

Appendectomy Deemed Safe During Pregnancy

BY FRAN LOWRY
Orlando Bureau

TORONTO — Laparoscopic appendectomy in pregnant patients is as safe as open appendectomy and has several advantages, according to a review presented at the annual meeting of the Canadian Association of Thoracic Surgeons. A retrospective study of 40 cases of suspected appendicitis treated laparoscopically at St. François d'Assise Hospital in

Quebec City showed that immediate complication rates and preterm labor rates were similar to those after open appendectomies, Dr. Patrice Lemieux said at the meeting.

The review, which Dr. Lemieux called the second-largest series of laparoscopic appendectomies in pregnancy in the literature, also showed that the laparoscopic approach was more versatile in cases where the appendix was displaced by the gravid uterus.

Appendicitis in pregnancy is a diagnostic challenge for the surgeon. CT scanning is not an option, and ultrasound is often suboptimal, said Dr. Lemieux, of Laval University, Quebec City.

He and his colleagues evaluated their institution's 10-year experience with laparoscopic appendectomy in 14 first-trimester, 20 second-trimester, and 6 third-trimester patients. They looked at the immediate preterm delivery rate, which they defined as delivery within 1 month of surgery,

short-term complications, and pregnancy outcomes. The women were contacted by telephone if relevant information was missing in their charts.

Three women experienced minor complications—wound infection, cystitis, and ileus—and were treated with medication. Major complications occurred in two women: an intra-abdominal abscess and a uterine perforation. This patient did well and delivered a healthy baby at 36 weeks and 4 days, he added.

There were no cases of immediate preterm labor in the month following surgery. The mean delivery time was 38 weeks. No differences were found between trimesters of pregnancy in preterm labor rates, complication rates, or operative time. The mean operative time was 49 minutes.

There were no fetal mortalities, which contrasted with published rates of 5%-14%. This may have been because of the low perforated appendix rate—9%—in the series, Dr. Lemieux said. ■

Antibiotics Resolve Some Appendicitis

MONTREAL — Antibiotic therapy is largely successful for treating acute, non-perforated appendicitis, but unlike surgery, it carries a risk of recurrence, according to long-term follow-up on the first randomized comparison of both treatments, Dr. Staffan Eriksson said at a meeting sponsored by the International Society of Surgery.

"This is a treatment with quite a high number of recurrences, but the treatment may have some advantages. It can be used in patients who do not want surgery, or in patients who are not fit for surgery," said Dr. Eriksson of Uppsala (Sweden) University. It might also be useful for post-poning night surgery until the next day, as has been shown in children, he said.

The multicenter study randomized 252 men, aged 15-50 years, from six Swedish centers, to surgery (124 patients) or antibiotic therapy (128 patients). Excluded from the study were patients in whom there was a high suspicion of perforation.

Patients in the antibiotic group received 2 days of intravenous therapy consisting of cefotaxime 2 g twice daily and tinidazole 0.8 g once daily. This was followed by 10 days of oral antibiotic therapy consisting of ofloxacin 0.2 g twice daily and tinidazole 0.5 g twice daily, he said.

In the surgery group, there was a 5% perforation rate and a 14% complication rate, mainly from wound infection.

The same rate of perforation was noted in the antibiotic group, in which 15 patients were treated surgically, 7 of whom had perforations. The remainder of patients in the antibiotic group (88%) recovered without surgery, said Dr. Eriksson. However, there was a 24% rate of recurrence within the 5-year follow-up.

—Kate Johnson



LIDODERM®
(Lidocaine Patch 5%)

Brief Summary (For full Prescribing Information and Patient Information, refer to package insert.)

INDICATIONS AND USAGE
LIDODERM is indicated for relief of pain associated with post-herpetic neuralgia. It should be applied only to intact skin.

CONTRAINDICATIONS
LIDODERM is contraindicated in patients with a known history of sensitivity to local anesthetics of the amide type, or to any other component of the product.

