Ozone Injections for the Knee?

While it may sound like something out of science fiction, ozone injections into the joint for knee osteoarthritis (KOA) are finding their way into therapy. This type of procedure has been around since 1983, but good data to support its use was lacking until recently.\(^1\) The mechanism of action for ozone injections is unknown in osteoarthritis. Suggested therapeutic mechanisms are increased tissue oxygenation or activation of the anti-nociceptive system which causes analgesia and anti-inflammatory effects.\(^1\)

Pain relief and functional improvement were similar between hypertonic dextrose and ozone injections in patients with mild to moderate KOA.\(^2\) The randomized clinical trial evaluated 80 patients aged 40-75 years old. The patients received either ozone (prolozone) injections (5-7 cm\(^3\) of ozone-oxygen mixture [15 g/mL]) or injections with 7 mL of 12.5% hypertonic dextrose. The injections were given every 7-10 days for three injections. Three months after the last injection, pain intensity and WOMAC functional scores were assessed and compared to baseline.\(^2\)

Pain scores decreased and WOMAC functional scores improved from baseline in both treatment groups. However, there were no statistically significant differences in pain and WOMAC scores between the two groups. Limitations to this study included the small patient population and the short duration of the study. Only the short-term results were analyzed.\(^2\)

Ozone’s place in therapy is similar to that of hypertonic dextrose injections.\(^1,3\) Both treatments are normally offered to patients after they have failed several other treatments or to patients who could not tolerate steroid injections. Ozone injections would be the last treatment option prior to replacement of a joint.\(^1,3\)

**REFERENCES:**


By Haiden Mohl, PharmD Candidate
The combination of indacaterol and glycopyrrolate (Utibron™ Neohaler®) has been approved for chronic obstructive pulmonary disease (COPD) maintenance therapy. Indacaterol is a long-acting beta-agonist (LABA), and glycopyrrolate is a long-acting muscarinic antagonist; both medications cause bronchodilation.¹

Utibron™ is a dry powder capsule, which is placed into the Neohaler® device for inhalation of the powder.¹,² The Neohaler® device has been designed to offer little resistance to inhalation, and allows medication delivery even in patients with severe airflow obstruction.²

Utibron™ is dosed twice daily—one capsule in the morning and one in the evening. Like other LABA combinations, Utibron™ is only indicated for maintenance use and should not be used for acute bronchospasms. LABAs are also associated with an increased risk of asthma-related death, so Utibron™ should not be used in patients with asthma.¹

Forced expiratory volume in the first second (FEV₁) was significantly improved with the use of Utibron™ compared to placebo and monotherapy with either indacaterol or glycopyrrolate in the FLIGHT1 and FLIGHT2 studies.¹,³ Both double-blind, randomized studies included a total of 2038 patients with COPD and a history of smoking. Patients were treated with either placebo, indacaterol/glycopyrrolate 27.5/15.6 mcg (Utibron™), indacaterol 27.5 mcg, or glycopyrrolate 15.6 mcg twice daily for 12 weeks. In addition to the improvement in FEV₁, the combination therapy was associated with improvements in health status, dyspnea, and COPD symptoms. Use of rescue medication was also reduced in patients taking Utibron™. The incidence of adverse effects was similar among the four treatment groups. However, because the studies were only 12 weeks in duration, the long-term safety and efficacy of Utibron™ was not assessed. Inspiratory capacity and other lung volumes were not measured, so the effect of Utibron™ on these values is unknown.¹,³

Commonly reported adverse effects with Utibron™ include nasopharyngitis, hypertension, back pain, and oropharyngeal pain. Bladder obstruction, urinary retention, atrial fibrillation, and tachycardia were reported by <1% of patients in clinical trials.¹

Utibron™ may have additive effects with other medications, such as other anticholinergic drugs.¹ Indacaterol may reduce potassium levels, so patients should be monitored for hypokalemia when using diuretics, steroids, and xanthine derivatives with Utibron™. Utibron™ may increase the effects of medications which increase the QTc interval and increase the risk of ventricular arrhythmias, so ECG monitoring may be warranted. Because indacaterol is cleared by P-gp and CYP3A4, drugs which inhibit P-gp and CYP3A4 may decrease the clearance of indacaterol. However, the dose of indacaterol included in Utibron™ is much lower than the maximum dose of indacaterol used in clinical trials. Therefore, concomitant use of Utibron™ with CYP3A4 and P-gp inhibitors should not affect the safety of Utibron™ and Utibron™ dose adjustment is not required.¹

