

# Sleepy Attending Docs = More OR Complications

BY MARY ANN MOON

Complication rates for elective surgical procedures were significantly higher when the attending physicians got less than 6 hours of sleep because of working during the previous night, according to a report in JAMA.

There was not a significantly increased rate of complications in the labor and delivery suite under the same conditions,

but larger studies are needed in this setting, said Dr. Jeffrey M. Rothschild of Brigham and Women's Hospital, Boston, and his associates (JAMA 2009;302:1565-72).

"These data suggest that attending physicians, like residents and nurses, may be at increased risk of making errors when sleep deprived or working extended shifts," the investigators noted. "The business as usual of a 'limitless

workweek' for attending physicians is not optimal for patient care."

The 2008 Institute of Medicine report on residents' working hours, which led to restrictions on those hours, "did not comment on attending physician work hour limitations," and it has not been clear whether older and more experienced attending physicians are more or less able to cope with the physiological effects of fatigue than are residents.

Dr. Rothschild and his colleagues studied the complication rates of 86 attending surgeons and 134 attending ob.gyns. for 1,876 elective procedures they performed after being on duty the previous night. They compared these with complication rates of the same physicians for 7,497 similar control procedures they performed after being off duty the previous night.

Overall, the procedures performed the day after nighttime duty were not associated with significantly increased complication rates, compared with control procedures, the investigators said.

However, there was wide variation in the duration of sleep attending physicians were able to get during on-duty

**Surgical but not ob.gyn. cases involving attending physicians who'd had 6 hours or less of sleep the night before showed a higher complication rate than when sleep exceeded 6 hours.**

nights. When these data were analyzed further, surgical but not ob.gyn. post-nighttime cases after 6 hours or less of sleep showed a substantially elevated rate of complications (6.2%), compared with cases in which sleep exceeded 6 hours (3.4%), they noted.

This difference was primarily a result of a higher complication rate in the operating room (8.5%) than in the labor and delivery suite (3.4%) on the day following nighttime duty with less than 6 hours of sleep.

Moreover, the risk of complications was higher, though not significantly so, for both surgery and ob.gyn. attending physicians who had just completed shifts of 12 hours or more, compared with when they had completed shifts of less than 12 hours.

Thus, both limited sleep and longer work shifts predicted higher complication rates, Dr. Rothschild and his associates said.

Several initiatives could counteract the risks of unsafe levels of fatigue during attending physicians' procedures.

"Large physician groups can avoid scheduling elective procedures following overnight on-call responsibilities or use hospital-based clinicians, such as obstetrical 'laborists' and surgical hospitalists, to cover nighttime emergencies. ...

"When possible, adequate backup personnel should be available to relieve physicians who detect impaired performance due to severe fatigue in themselves and others," the investigators said.

In addition, "attending physicians should consider canceling or postponing elective procedures if they are not alert enough to safely operate," they said.

This study was supported by a grant from the Rx Foundation, Cambridge, Mass. Dr. Rothschild reported no financial conflicts of interest. ■



## BRIEF SUMMARY

Please see package insert for full Prescribing Information.

## INDICATIONS AND USAGE

GELNIQUE is indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency.

GELNIQUE is for topical application only and should not be ingested.

## CONTRAINDICATIONS

The use of GELNIQUE is contraindicated in the following conditions:

- Urinary retention
- Gastric retention
- Uncontrolled narrow-angle glaucoma
- Known hypersensitivity to GELNIQUE, including skin hypersensitivity

## PRECAUTIONS

### Urinary Retention

Administer GELNIQUE with caution in patients with clinically significant bladder outflow obstruction because of the risk of urinary retention.

### Patients with Gastrointestinal Disorders

Administer GELNIQUE with caution to patients with gastrointestinal obstructive disorders because of the risk of gastric retention.

GELNIQUE, like other anticholinergic drugs, may decrease gastrointestinal motility and should be used with caution in patients with conditions such as ulcerative colitis or intestinal atony. GELNIQUE should be used with caution in patients who have gastroesophageal reflux and/or who are concurrently taking drugs (such as bisphosphonates) that can cause or exacerbate esophagitis.

### Skin Hypersensitivity

In a controlled clinical trial of skin sensitization, 1 of 200 patients (0.5%) demonstrated skin hypersensitivity to GELNIQUE. Patients who develop skin hypersensitivity to GELNIQUE should discontinue drug treatment.

### Skin Transference

Transfer of oxybutynin to another person can occur when vigorous skin-to-skin contact is made with the application site. To minimize the potential transfer of oxybutynin from GELNIQUE-treated skin to another person, patients should cover the application site with clothing after the gel has dried if direct skin-to-skin contact at the application site is anticipated. Patients should wash their hands immediately after application of GELNIQUE.

### Flammable Gel

GELNIQUE is an alcohol-based gel and is therefore flammable. Avoid open fire or smoking until gel has dried.

### Myasthenia Gravis

Administer GELNIQUE with caution in patients with myasthenia gravis, a disease characterized by decreased cholinergic activity at the neuromuscular junction.

## ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trial of another drug and may not reflect the rates observed in practice.

The safety of GELNIQUE was evaluated in 789 patients (389 randomized to GELNIQUE 1 g and 400 randomized to placebo) during a randomized, placebo-controlled, double-blind, 12-week clinical efficacy and safety study. A subset of these 789 patients (N=216) participated in the 14-week open-label safety extension that followed the placebo-controlled study. Of 216 patients in the safety extension, 107 were randomized to placebo gel during the double-blind, placebo-controlled 12-week study. In the combined double-blind, placebo-controlled study and the open-label safety extension, a total of 496 patients were exposed to at least one dose of GELNIQUE. Four hundred thirty-one (431) patients received at least 12 weeks of GELNIQUE treatment and 85 patients received 26 weeks of GELNIQUE treatment. The study population primarily consisted of Caucasian women (approximately 90%) with an average age of 59 years who had overactive bladder with urge urinary incontinence.

