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Omalizumab in the Treatment of Chronic Urticaria during Pregnancy

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Abstract: Chronic urticaria during pregnancy represents a prevalent dermatological condition, with some patients experiencing severe symptoms including intense pruritus, sleep disturbances, and potentially life-threatening manifestations. However, due to the unique physiological state of pregnancy, treatment options are significantly constrained. Conventional antihistamine therapy remains the primary pharmacological approach, yet exhibits suboptimal efficacy in certain cases. Prolonged glucocorticoid administration may elevate risks of gestational hypertension and preterm delivery. Omalizumab, a humanized monoclonal antibody targeting immunoglobulin E (IgE), has emerged in recent years as a potential therapeutic alternative for refractory chronic urticaria in pregnant populations. This article reviews the relevant studies on the treatment of chronic urticaria during pregnancy with omalizumab, elaborates the mechanism of action of omalizumab, analyzes the treatment needs and traditional treatment methods of chronic urticaria during pregnancy, explores the treatment of chronic urticaria during pregnancy with omalizumab, and compares the differences in safety and effectiveness between omalizumab and traditional treatments, so as to provide reference for clinical treatment.

1. Introduction

Chronic urticaria (CU), characterized by recurrent wheals and/or angioedema persisting for over six weeks, represents a persistent dermatological condition. [1]Second-generation H1 antihistamines remain first-line pharmacotherapy for CU; [2]however, suboptimal therapeutic responses are observed in certain pregnant patients. When conventional antihistamine therapy fails in gestational CU cases, adjunctive systemic glucocorticoids may be considered but carry risks of fetal growth restriction, cleft palate, maternal hypertension, and gestational diabetes, [3]underscoring the urgent need for safer and more effective treatment strategies in this population.

2. Mechanism of action of omalizumab treatment in chronic urticaria

Omalizumab is a recombinant humanized anti-IgE monoclonal antibody. [4]Its primary mechanism of action involves specific binding to free IgE, thereby preventing IgE from interacting with the high-affinity IgE receptor (FcεRI) on mast cells and basophils. This inhibition blocks the activation and degranulation of mast cells and basophils, reducing the release of inflammatory mediators such as histamine and leukotrienes, which consequently alleviates allergic and

inflammatory responses.[5]

3. Treatment of chronic urticaria during pregnancy is needed

Studies by Marcus Maurer et al. have shown that the incidence of chronic urticaria is higher in women than in men. [6]When female patients are pregnant, symptoms such as skin itching and wheals caused by CU may seriously affect the daily life and sleep quality of pregnant women, further affecting their mental state and physical health, reducing their quality of life and bringing physical and mental distress to them.A multicenter study has shown that about half of the patients withCU during pregnancy believe that their CU condition has improved during pregnancy, about one-fifth of the patients feel that their condition has not changed, and about one-third of the patients feel that their condition has worsened.[7]However, for patients with CU during pregnancy, due to their special condition, the treatment options are limited, and the treatment needs to take into account both the control of the patients' symptoms and the safety of the fetus. Therefore, patients with CU during pregnancy are in urgent need of a safe and effective treatment method.

4. General treatment of chronic urticaria during pregnancy

4.1 Antihistamine treatment

Antihistamine drugs are recommended as a first - line treatment option in international guidelines. [10]Most patients with CU during pregnancy choose antihistamine drugs for treatment, but their use during pregnancy remains controversial.

4.1.1 Guideline Recommendations

The international EAACI/GA2LEN/EuroGuiDerm/APAAACI urticaria guidelines indicate that the same management strategy is recommended for patients with CU during pregnancy. Treatment should be initiated with the standard dose of second-generation (non-sedating) H1 antihistamines, and the dose should be increased up to four times in case of no response. [8]The US FDA has classified H1 receptor antagonists as category B drugs, including loratadine, cetirizine, levocetirizine, chlorpheniramine maleate, cyproheptadine, montelukast, etc. After assessing the individual risks and benefits of the disease, it is currently believed that the use of standard doses of the second-generation H1 receptor antagonists loratadine and cetirizine is relatively safe during pregnancy. Among the antihistamine drugs, hydroxyzine is the only antihistamine drug that is prohibited during pregnancy.

4.1.2 Current Status of Clinical Research

Studies have demonstrated that second-generation H1-antihistamines are the most commonly prescribed medications for pregnant women with CU, among which cetirizine is the most frequently utilized. Notably, approximately one-fifth of patients receiving second-generation H1-antihistamine therapy were administered higher-than-standard doses of these medications.[9]Limited studies have suggested potential associations between loratadine/cetirizine and congenital malformations.[10-11] However, multiple studies have demonstrated the safety profile of second-generation H1-antihistamines (including loratadine, cetirizine, among others) during pregnancy, with no significant associations observed with congenital malformations.[9.12-14]

4.2 Treatment with corticoids

Corticoids are less frequently used in the treatment of CU during pregnancy and are typically employed during acute exacerbations.