**Patient Counseling Points:**

- Utibron™ is not a treatment for an acute exacerbation; it is to be taken daily, regardless of COPD symptom occurrence.
- The capsules are not to be taken orally but are to be used inside the inhaler.
- Patients need to be counseled on how to use the Neohaler® at the pharmacy and should read the instructions thoroughly before use.
- Narrow angle glaucoma and urinary retention may worsen with use of Utibron™.
- Patients should not use any other long-acting beta-agonists with Utibron™.

**By Kaja Wagner, PharmD Candidate**

**REFERENCES:**


What is influenza?

Influenza (the flu) is a contagious illness caused by the influenza virus. Most cases of the flu are mild, but some can be severe and lead to hospitalization or even death. Children and older adults are at higher risk of severe flu. Getting a flu vaccination every year is the best way to prevent the flu.

How does influenza spread?

The flu virus is usually spread through the air by saliva when people with the flu cough, talk, or sneeze. You may even spread the flu before you know that you are sick. People with the flu can spread the virus starting the day before they feel sick and for 5-7 days after they become sick.

Signs/symptoms of influenza

- Fever or chills
- Body aches and fatigue
- Sore throat and cough
- Runny/stuffy nose
- Vomiting/diarrhea (more common in children)

Cold vs. flu

Telling the difference between a cold and the flu can be difficult because their symptoms are similar. Generally, a cold has milder symptoms than the flu. People with a cold are more likely to have a runny/stuffy nose. Special tests are available to determine if people have the flu.

Flu vaccine facts

⇒ The flu vaccine is “inactivated” and cannot cause the flu.
⇒ You must get a flu vaccine every year. The vaccine’s ability to work declines over a year, and there is a different flu virus causing illness each year.
⇒ Getting the flu is not safer than getting the vaccine. The flu virus can cause serious health issues, especially in children and older people.

Preventing influenza

Besides getting the flu vaccine, here are some helpful tips for preventing the flu:

- Wash your hands with warm soapy water; use hand sanitizer if warm soapy water is not available.
- Avoid touching your nose, mouth, and eyes.
- Avoid close contact with people who have influenza.
- Get plenty of sleep.
- Drink lots of fluids.
- Exercise regularly.
- Minimize stress.

Treatment of influenza

Besides rest, fluids, and over-the-counter medicines (Advil® [ibuprofen], Tylenol® [acetaminophen], cough syrups), three prescription drugs are available to treat the flu. None of these drugs will cure influenza, but they will shorten the amount of time that you are sick.

⇒ Tamiflu® (oseltamivir)

- Can be used in people of all ages
- Adult dose: 1 tablet taken by mouth twice daily for 5 days
- Child dose: based on child’s weight; consult healthcare provider
- Side effects: flu-like symptoms
- Best if taken within the first two days of illness
- Take with a meal to decrease the chance of upset stomach
- If you have kidney problems, the drug dose may need to be decreased

⇒ Relenza® (zanamivir)

- Only for people at least 7 years of age
- Adult dose: 2 inhalations by mouth twice daily for 5 days
- NOT for use in children
- Side effects: flu-like symptoms
- If you have asthma or COPD, do not use this drug because it can worsen these conditions

⇒ Rapivab® (peramivir)

- For adults 18 and older
- Adult dose: one IV infusion over 15-30 minutes
- NOT for use in children
- Side effects: diarrhea
- If you have kidney problems, the drug dose may need to be decreased

By Matthew Colby, PharmD Candidate

REFERENCES:


Pregnancy References (from page 6)


What is rosacea (rose-AY-sha)?
Rosacea is a common skin disease, characterized by flushing and persistent redness on the face. The redness usually appears across the nose and cheeks and is equal on both sides of the face. The redness can spread to the rest of the face and affect the ears, chest, and back.

