

Hormone Therapy Tied to Cataract Surgery

BY SHERRY BOSCHERT

Women who used hormone therapy were more likely to need cataract surgery, a risk potentiated by drinking alcohol, a large Swedish prospective study found.

In a 98-month study of 30,861 postmenopausal women, those who had ever used hormone therapy (HT) had a 14% higher risk for cataract extraction and

current HT users had an 18% higher risk, compared with women who never used HT in a multivariate analysis, Dr. Birgitta Ejderik Lindblad and her associates reported (Ophthalmology 2010 Jan. 4 [doi:10.1016/j.opht.2009.07.046]).

Cataract extraction was even more likely in women who were using HT and drank alcohol. Among current HT users, any alcohol consumption was associated with a 29% higher risk for cataract ex-

traction, and those who drank more than one alcoholic drink per day had a 42% higher risk, compared with women who were neither using HT nor drinking alcohol. (One drink was defined as about 13 g of alcohol, roughly equal to one glass of wine, bottle of beer, or drink of liquor.) Drinking alcohol has been associated with increased levels of plasma estrogen in postmenopausal women in prior studies.

Investigators collected data from women in the Swedish Mammography Cohort who completed questionnaires in September 1997 about hormone status, use of hormone therapy, and lifestyle factors. The researchers followed them through October 2005 and compared their names with those on Swedish registers of cataract surgeries, which identified 4,324 women who underwent cataract surgery during the study period.

Among women aged 65 years or older, the risk for cataract surgery was 73% higher in those using hormone therapy, compared with women who never used HT, after the researchers adjusted for the effects of alcohol consumption, smoking, diabetes, hypertension, steroid or vitamin use, body mass index, and education level.

Longer use of HT was associated with

Women who used hormone therapy for more than 10 years had a 20% higher risk of cataract extraction, compared with women who never used hormone therapy.

higher risk for cataract extraction in a linear fashion, added Dr. Lindblad of the Karolinska Institute, Stockholm. Current users of hormone therapy reported longer duration of HT (a mean of 6 years) compared with past users (4 years). Women who used HT for more than 10 years had a 20% higher risk of cataract extraction, compared with women who never used HT.

If the current study's findings can be confirmed, the increased risk for cataract extraction should be added to the list of increased risks for breast cancer and cardiovascular disease that are associated with HT use, the investigators suggested.

Previous studies provided scarce and inconsistent evidence of any potential association between HT use and the risk of age-related cataracts.

Dr. Lindblad and her associates advised caution in comparing their study with those conducted outside of Sweden because HT preparations and clinical practices vary between countries. The different chemistries might have different effects on the body.

At the start of the study, 39% of women were using hormone therapy, 11% had used HT in the past, and 50% had never used HT. Half of current users took HT to relieve hot flushes, 33% used it for urogenital symptoms, and 17% took HT for both types of symptoms.

The risk for cataract extraction in women using HT did not differ significantly based on current or past cigarette smoking. ■

Disclosures: The researchers reported having no conflicts of interest related to the study, funded by Swedish government agencies and research foundations.

BRIEF SUMMARY - Consult full prescribing information before use.

Tussicaps®
(Hydrocodone Polistirex and Chlorpheniramine Polistirex)
Extended-Release Capsules



Rx only

CONTRAINDICATIONS

Tussicaps® extended-release capsules are contraindicated in patients with a known allergy or sensitivity to hydrocodone or chlorpheniramine.

The use of Tussicaps® extended-release capsules are contraindicated in children less than 6 years of age due to the risk of fatal respiratory depression.

WARNINGS

Respiratory Depression – As with all narcotics, Tussicaps® extended-release capsules produce dose-related respiratory depression by directly acting on brain stem respiratory centers. Hydrocodone affects the center that controls respiratory rhythm, and may produce irregular and periodic breathing. Caution should be exercised when Tussicaps® extended-release capsules are used postoperatively and in patients with pulmonary disease, or whenever ventilatory function is depressed. If respiratory depression occurs, it may be antagonized by the use of naloxone hydrochloride and other supportive measures when indicated (see **OVERDOSAGE**).

Head Injury and Increased Intracranial Pressure – The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a pre-existing increase in intracranial pressure. Furthermore, narcotics produce adverse reactions, which may obscure the clinical course of patients with head injuries.

Acute Abdominal Conditions – The administration of narcotics may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

Obstructive Bowel Disease – Chronic use of narcotics may result in obstructive bowel disease especially in patients with underlying intestinal motility disorder.

Pediatric Use – The use of Tussicaps® extended-release capsules are contraindicated in children less than 6 years of age (see **CONTRAINDICATIONS**).

In pediatric patients, as well as adults, the respiratory center is sensitive to the depressant action of narcotic cough suppressants in a dose-dependent manner. Caution should be exercised when administering Tussicaps® extended-release capsules to pediatric patients 6 years of age and older. Overdose or concomitant administration of Tussicaps® extended-release capsules with other respiratory depressants may increase the risk of respiratory depression in pediatric patients. Benefit to risk ratio should be carefully considered, especially in pediatric patients with respiratory embarrassment (e.g., croup) (see **PRECAUTIONS**).

PRECAUTIONS

General

Caution is advised when prescribing this drug to patients with narrow-angle glaucoma, asthma, or prostatic hypertrophy.

Special Risk Patients – As with any narcotic agent, Tussicaps® extended-release capsules should be used with caution in elderly or debilitated patients and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy, or urethral stricture. The usual precautions should be observed and the possibility of respiratory depression should be kept in mind.