WARNINGS

Accidental Exposure in Children
Even a used LIDODERM patch contains a large amount of lidocaine (at least 665 mg). The potential exists for a small child or a pet to suffer serious adverse effects from chewing or ingesting a new or used LIDODERM patch, although the risk with this formulation has not been evaluated. It is important for patients to **store and dispose of LIDODERM out of the reach of children, pets, and others.** (See HANDLING AND DISPOSAL)

Excessive Dosing

Excessive dosing by applying LIDODERM to larger areas or for longer than the recommended wearing time could result in increased absorption of lidocaine and high blood concentrations, leading to serious adverse effects (see ADVERSE REACTIONS, Systemic Reactions). Lidocaine toxicity could be expected at lidocaine blood concentrations above 5 µg/mL. The blood concentration of lidocaine is determined by the rate of systemic absorption and elimination. Longer duration of application, application of more than the recommended number of patches, smaller patients, or impaired elimination may all contribute to increasing the blood concentration of lidocaine. With recommended dosing of LIDODERM, the average peak blood concentration is about 0.13 µg/mL, but concentrations higher than 0.25 µg/mL have been observed in some individuals.

PRECAUTIONS

General

Hepatic Disease: Patients with severe hepatic disease are at greater risk of developing toxic blood concentrations of lidocaine, because of their inability to metabolize lidocaine normally.

Allergic Reactions: Patients allergic to para aminobenzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine. However, LIDODERM should be used with caution in patients with a history of drug sensitivities, especially if the etiologic agent is uncertain.

Non-intact Skin: Application to broken or inflamed skin, although not tested, may result in higher blood concentrations of lidocaine from increased absorption. LIDODERM is only recommended for use on intact skin.

Eye Exposure: The contact of LIDODERM with eyes, although not studied, should be avoided based on the findings of severe eye irritation with the use of similar products in animals. If eye contact occurs, immediately wash out the eye with water or saline and protect the eye until sensation returns.

Drug Interactions

Antiarrhythmic Drugs: LIDODERM should be used with caution in patients receiving Class I antiarrhythmic drugs (such as tocainide and mexiletine) since the toxic effects are additive and potentially synergistic.

Local Anesthetics: When LIDODERM is used concomitantly with other products containing local anesthetic agents, the amount absorbed from all formulations must be considered.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis: A minor metabolite, 2, 6-xylidine, has been found to be carcinogenic in rats. The blood concentration of this metabolite is negligible following application of LIDODERM.

Mutagenesis: Lidocaine HCl is not mutagenic in Salmonella/mammalian microsome test nor clastogenic in chromosome aberration assay with human lymphocytes and mouse micronucleus test.

Impairment of Fertility: The effect of LIDODERM on fertility has not been studied.

Pregnancy

Teratogenic Effects: Pregnancy Category B. LIDODERM (lidocaine patch 5%) has not been studied in pregnancy. Reproduction studies with lidocaine have been performed in rats at doses up to 30 mg/kg subcutaneously and have revealed no evidence of harm to the fetus due to lidocaine. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, LIDODERM should be used during pregnancy only if clearly needed.

Labor and Delivery

LIDODERM has not been studied in labor and delivery. Lidocaine is not contraindicated in labor and delivery. Should LIDODERM be used concomitantly with other products containing lidocaine, total doses contributed by all formulations must be considered.

Nursing Mothers

LIDODERM has not been studied in nursing mothers. Lidocaine is excreted in human milk, and the milk: plasma ratio of lidocaine is 0.4. Caution should be exercised when LIDODERM is administered to a nursing woman.

R_x only

LIDODERM® is a registered trademark of Hind Health Care, Inc.



CHADDS FORD, PENNSYLVANIA 19317

© 2007 Endo Pharmaceuticals

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

Application Site Reactions

During or immediately after treatment with LIDODERM (lidocaine patch 5%), the skin at the site of application may develop blisters, bruising, burning sensation, depigmentation, dermatitis, discoloration, edema, erythema, exfoliation, irritation, papules, petechia, pruritus, vesicles, or may be the locus of abnormal sensation. These reactions are generally mild and transient, resolving spontaneously within a few minutes to hours.

Allergic Reactions

Allergic and anaphylactoid reactions associated with lidocaine, although rare, can occur. They are characterized by angioedema, bronchospasm, dermatitis, dyspnea, hypersensitivity, laryngospasm, pruritus, shock, and urticaria. If they occur, they should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.

Other Adverse Events

Due to the nature and limitation of spontaneous reports in postmarketing surveillance, causality has not been established for additional reported adverse events including:

Asthenia, confusion, disorientation, dizziness, headache, hyperesthesia, hypoesthesia, lightheadedness, metallic taste, nausea, nervousness, pain exacerbated, paresthesia, somnolence, taste alteration, vomiting, visual disturbances such as blurred vision, flushing, tinnitus, and tremor.

