Omalizumab (Xolair) for Allergy-Induced Asthma

Expires Thursday, October 31, 2019 Nursing Colleen Symanski-Sanders , RN

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1. Discuss the significance of asthma as a healthcare disorder.
2. Explain the relationship of IgE to the symptoms that are seen in patients with an allergic response.
3. Describe the mechanism of action of omalizumab (Xolair), the dosing, the administration, and the required injection technique.
4. Describe the findings in the clinical trials, the identified side effects, and how patient education for using omalizumab (Xolair) should occur.

Article

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Author: Colleen Symanski-Sanders, RN, Forensic Nurse Specialist

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Imagine if there was a substance made from living organisms or a by-product of living organisms that could stimulate or restore the ability of the immune system to battle allergies in individuals with asthma. The occurrence of allergy asthmatic attacks would be reduced, trips to the emergency room would decrease, and individuals sensitive to climate changes (especially those who travel frequently) would be able to do so without the telephone number of local hospitals. In mid 2003, the approval for such a product was granted.

Brief Overview

Asthma is a very common medical disorder in the United States. Though exact numbers regarding the incidence of asthma do not exist, because of differences in location and a lack of a uniform diagnosis, it has been suggested that approximately 7% to 10% of children and 4% to 5% of adults have some form of the disease. Overall, there are two broad groups of asthma, which are allergic (associated with an IgE response) and idiosyncratic. The idiosyncratic form has several subtypes, including drug-induced (aspirin, etc.), exercise-induced, stress-induced, or brought on by a viral upper respiratory tract infection, wide changes in temperature, or an occupational exposure. The allergy-induced form of the disease accounts for approximately one-third of asthma cases, with the remaining two-thirds split up amongst the idiosyncratic forms.

Until recently, treatment was grouped into 5 major categories: beta-adrenergic agonists (such as epinephrine, etc.); methylxanthines (such as theophylline, etc.); glucocorticoids (cortisol, etc.); chromones (cromolyn sodium, etc.); and anticholinergics (atropine, etc.). However, now there is a sixth category.

The First Biological for Treatment of Allergy-Induced Asthma

The FDA approved the first biological for the treatment of allergen-induced asthma – Omalizumab (Xolair). Xolair is administered via subcutaneous injection and the expectations are that the user can eventually self-administer the

medication; however; it does require reconstitution and it is viscous. The manufacturers do provide patient education for the injection and clinical support to Xolair users, so chances are that when you come across a patient using it, they will have received education. The exception to this would probably be if you work in a medical practice and will be administering the injection or your employer has set you up to be teaching patients how to use the medication. While it is hoped that Xolair will be an exciting break through in the biological therapy for sufferers of allergy-induced asthma, success will lie with the patient. Clinicians play a valuable role in this area in being knowledge about the indications for use, administration technique, side effects, and patient education.

IgE, Asthma, and Xolair

Dr. Ken Adams, Chief of the National Institute of Allergy and Infectious Disease's Asthma and Inflammation Division, promotes the understanding that asthma is not a single disease but rather is a group of related diseases or sub-types of asthma. Each type of asthma acts differently and is triggered by various stimuli. Whether it is allergy-induced, aspirin-induced, exercise-induced, or caused by something else, the treatment is different, and thus, having an understanding of this fact will result in better management for adolescents and adults, who suffer from asthma. Xolair's benefit to patients, once it reaches a therapeutic level, is a decrease in the number of allergy-induced asthma attacks or episodes. Thus therapy is no longer isolated to the treatment of acute episodes.