People with rosacea often have persistent breakouts of acne, commonly in clusters.

Who is at risk for rosacea?
- People who flush or blush easily
- People of Celtic descent
- Women
- People with a family history of rosacea
- People over 30 years old
- People of white, non-Hispanic ethnicity

What triggers rosacea?
- Exposure to the sun
- Emotional stress
- Temperature extremes—either hot or cold
- Wind exposure
- Physical exercise
- Alcohol consumption
- Eating spicy foods
- Humidity
- Some skin care products

The 4 subtypes of rosacea (see photo at left)
1. Facial redness
2. Bumps and pimples (often with subtype 1—facial redness)
3. Skin thickening, usually around the nose
4. Eye irritation

The same person can have more than one subtype of rosacea.

Rosacea or acne?
People often confuse rosacea with acne. Here are a few key differences to keep in mind:
- Age of onset—acne usually starts around puberty, while rosacea does not occur until early adulthood
- Presence of whiteheads—more common in acne
- Skin thickening and redness of nose—more common in rosacea
- Area involved—rosacea appears on central face and eyes, while acne may appear on face, back, and neck
- Triggers—rosacea can often be triggered by factors such as weather and food, while acne is not

Rosacea cannot be cured, but symptoms can be managed with medications and lifestyle changes. Avoid known triggers to help decrease rosacea flare-ups. Rosacea is not the same as adult acne, and cannot be treated with over-the-counter medications. If you think you may have rosacea, talk with your healthcare provider about treatment options.

By Halley Lopez, PharmD Candidate

REFERENCES:
Patient Information: Nausea and Vomiting During Pregnancy—What to do when you are sick of being sick

Approximately 50-80% of women experience nausea and vomiting of pregnancy, or NVP. This condition is commonly referred to as “morning sickness”, although the symptoms may be present at any time of day. NVP may be caused by an increase in hormones such as hCG (human chorionic gonadotropin) and estrogen during pregnancy. Most NVP occurs during the first trimester, with symptoms typically beginning around week six and ending by the 12th week.

The good news is that people with severe NVP usually have healthy babies. Experts from the American College of Obstetricians and Gynecologists recommend treating NVP early to prevent it from progressing to a more severe condition known as hyperemesis gravidarum. Hyperemesis gravidarum is a less common but more serious form of NVP that occurs in about 0.3-3% of pregnancies. This condition causes dehydration, electrolyte imbalances, and weight loss as a result of nausea with severe vomiting. Another reason for treating NVP is to reduce symptoms and make you more comfortable.

Recommended non-drug treatments:

Take a prenatal multivitamin for at least 3 months before becoming pregnant to reduce your risk of NVP. Continue the multivitamin during pregnancy.

Ginger may help reduce symptoms of nausea in pregnant women. Ginger-powder capsules were used in most of the studies done in pregnant women with NVP.

Get as much rest as you need and avoid things that seem to trigger your nausea/vomiting. Certain odors, heat, noise, and light are common triggers.

Avoid large meals by eating a small amount every 1-2 hours. Eating meals with more protein and less fats/carbohydrates may be beneficial in reducing NVP. Some people also find eating bland or dry foods to be helpful.

Stay hydrated by drinking at least two liters of water a day.

Acupressure and acupuncture at the pressure point on the wrist (known as P6) have not been shown to be effective for NVP. However, these treatments are probably safe in pregnancy.

Recommended drug treatments:

Vitamin B6 alone or in combination with doxylamine are recommended as first-line drug treatments for NVP. Most forms of doxylamine are available over-the-counter (OTC). Vitamin B6, or pyridoxine, is also available as an OTC supplement. Both drugs have been found to be safe and effective for treatment of nausea and vomiting in pregnant women.

Diclegis®:

Diclegis® is a combination of doxylamine and pyridoxine that was approved by the FDA in 2013 for treatment of NVP. Diclegis® is only available by a prescription from your doctor.

Take Diclegis® on an empty stomach. This helps your body absorb as much of the medication as possible. Avoid chewing, crushing, or cutting the tablets. The most common side effects of Diclegis® are drowsiness, dizziness, and headache. Be careful when taking it before driving or with other medications that make you sleepy.