Systemic (Dose-Related) Reactions

Systemic adverse reactions following appropriate use of LIDODERM are unlikely, due to the small dose absorbed (see CLINICAL PHARMACOLOGY, Pharmacokinetics). Systemic adverse effects of lidocaine are similar in nature to those observed with other amide local anesthetic agents, including CNS excitation and/or depression (light headedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred or double vision, vomiting, sensations of heat, cold, or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression, and arrest). Excitatory CNS reactions may be brief or not occur at all, in which case the first manifestation may be drowsiness merging into unconsciousness. Cardiovascular manifestations may include bradycardia, hypotension, and cardiovascular collapse leading to arrest.

OVERDOSAGE

Lidocaine overdose from cutaneous absorption is rare, but could occur. If there is any suspicion of lidocaine overdose (see ADVERSE REACTIONS, Systemic Reactions), drug blood concentration should be checked. The management of overdose includes close monitoring, supportive care, and symptomatic treatment. Dialysis is of negligible value in the treatment of acute overdose with lidocaine.

In the absence of massive topical overdose or oral ingestion, evaluation of symptoms of toxicity should include consideration of other etiologies for the clinical effects, or overdosage from other sources of lidocaine or other local anesthetics.

The oral LD₅₀ of lidocaine HCl is 459 (346-773) mg/kg (as the salt) in non-fasted female rats and 214 (159-324) mg/kg (as the salt) in fasted female rats, which are equivalent to roughly 4000 mg and 2000 mg, respectively, in a 60 to 70 kg man based on the equivalent surface area dosage conversion factors between species.

DOSAGE AND ADMINISTRATION

Apply LIDODERM to intact skin to cover the most painful area. Apply up to three patches, only once for up to 12 hours within a 24-hour period. Patches may be cut into smaller sizes with scissors prior to removal of the release liner. (See HANDLING AND DISPOSAL) Clothing may be worn over the area of application. Smaller areas of treatment are recommended in a debilitated patient, or a patient with impaired elimination.

If irritation or a burning sensation occurs during application, remove the patch (es) and do not reapply until the irritation subsides.

When LIDODERM is used concomitantly with other products containing local anesthetic agents, the amount absorbed from all formulations must be considered.

HANDLING AND DISPOSAL

Hands should be washed after the handling of LIDODERM, and eye contact with LIDODERM should be avoided. Do not store patch outside the sealed envelope. Apply immediately after removal from the protective envelope. Fold used patches so that the adhesive side sticks to itself and safely discard used patches or pieces of cut patches where children and pets cannot get to them. LIDODERM should be kept out of the reach of children.

Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F). [See USP Controlled Room Temperature].

Manufactured for:

Endo Pharmaceuticals Inc.
Chadds Ford, Pennsylvania 19317

Manufactured by:
Teikoku Seiyaku Co., Ltd.
Sanbonmatsu, Kagawa 769 2695
Japan

LIDODERM® is a Registered Trademark of Hind Health Care, Inc.

Copyright© Endo Pharmaceuticals Inc. 2007

Rev. April, 2007
6524-10 E1

References: 1. Lidoderm Prescribing Information. Chadds Ford Pa: Endo Pharmaceuticals Inc; 2006. 2. Galer BS. Advances in the treatment of postherpetic neuralgia: the topical lidocaine patch. *Today's Therapeutic Trends* 2000; 18:1-20. 3. Argoff CE. Targeted topical peripheral analgesics in the management of pain. *Curr Pain Headache Rep*. 2003;7:34-38. 4. Rowbotham MC, Davies PS, Verklempink C, Galer BS. Lidocaine patch: double-blind controlled study of a new treatment method for post-herpetic neuralgia. *Pain*. 1996;65:39-44. 5. Data on file. 6. Galer BS, Jensen MP, Ma T, Davies PS, Rowbotham MC. The lidocaine patch 5% effectively treats all neuropathic pain qualities: results of a randomized, double-blind, vehicle-controlled, 3-week efficacy study with use of the neuropathic pain scale. *Clin J Pain*. 2002;18:297-301.

LD-1486B/OCTOBER 2007

1-800-462-ENDO

www.lidoderm.com