Allergy-induced asthma is a chronic inflammatory disorder of the airways, in which exposure to an aeroallergen triggers an allergic surge that can result in airway inflammation and obstruction. When allergens enter the body, the body responds by producing immunoglobulin E, or IgE antibodies, which in turn circulate in the blood. IgE circulating in the blood attaches to mast cells and triggers the release of inflammatory chemicals such as histamine and leukotrienes. Organs that contain mast cells include the eyes, nose, skin, respiratory tract, and gastrointestinal tract. The common allergic reactions of mucus production, sneezing, itching, coughing, tear production, and inflammation, are the body's attempt to expel the allergenic proteins. The clinical symptoms, produced by this IgE antibody response, result in the "allergic disease" that is seen. In addition, the released inflammatory chemicals cause the bronchial airway constriction and coughing that is seen in individuals with asthma.

Xolair binds to the circulating IgE antibodies in the blood, decreasing the amount of IgE antibodies that are available to attach to mast cells. This means, that patients using Xolair, will have fewer IgE antibodies binding to mast cells, therefore inhibiting the mast cell's release of chemicals that produce the asthma symptoms. Instead of treating the symptoms, Xolair reduces the incidence of allergy-induced asthma.

Clinical Studies

The clinical trials on Xolair consisted of patients between the ages of 12 to 76, diagnosed with moderate to severe persistent asthma for at least one year, and who had a positive skin test reaction to a perennial aeroallergen. Doses were based on body weight and baseline serum total IgE concentration. All patients had a baseline IgE between 30 and 700 IU/mL and a body weight not more than 150 kg. The maximum Xolair dose patients received, who were included in the study, was 750 mg per four weeks.

When Xolair was used in conjunction with inhaled corticosteroids, in both clinical trials, it reduced the mean number of asthma exacerbations per patient by 33% to 75% during the stable-steroid phase and by 33% to 50% during the steroid-reduction phase. Reduction in asthma exacerbations was confirmed by improvements in other measures of asthma control, including symptom scores, such as nocturnal awakenings and daytime asthma symptoms.

Special Populations

Special populations include, but are not limited to, women who are nursing, pregnant, or expecting to conceive. IgG molecules are known to cross the placental barrier and IgG is also excreted in human milk. Though less is known about the IgE antibody, researchers have concluded that it is reasonable to expect the presence of Xolair in human milk as well. There were no well-controlled studies of Xolair use by pregnant women. In addition, no studies have fully analyzed whether it is present in human milk. Though animal studies are part of a new drug approval process, reproduction studies in animals are not always able to predict human reproduction outcomes. Xolair should only be used during pregnancy if clearly needed and used cautiously by nursing mothers. Pediatric use is limited to those 12 years of age and older. Children under the age of 12 were excluded from the clinical trials. Though obvious, Xolair should not be given to individuals who have had an adverse reaction to Xolair.

Dosage

Xolair 150 mg to 375 mg is administered subcutaneously every 2 to 4 weeks. Dosages and dosing frequency are determined by the total serum IgE level in IU/mL (measured before the start of treatment) and body weight in kilograms. Doses of more than 150 mg require multiple injections with a limit of 150 mg per injection site.

Administration

Medications are increasingly being developed for the treatment of chronic illnesses that require regular injection. The preference is that the patient learns to self-inject because of better compliance. Insulin is probably the obvious example. Other examples of injectable medications are growth hormone and interferon beta-1a. Xolair is intended for self-injection after willing and able individuals have received training.

The injection of Xolair can take up to 15 seconds because of its viscosity. There is also some sophistication in the preparation and the injection that is required. Patients do have difficulty learning to self-inject and a challenge to clinicians is often assisting them in overcoming their fears or phobias regarding needles and self-injection. The following information is specific to Xolair administration.

- Xolair is injected subcutaneously, not intramuscularly.
- The lyophilized product takes 15-20 minutes to dissolve
- A fully reconstituted product appears clear or slightly opalescent and may have a few small bubbles or foam around the edge of the vial.
- The reconstituted product is viscous; in order to obtain the full 1.2 mL dose the entire product must be withdrawn from the vial before expelling any air or excess solution from the syringe.

Injection Technique

Instructions from the product insert are provided below. Statements critical to successful injection are presented in bold font.