4.2.1 Guideline Recommendations

According to the guidelines, systemic corticosteroids are limited to short-term use during exacerbation in CU .[8] In the United States, the FDA has designated Prednisone and Prednisolone as Class B drugs for pregnancy, classified as the first-line emergency rescue drug. On the other hand, betamethasone and dexamethasone belong to long-acting corticosteroids, capable of crossing the placenta to reach the fetal compartment, with the ability to inhibit the maturation of the placenta, classified as Class C drugs for pregnancy (Class D drugs during early pregnancy). The glucocorticoids classified as Pregnancy Category C medications also include hydrocortisone (classified as Category D during the first trimester), methylprednisolone, budesonide, clobetasol, and fluorometholone. For pregnant patients with severe urticaria refractory to antihistamine therapy or experiencing acute severe exacerbations, short-term, low-dose glucocorticoid therapy may be considered during pregnancy.[7]

4.2.2 Current Status of Clinical Research

Although systemic glucocorticoids have a good effect on acute-onset CU, for pregnant patients, the systemic use of glucocorticoids may lead to maternal side effects, such as gestational diabetes mellitus, preeclampsia, etc, and may also lead to adverse pregnancy outcomes such as miscarriage. [3]For the fetus, some studies have shown that the use of glucocorticoids during pregnancy may increase the risk of fetal cleft lip and palate.[15-16]Therefore, the use of glucocorticoids should be avoided as much as possible during pregnancy.

5. Omazumab for chronic urticaria during pregnancy

Omalizumab has shown good efficacy and safety in the treatment of CU, but research on its use in treating CU during pregnancy is limited.

5.1 Guideline Recommendations

The international EAACI/GA2LEN/EuroGuiDerm/APAAACI urticaria guidelines indicate that for refractory pregnant patients with CU who are unresponsive to antihistamines, omalizumab can be used after full informed consent, but also emphasize the lack of evidence-based information on the safety and effectiveness of urticaria treatment during pregnancy. [8]The US FDA has also classified omalizumab as a category B drug during pregnancy.

5.2 Therapeutic Regimen

Generally, according to the conventional treatment dose for chronic urticaria, omalizumab is administered subcutaneously to patients based on their body weight, once every 2 to 4 weeks. During the treatment process, it is necessary to closely monitor the patient's symptom changes, adverse reactions and the development of the fetus.

5.3 Current Status of Clinical Research

At present, there are relatively few studies on the treatment of chronic urticaria during pregnancy with omalizumab, and only 41 patients have been reported in the medical records. [17-23]The conditions of these 41 patients have improved significantly, and almost none of the patients had adverse reactions during pregnancy or in the newborns. Among them, there were 2 patients who had an increased dose of omalizumab or a shortened dosing interval (150 mg/2 weeks, 450 mg/4 weeks), and 5 advanced - age parturient were known to be over 35 years old. These patients all had a good therapeutic effect and no adverse reactions during pregnancy or in the newborns. A multicenter study also shows that the use of omalizumab during pregnancy is not an important risk factor for premature birth.[9]Shakuntulla et al. retrospectively collected 298 patients who received omalizumab treatment during pregnancy (the majority were asthmatic patients, with a minority being chronic urticaria patients), indicating that omalizumab is relatively safe and effective for both the mother and the fetus.[24]

6. Efficacy and safety of omalizumab versus conventional therapy

6.1 Efficacy Contrast

Comparison of efficacy between general treatment and Omalizumab treatment in pregnant patients with CU.

6.1.1 General treatment

Antihistamines demonstrate efficacy in certain patient populations, yet a substantial proportion of cases exhibit inadequate symptom control, particularly showing limited therapeutic effectiveness in severe CU patients. Although glucocorticoids exhibit rapid onset of action, their long-term use is constrained by safety concerns and clinical restrictions, with patients being prone to relapse following discontinuation.

6.1.2 Omizumab treatment

Multiple studies have shown that omalizumab can effectively improve the symptoms of pregnant patients with CU who have a poor response to antihistamines or glucocorticoids. [17-23]

6.2 Safety Contrast

Comparison of safety between general treatment and Omalizumab treatment in pregnant patients with CU.

6.2.1 General treatment

As mentioned earlier, although there are individual reports suggesting that antihistamines may have a teratogenic risk to the fetus, multiple studies have shown that second-generation H1 antihistamines are safe and feasible for use in pregnant patients with CU. The risks of using glucocorticoids are more definite, and long-term use can cause many adverse reactions in both pregnant women and fetuses.

6.2.2 Omizumab treatment

To date, existing limited research has not identified that the application of omalizumab in the

treatment of chronic urticaria during pregnancy gives rise to severe adverse outcomes, including fetal malformations, growth restriction, or miscarriage. Based on the current body of research, omalizumab demonstrates favorable safety profiles for both the maternal body and the fetus. Nevertheless, owing to the relatively scarce experience in its clinical utilization, additional large - scale, long - term investigations are imperative to conduct a more in - depth evaluation of its safety.

7. Conclusion

The management of chronic urticaria during pregnancy requires effective symptom control while ensuring maternal and fetal safety. Omalizumab, as a novel biological agent, demonstrates favorable efficacy and safety in treating chronic urticaria during pregnancy, providing a new therapeutic option for patients unresponsive to or contraindicated for conventional therapies. However, current research on omalizumab use during gestation remains insufficient, and its long-term safety profile requires further investigation. With accumulating clinical experience and advancing research, omalizumab is anticipated to emerge as a crucial therapeutic tool for chronic urticaria management in pregnancy, potentially improving maternal-fetal health outcomes. In clinical practice, physicians should develop tailored treatment plans through comprehensive evaluation of therapeutic options based on individual patient characteristics, carefully weighing benefits and risks of various approaches.

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