Table 1 lists adverse events, regardless of causality, that were reported in the randomized, double-blind, placebo-controlled 12-week study at an incidence greater than placebo and in greater than 2% of patients treated with GELNIQUE.

**Table 1: Common Adverse Events in the Randomized, Double-blind, Placebo-controlled 12-Week Study (>2% and > placebo)**

Adverse Event	GELNIQUE 1 gram N=389 n (%)	Placebo N=400 n (%)
Dry mouth	29 (7.5)	11 (2.8)
Urinary tract infection	27 (6.9)	17 (4.3)
Application site reactions*	21 (5.4)	4 (1.0)
Upper respiratory tract infection	21 (5.4)	20 (5.0)
Dizziness	11 (2.8)	4 (1.0)
Nasopharyngitis	11 (2.8)	9 (2.3)
Fatigue	8 (2.1)	4 (1.0)
Gastroenteritis viral	8 (2.1)	7 (1.8)

\*Includes application site pruritus, dermatitis, papules, anesthesia, erythema, irritation, pain and papules

The most common adverse reactions, defined as adverse events judged by the investigator to be reasonably associated with the use of study drug, that were reported in ≥ 1% of GELNIQUE-treated patients were dry mouth (6.9%), application site reactions (5.4%), dizziness (1.5%), headache (1.5%), constipation (1.3%), and pruritus (1.3%). Application site pruritus (2.1%) and application site dermatitis (1.8%) were the most commonly reported application site reactions. A majority of treatment-related adverse events were described as mild or moderate in intensity, except for two patients reporting severe headache.

No serious adverse events were judged by the investigator to be treatment-related during the randomized, double-blind, placebo-controlled 12-week study. The most common adverse reaction leading to drug discontinuation was application site reaction (0.8% with GELNIQUE versus 0.3% with placebo).

The most common adverse reactions reported during the 14-week open-label extension study were application site reactions (6.0%) and dry mouth (1.9%). The most common reason for premature discontinuation was application site reactions (9 patients or 4.2%). Two of these 9 patients experienced application site reactions of severe intensity (dermatitis, urticaria, and erythema).

## DRUG INTERACTIONS

No specific drug-drug interaction studies have been performed with GELNIQUE.

### Use With Other Anticholinergics

The concomitant use of GELNIQUE with other anticholinergic (antimuscarinic) agents may increase the frequency and/or severity of dry mouth, constipation, blurred vision, somnolence and other anticholinergic pharmacological effects.

## USE IN SPECIFIC POPULATIONS

### Pregnancy

Pregnancy Category B

There are no adequate and well-controlled studies of topical or oral oxybutynin use in pregnant women. Subcutaneous administration to rats at doses up to 25 mg/kg (approximately 50 times the human exposure based on surface area) and to rabbits at doses up to 0.4 mg/kg (approximately 1 times the human exposure) revealed no evidence of harm to the fetus due to oxybutynin chloride. The safety of GELNIQUE administration to women who are or who may become pregnant has not been established. Therefore, GELNIQUE should not be given to pregnant women unless, in the judgment of the physician, the probable clinical benefits outweigh the possible hazards.

### Nursing Mothers

It is not known whether oxybutynin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when GELNIQUE is administered to a nursing woman.

### Geriatric Use

Of the 496 patients exposed to GELNIQUE in the randomized, double-blind, placebo-controlled 12-week

study and the 14-week safety extension study, 188 patients (38%) were 65 years of age and older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

### Pediatric Patients

The pharmacokinetics of oxybutynin and N-desethyloxybutynin have not been evaluated in individuals younger than 18 years of age.

### Renal Impairment

There is no experience with the use of GELNIQUE in patients with renal impairment.

### Hepatic Impairment

There is no experience with the use of GELNIQUE in patients with hepatic impairment.

### Race

The effect of race on the pharmacokinetics of GELNIQUE has not been studied.

### Gender

Available data suggest that there are no significant differences in the pharmacokinetics of oxybutynin based on gender in healthy volunteers following administration of GELNIQUE.

### Use of Sunscreen

The effect of sunscreen on the absorption of oxybutynin when applied 30 minutes before or 30 minutes after GELNIQUE application was evaluated in a single-dose randomized crossover study (N=16). Concomitant application of sunscreen, either before or after GELNIQUE application, had no effect on the systemic exposure of oxybutynin.

### Showering

The effect of showering on the absorption of oxybutynin was evaluated in a randomized, steady-state crossover study under conditions of no shower, or showering 1, 2 or 6 hours after GELNIQUE application (N=20). The results of the study indicate that showering after one hour does not affect the overall systemic exposure to oxybutynin.

## OVERDOSAGE

Overdosage with oxybutynin has been associated with anticholinergic effects including central nervous system excitation, flushing, fever, dehydration, cardiac arrhythmia, vomiting, and urinary retention. Oral ingestion of 100 mg oxybutynin chloride in association with alcohol has been reported in a 13-year-old boy who experienced memory loss, and in a 34-year-old woman who developed stupor, followed by disorientation and agitation on awakening, dilated pupils, dry skin, cardiac arrhythmia, and retention of urine. Both patients recovered fully with symptomatic treatment.

Plasma concentrations of oxybutynin begin to decline 24 hours after GELNIQUE application. If overexposure occurs, monitor patients until symptoms resolve.

### Keep out of reach of children.

### Storage

Store at room temperature, 25°C (77°F). Temporary storage between 15 - 30°C (59 - 86°F) is also permitted. Keep GELNIQUE and all medications in a safe, secure place and out of the reach of children.

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