- STEP 1: Draw 1.4 mL of SWFI, USP into a 3-cc syringe equipped with a 1-inch, 18-gauge needle.
- STEP 2: Place the vial upright on a flat surface and using standard aseptic technique, insert the needle and inject the SWFI, USP directly onto the Xolair powder.
- STEP 3: Keeping the vial upright, gently swirl the upright vial for approximately 1 minute to evenly wet the powder. **Do not shake**.
- STEP 4: After completing STEP 3, gently swirl the vial for 5-10 seconds approximately every 5 minutes in order to dissolve any remaining solids. There should be no visible gel-like particles in the solution. **Do not use if foreign particles are present.**
- **Note**: Some vials may take longer than 20 minutes to dissolve completely. If this is the case, repeat STEP 4 until there are no visible gel-like particles in the solution. It is acceptable to have small bubbles or foam around the edge of the vial. Do not use if the contents of the vial do not dissolve completely by 40 minutes.
- STEP 5: Invert the vial for 15 seconds in order to allow the solution to drain toward the stopper. Using a new 3-cc syringe equipped with a 1-inch, 18-gauge needle, insert the needle into the inverted vial. Position the needle tip at the very bottom of the solution in the vial stopper when drawing the solution into the syringe. Before removing the needle from the vial, pull the plunger all the way back to the end of the syringe barrel in order to remove all of the solution from the inverted vial.
- STEP 6: Replace the 18-gauge needle with a 25-gauge needle for subcutaneous injection.
- STEP 7: Expel air, large bubbles, and any excess solution in order to obtain the required 1.2 mL dose. A thin layer of small bubbles may remain at the top of the solution in the syringe. Because the solution is very viscous, the injection may take 5-15 seconds to administer.

Side Effects and Warnings

Current federal law requires that all new drugs have proof of their effectiveness and safety before they can be approved for marketing. Safety does not imply free from risks, because no drug is absolutely safe; however, drug manufactures need to prove that the benefits outweigh the risks before the FDA considers it safe enough to approve. Asthma is not a life-threatening disease, so the FDA's threshold for safety is higher than if the drug were designed to treat AIDS, for example.

The most common adverse reaction reported in the Xolair clinical trials was injection site reactions. Other commonly observed side effects were viral infections in 23% of the study population, upper respiratory tract infections in 20%, sinusitis in 16%, and pharyngitis in 11%. The most serious adverse reactions during the Xolair clinical trials were malignancies and anaphylaxis.

1. Injection Site Reactions

Injection site reactions, regardless of severity, occurred at a rate of 45% in the Xolair-treated patients compared with 43% in the placebo-treated patients. This was not significantly different and may just be the result of injecting a viscous liquid subcutaneously, rather than a reaction to the drug itself. The types of injection site reactions that occurred during the clinical trials were bruising, redness, warmth, burning, stinging, itching, pain, hives, indurations, mass effect, and inflammation. Most of the site reactions happened within one hour post injection and lasted less than 8 days. Reactions tended to decrease in frequency after subsequent injections.

2. Malignancies

Malignant neoplasms were observed in 20 of 4127 (0.5%) Xolair-treated patients compared with 5 of 2236 (0.2%) control patients in the clinical studies of asthma and other allergic disorders. This did not reach statistical significance but did show a trend based on the Fischer's Exact test. The observed malignancies in the Xolair-treated patients were a variety of types, with breast, non-melanoma skin, prostate, melanoma, and parotid gland cancers occurring more than once, and five other types occurring once each. The majority of patients were observed for less than 1 year. Therefore, the issue of whether or not there is a higher risk for malignancy if the drug is used will require further investigation. In addition, the impact of longer exposure to Xolair or use in patients at higher risk for malignancy (i.e. the elderly or smokers) is currently not known.