If you get a headache from Diclegis®, some OTC medications used to treat headache are NOT SAFE during pregnancy. These include ibuprofen and aspirin. Tylenol® (acetaminophen) is usually preferred over other drugs for headache during pregnancy.

Zofran®:

The anti-nausea drug Zofran® (ondansetron) and its use in pregnant women have received a lot of media coverage lately. When a drug is used in pregnant women, it needs to be effective as well as safe for both the mother and unborn baby. For the mother, Zofran® can cause changes in heart rhythm. This risk may be increased in people who have been vomiting, such as pregnant women with NVP.

In some studies, Zofran® has appeared to be safe with no observed increase in birth defects in babies when mothers used the drug during pregnancy. However, a recent analysis found that infants whose mothers used Zofran® during the first trimester may have twice the risk of heart birth defects compared with babies who were not exposed to Zofran®. These infants may also have an increased risk of cleft palate.

One small study found that Zofran® worked better than the combination doxylamine and pyridoxine in treatment of NVP. With only 36 patients, this study was too small to know how the two treatments might compare in a larger population of pregnant women.

Zofran® is not a recommended first-line drug treatment for NVP because there are not as many studies on its safety and effectiveness for NVP as there are with doxylamine and pyridoxine. Because Zofran® is inexpensive and may work better than other drugs for more severe cases of NVP, it may be a useful option after other treatments have failed.

By Shelby White, PharmD Candidate

References on Page 4
**Praxbind® (idarucizumab)**

**Specific Reversal Agent for Pradaxa® (dabigatran)**

Pradaxa® (dabigatran) is an alternative to warfarin in patients with non-valvular atrial fibrillation for stroke prophylaxis.¹ Dabigatran inhibits factor Xa in the clotting cascade to prevent the formation of blood clots. Unlike warfarin, dabigatran and the other newer anticoagulation agents cannot be reversed with vitamin K. This means that life-threatening, uncontrolled bleeding can occur in patients taking dabigatran when in emergent or surgical situations, especially since an immediate anticoagulation reversal option was previously lacking.¹

A new agent, Praxbind® (idarucizumab), is now available to reverse the anticoagulation effects of dabigatran.² Idarucizumab is a monoclonal antibody which specifically binds to dabigatran and the dabigatran-thrombin complex. Idarucizumab is only effective for reversing the anticoagulant effects of dabigatran and will not reverse other anticoagulant medications.²

Idarucizumab comes in a unit-of-use package containing two 50 mL vials of idarucizumab 2.5 g solution.²³ Idarucizumab must be prepared using proper aseptic technique. The IV port must be flushed with normal saline before and after administration of idarucizumab. Both bottles of idarucizumab are administered 15 minutes apart via IV access.²³

Dabigatran’s anticoagulation effects are reversed very quickly upon administration of idarucizumab. Full reversal is achieved in 89% of patients within 4 hours.²³ After 6 hours, dabigatran blood levels may begin to rise due to migration from third-space compartments. If this occurs, a second course of idarucizumab may be warranted.²³

**Clinical Pearls for using Idarucizumab**

- Confirm the uncontrolled bleeding event is truly caused by dabigatran
- Discontinue dabigatran while initiating idarucizumab
- Initiate idarucizumab as soon as possible
- Do not give a partial dose of idarucizumab—give the complete 2-vial dose
- Idarucizumab completely reverses the anticoagulant effect of dabigatran within 4 hours in 89% of patients²
- Idarucizumab will only reverse dabigatran-induced anticoagulation
- **Restart anticoagulation therapy as soon as reasonably possible to reduce the risk of thrombosis**

By Markpaul Santos, PharmD Candidate

**REFERENCES:**


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College of Health Professions and Biomedical Sciences
Drug Information Service

The University of Montana
Skaggs School of Pharmacy
32 Campus Drive
Missoula, MT 59812-1522

Phone: 406-243-5254
Fax: 406-243-5256
Email: druginfo@umontana.edu

[www.health.umt.edu/DIS](http://www.health.umt.edu/DIS)