p = 0.248$  according to F-test) and by 5.9% of the

physicians participated in the All-Russian survey (7.0% of OGs and 3.6% of GPs,  $p < 0.03$ ), desloratadine ('Erius') was chosen by 10.6% of the surveyed OGs and GPs in Belgorod (6.5% and 29.4%, respectively,  $p = 0.06$  by F-test) and by 5.9% of the physicians of the national survey (7.1% of OGs and 3.3% of GPs,  $p < 0.01$ ).

According to the questionnaire, Clemastin ('Tavegil'), cetirizine ('Zirtek') and promethazine ('Pipolphen') were determined as drugs of choice during pregnancy by only the OGs of Belgorod region (9.1%, 7.8% and 1.3%, respectively,  $p > 0.05$ ), while GPs rejected to prescribe these drugs. On the contrary, OGs and GPs from four federal districts actively prescribed the above mentioned drugs to pregnant women: clamastine 'Tavegil' was chosen by 9.1% of OGs and by 12.1% of GPs ( $p < 0.1$ ), cetirizine 'Zirtek'- by 7.8% of obstetricians and 17.2% of GPs ( $p < 0.0001$ ), promethazine 'Pipolphen' was indicated by 1.8% and 0.9% of OGs and GPs respectively.

Loratadine ('Claritine') was given approximately an equal number of preferences by OGs and GPs in Belgorod region (6.5% and 5.9% respectively,  $p > 0.05$ ) while within the All-Russian questionnaire it occupied one of the leading positions with such

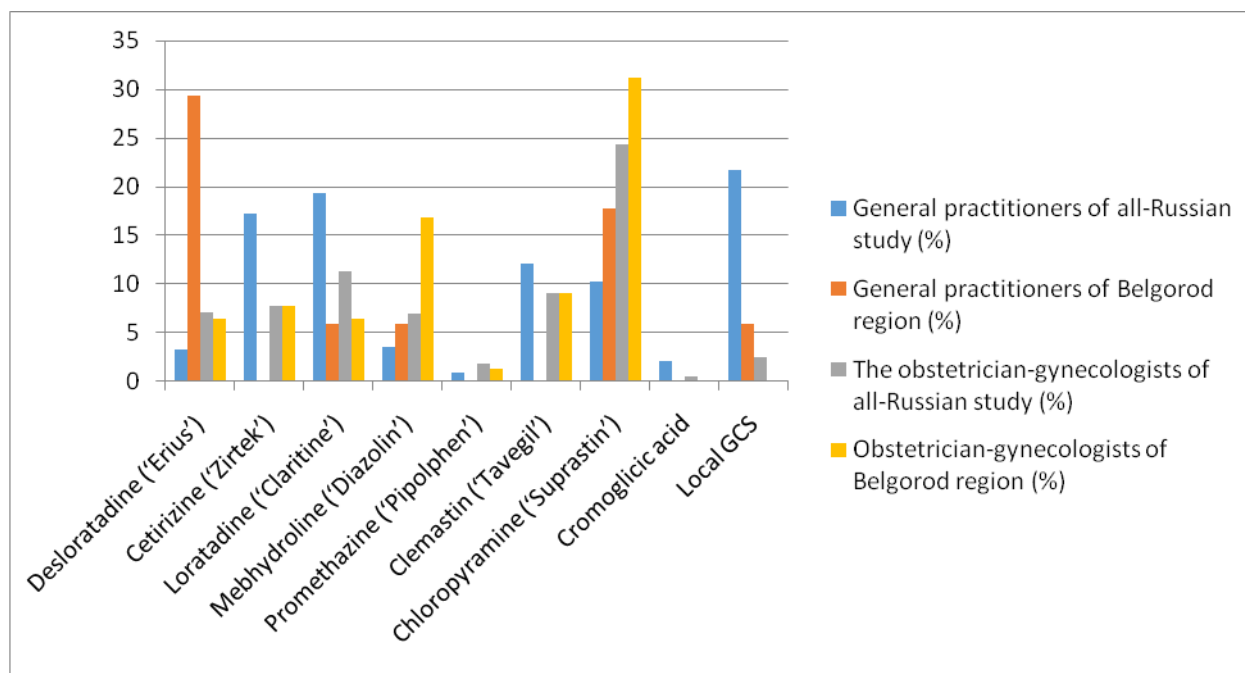
preferences: 11.3% of OGs and 19.3% of GPs ( $p < 0.0005$ ).