3. Anaphylaxis

Anaphylaxis is the most severe form of allergic reaction, occurring rapidly without anticipation, and can be fatal. In most cases, anaphylaxis results when several organ systems react to a stimulus at the same time, which causes the multitude of signs and symptoms that are seen. Some patients may receive their first dose of Xolair at home and others may have it administered in their physician's office. It is important for clinicians to take into account that anaphylactic reactions are possible on subsequent injections and are not isolated to the first dose. Symptoms of anaphylaxis generally start within 15 to 30 minutes after exposure to an allergen; occasionally they begin after 1 hour; and rarely may occur hours later. For patients on Xolair, a two-hour reaction window is advised. Patients should be observed after an injection of Xolair, and medications for the treatment of severe hypersensitivity reactions (including anaphylaxis) should be available. If a severe hypersensitivity reaction to Xolair occurs, therapy should be discontinued. During the clinical trials, 3 cases of anaphylaxis were observed within 2 hours of Xolair administration. It has been suggested (but currently is not a requirement) that patients, who are self-administering Xolair for the first time at home, be given a self-injectable form of epinephrine as a precaution.

Patient Education

Patient education requires clinicians to translate their knowledge and to communicate that information in a manner that best serves the patient. There can be no room for assumptions. What may be obvious to the clinician will not always be perceptible to the patient. The following educational material will assist patients in the self-injection of Xolair and will facilitate a better understanding of the drug.

1. Do not decrease the dose of, or stop taking any other asthma medication, unless instructed to do so by your physician. Xolair is not meant for the treatment of acute bronchospasm or status asthmaticus.
2. You may not see immediate improvement in your asthma after beginning Xolair therapy. An effect may take up to 12 weeks.
3. Keep Xolair refrigerated at 36^0F to 46^0F.
4. Do not use Xolair if it has expired. The expiration date is stamped on the medication carton.
5. Xolair contains no preservatives. Xolair may be used for subcutaneous administration within 8 hours following reconstitution when stored in the vial at 36^0F to 46^0F, or within 4 hours of reconstitution when stored at room temperature.
6. Utilize an injection site map to make injections easier. Start numbering the injections you give yourself and write the number in each square. This will help you to properly rotate your injections so the same spot isn't used too

frequently.

7. Select your injection site. This must be an area that has a layer of fat between the skin and the muscle and this is called the subcutaneous layer. The following parts of your body have subcutaneous layers:

    - Outer surface of the upper arm
    - Top of thighs
    - Buttocks
    - Abdomen, except at the navel or waistline locations (If you are very thin, you may need to avoid the abdomen as an injection site)

8. Inject at least 1 1/2 inches away from the last injection site.
9. Do not inject within two inches of your naval, near scars or bruises, or close to the groin or joint areas.
10. Always follow the instructions provided during training and those of your physician. If you have access to a computer, consult the drug company's website for additional information and patient education.
11. Discard used needles as directed.

Conclusion

Xolair is the first of its kind in an entirely new class of a monoclonal antibody designed to treat asthma, a lifetime disease for many people. There are very few monoclonal antibodies that are prescribed for such a length of time. Though asthma is not considered life threatening, it does threaten the quality of life for millions of people.

Our work as clinicians is very much like that of new drug researchers. The care we provide, the knowledge we impart, and the advocacy for public health and safety changes constantly as new information and technology is made available. Hopefully, as Xolair use increases in society, the results seen in the clinical trials will persist and the side effects will remain at a minimum. Only time will answer this question. Wouldn't it be nice to see more kids participate in sports with less emergency room visits for allergy-induced asthma attacks?

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About the Author(s)

Colleen Symanski-Sanders, RN, Forensic Nurse Specialist, has been a Registered Nurse for over 18 years. She has extended her education into forensic nursing, criminal profiling, and psychopathy receiving a Certificate as a Forensic Nurse Specialist. She has over 16 years experience in public health and home care nursing.

Colleen has been an author of educational material for St. Petersburg College, St. Petersburg, Florida. She has also lectured on a variety of topics at numerous nursing symposiums and conferences across the country. She is on the Editorial Board for "Home Health Aide Digest" and "Private Duty Homecare" publications.

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