Information for Patients

As with all narcotics, Tussicaps® extended-release capsules may produce marked drowsiness and impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery; patients should be cautioned accordingly. Tussicaps® extended-release capsules must not be diluted with fluids or mixed with other drugs as this may alter the resin-binding and change the absorption rate, possibly increasing the toxicity.

Keep out of the reach of children.

Cough Reflex – Hydrocodone suppresses the cough reflex; as with all narcotics, caution should be exercised when Tussicaps® extended-release capsules are used postoperatively, and in patients with pulmonary disease.

Drug Interactions

Patients receiving narcotics, antihistamines, antipsychotics, anti-anxiety agents, or other CNS depressants

(including alcohol) concomitantly with Tussicaps® extended-release capsules may exhibit an additive CNS depression. When combined therapy is contemplated, the dose of one or both agents should be reduced.

The use of MAO inhibitors or tricyclic antidepressants with hydrocodone preparations may increase the effect of either the antidepressant or hydrocodone.

The concurrent use of other anticholinergics with hydrocodone may produce paralytic ileus.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity, mutagenicity and reproductive studies have not been conducted with Tussicaps® extended-release capsules.

Pregnancy

Teratogenic Effects. *Pregnancy Category C* – Hydrocodone has been shown to be teratogenic in hamsters when given in doses 700 times the human dose. There are no adequate and well-controlled studies in pregnant women. Tussicaps® extended-release capsules should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects – Babies born to mothers who have been taking opioids regularly prior to delivery will be physically dependent. The withdrawal signs include irritability and excessive crying, tremors, hyperactive reflexes, increased respiratory rate, increased stools, sneezing, yawning, vomiting, and fever. The intensity of the syndrome does not always correlate with the duration of maternal opioid use or dose.

Labor and Delivery

As with all narcotics, administration of Tussicaps® extended-release capsules to the mother shortly before delivery may result in some degree of respiratory depression in the newborn, especially if higher doses are used.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Tussicaps® extended-release capsules, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

The use of Tussicaps® extended-release capsules are contraindicated in children less than 6 years of age (see **CONTRAINDICATIONS** AND **ADVERSE REACTIONS, Respiratory, Thoracic and Mediastinal Disorders**).

Tussicaps® extended-release capsules should be used with caution in pediatric patients 6 years of age and older (see **WARNINGS, Pediatric Use**).

Geriatric Use

Clinical studies of hydrocodone polistirex and chlorpheniramine polistirex extended-release did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

ADVERSE REACTIONS

Gastrointestinal Disorders

Nausea and vomiting may occur; they are more frequent in ambulatory than in recumbent patients. Prolonged administration of Tussicaps® extended-release capsules may produce constipation.

General Disorders and Administration Site Conditions

Death

Nervous System Disorders

Sedation, drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, euphoria, dizziness, psychic dependence, mood changes.

Renal and Urinary Disorders

Ureteral spasm, spasm of vesical sphincters, and urinary retention have been reported with opiates.

Respiratory, Thoracic and Mediastinal Disorders

Dryness of the pharynx, occasional tightness of the chest, and respiratory depression (see **CONTRAINDICATIONS**).

Tussicaps® extended-release capsules may produce

dose-related respiratory depression by acting directly on brain stem respiratory centers (see **OVERDOSAGE**). Use of Tussicaps® in children less than 6 years of age has been associated with fatal respiratory depression. Overdose with Tussicaps® extended-release capsules in children 6 years of age and older, in adolescents, and in adults has been associated with fatal respiratory depression.

Skin and Subcutaneous Tissue Disorders

Rash, pruritus.

DRUG ABUSE AND DEPENDENCE

Tussicaps® extended-release capsules are Schedule III narcotics. Psychic dependence, physical dependence and tolerance may develop upon repeated administration of narcotics; therefore, Tussicaps® extended-release capsules should be prescribed and administered with caution. However, psychic dependence is unlikely to develop when Tussicaps® extended-release capsules are used for a short time for the treatment of cough. Physical dependence, the condition in which continued administration of the drug is required to prevent the appearance of a withdrawal syndrome, assumes clinically significant proportions only after several weeks of continued oral narcotic use, although some mild degree of physical dependence may develop after a few days of narcotic therapy.

OVERDOSAGE

Signs and Symptoms – Serious overdose with hydrocodone is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. Although miosis is characteristic of narcotic overdose, mydriasis may occur in terminal narcosis or severe hypoxia. In severe overdose, apnea, circulatory collapse, cardiac arrest and death may occur. The manifestations of chlorpheniramine overdose may vary from central nervous system depression to stimulation.

Treatment – Primary attention should be given to the reestablishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonist naloxone hydrochloride is a specific antidote for respiratory depression which may result from overdose or unusual sensitivity to narcotics including hydrocodone. Therefore, an appropriate dose of naloxone hydrochloride should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. Since the duration of action of hydrocodone in this formulation may exceed that of the antagonist, the patient should be kept under continued surveillance and repeated doses of the antagonist should be administered as needed to maintain adequate respiration. For further information, see full prescribing information for naloxone hydrochloride. An antagonist should not be administered in the absence of clinically significant respiratory depression. Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated. Gastric emptying may be useful in removing unabsorbed drug.

A Schedule CIII Narcotic.

For Medical Information

Contact: Product Monitoring Department
Phone: 800-778-7898

Manufactured by:
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