Among the surveyed physicians in Belgorod no one chose cromoglycic acid for pollinosis treatment during pregnancy. In the All-Russian study, the medication was not in the lead list as well and was mentioned by 0.5% of OGs and 2.1% of GPs.

Off-brand external GCS was chosen as suitable treatment by only GPs of Belgorod region (5.9% of respondents,  $p < 0.001$ ). The all-Russian study showed that 8.4% of physicians prescribe external GCS (2.5% of OGs and 21.7% of GPs,  $p < 0.0001$ ). Unfortunately, the majority of physicians had lack of confidence in treatment for seasonal allergic diseases - 47.9% of the surveyed in Belgorod region (50.7% of OGs and 35.3% of GPs,  $p > 0.05$ ) decided not to treat, but to redirect their patients to another specialist. Almost the same tendency was revealed in the analysis of the All-Russian questionnaire - 42.8% of the physicians (60.9% of obstetricians and 49.1% of GPs,  $p < 0.05$ ) do not treat their patients discretionary. The choice of drugs for seasonal allergic rhinitis in pregnant women by physicians of various specialties is presented in Table 1 and in Figure 1.

**Table 1: The choice of drugs for seasonal allergic rhinitis treatment in pregnant women: physicians' preferences in the Russian Federation and Belgorod region**

Drug	Obstetrician-gynecologists of Belgorod region (n=77), %	The obstetrician-gynecologists of all-Russian study (n=734), %	p	General practitioners of Belgorod region (n=17), %	General practitioners of all-Russian study (n=332), %	p
Local GCS	0	18 (2.5%)	0.164	1 (5.9%)	72 (21.7%)	0.118
Cromoglycic acid	0	4 (0.5%)	0.516	0	7 (2.1%)	0.545
Chloropyramine ('Suprastin')	25 (30.5%)	179 (24.4%)	0.120	3 (17.7%)	34 (10.2%)	0.333
Clemastin ('Tavegil')	7 (8.5%)	67 (9.1%)	0.991	0	40 (12.1%)	0.128
Promethazine ('Pipolphen')	1 (1.2%)	13 (1.8%)	0.762	0	3 (0.9%)	0.693
Mebhydroline ('Diazolin')	13 (15.9%)	51 (7.0%)	<b>0.002</b>	1 (5.9%)	12 (3.6%)	0.630
Loratadine ('Claritine')	5 (6.1%)	83 (11.3%)	0.196	1 (5.9%)	64 (19.3%)	0.166
Cetirizine ('Zirtek')	6 (7.3%)	57 (7.8%)	0.993	0	57 (17.2%)	0.061
Desloratadine ('Erius')	9 (10.9%)	52 (7.1%)	0.145	5 (29.4%)	11 (3.3%)	<b>&lt;0.001</b>
Do not treat and redirect to another specialist	39 (47.6%)	447 (60.9%)	0.080	6 (35.3%)	163 (49.1%)	0.266



**Fig. 1: The frequency (%) of drugs prescription for seasonal allergic rhinitis treatment in pregnant women: physicians' preferences in the Russian Federation and Belgorod region**

Currently, there is no common opinion in national and foreign literature on treatment for seasonal allergic diseases in pregnant women. That raises a difficult matter of choice of treatment prescription in practicing physicians.

Obviously, the preference is given to drug-free treatment methods: allergen elimination (removal) or allergen contact minimization [18]. For this purpose, pregnant women are recommended to hold antiallergic arrangements, including ventilation of rooms, frequent wet mopping, respiratory tract irritants reduction (tobacco smoke, fine aerosols), avoidance of histamine-liberators (products that increase the degranulation of mast cells and support allergic reactions in the body) – strawberries, citrus fruits, chocolate, coffee, smoked products, tomatoes, eggplant, bee products, spices, nuts, alcohol, etc.

In cases of pollinosis it is recommended to change the climate zone for a while, avoid use of perfume and cosmetic compositions on a plant basis, limit walks in the country during rapid plants bloom and in windy weather, install air cleaners and humidifiers. In cases of house dust and dust mites' allergy it is required to stop using dense curtains and blankets, carpets, old things and soft toys in the interior. If one is allergic to the wool and petscruf, animals should be removed from the house; fish tank owners should replace dry fish food with wet one.

During pregnancy women are actively encouraged to use elimination-barrier methods for protection from causative allergens. Safe and effective methods to withstand allergens are nasal-and mouthwash with sea- or ocean-based saline dilution

that have moisturizing and decongesting effects several times a day [19]. It is also recommended to use gel-barrier substances that sink on nasal cavity walls and thus delay allergic agents and respiratory infections invaders (microcellulose-, glycerin-based medications).

Only when the mentioned above measures are insufficient for maintaining the normal well-being of a pregnant woman, it is recommended to prescribe pharmacological medications. The key factors of drug therapy during pregnancy are the following: treatment safety for a fetus, priority of monotherapy to a combination of drugs, minimum effective dose use and minimum drug use duration, excluding, if possible, any other route of administration except local.

Those criteria are best met when prescribing intranasal GCS for treatment of allergic disease in active phase as GCS have minimal absorption into the blood stream and, thus, have minimal effect on a fetus. In terms of fetus influence they are classified as B-medications according to the Food and Drug Administration (FDA) (particularly, there was considered the most studied drug – budesonide) [20]. That medication is reckoned as the drug of choice for allergic rhinitis treatment in pregnant women. The rest topical GCS are C-drugs according to the FDA classification.

In addition, intranasal cromones -cromoglycic acid - are classified as B-drugs according to the FDA classification. Despite the obvious safety of use in the pregnancy, cromoglycic acid was rarely chosen by the surveyed physicians due to its low efficiency in treating seasonal pollinosis [5].

The majority of physicians indicated antihistamines as the most optimal drugs for allergic rhinitis treatment in pregnant women. In terms of use safety antihistamines are related to the second-line medications. They are applied when drug-free methods and topical GCS do not have positive effect on the disease course. The 2<sup>nd</sup> gen H1HA are preferably prescribed in pregnant women since these drugs have less significant sedative effect compared to the 1<sup>st</sup> gen H1HA [21]. The most studied antihistamine drugs include loratadine, cetirizine and clemastine (B-class, FDA). ARIA (2010) [6] does not recommend the administration of systemic antihistamines during pregnancy (in particular, the 1<sup>st</sup> gen H1HA), especially in the first trimester. If the benefit from drug use exceeds the maximum acceptable risk for the fetus, then systemic antihistamines should be used in a minimal permissible dose in a short course.

### RESULTS:

The analysis of data showed that physicians rarely prescribe the safest drugs (local GCS and cromoglycic acid) that meet the basic requirements in pregnant women therapy. Much more often respondents preferred the second-line drugs - systemic H1HA of the 1<sup>st</sup> and the 2<sup>d</sup> generation. Approximately the half of the surveyed did not treat their patients and redirect them to another specialist. That choice is partly explained by the lack of clear recommendations and guidelines for managing pregnant women.

### CONCLUSION:

The conducted questioning among the obstetrician-gynecologists and general practitioners in Belgorod region welfare centers, city polyclinics and Central District Hospital, as well as among the physicians in four federal districts (Central, Volga, Urals and Far East), revealed the low level of physicians' awareness in tactics of managing pregnant women with allergic rhinitis and the slight difference in answers of these two groups.

The obtained results show the necessity of carrying out educational activities on tactics of managing pregnant women with seasonal allergic diseases among the obstetrician-gynecologists and general practitioners.

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