

# Simple Screen IDs Medication Overuse Headache

BY DAMIAN McNAMARA

FROM THE INTERNATIONAL HEADACHE CONGRESS

BERLIN – “Do you take an attack treatment more than 10 days per month?” “Is this intake on a regular basis?”

With these two questions, clinicians at a headache treatment center in France quickly screened and identified patients with medication overuse headache, ac-

ording to a validation study of the screening questions.

The traditional approach to diagnosis of medication overuse headache involving the revised International Classification of Headache Disorders (ICHD-II) criteria requires a face-to-face interview that takes considerable clinician time and expertise, Dr. Virginie Dousset said at the congress, which was sponsored by the International Headache Society and

the American Headache Society.

Dr. Dousset and her colleagues transformed the second edition ICHD-II criteria into four simplified questions for a patient self-administered screening tool. To determine its sensitivity and specificity, they recruited 79 consecutive patients between September 2009 and February 2010. All participants presented for their first evaluation at the Bordeaux Headache Centre at the University of

VITALS

**Major Finding:** Asking patients if they take attack treatments for headache more than 10 days per month and if this practice is regular identifies medication overuse headache with 95% sensitivity and 80% specificity.

**Data Source:** Validation study of 77 headache patients treated at a headache treatment center.

**Disclosures:** Dr. Dousset said that she had no relevant financial disclosures.

Bordeaux, where Dr. Dousset is director.

After 2 participants withdrew, 42 patients with medication overuse headache and 35 migraine sufferers without medication overuse were assessed further. Investigators compared their responses to the questions with diagnoses made by headache specialists using the formal ICHD-II criteria.

The initial screen featured four questions. But when the two questions regarding attack treatment frequency and regular use of medications were combined, they had the best sensitivity (95%) and specificity (80%) for identification of medication overuse headache.

The question, “Do you have headache on 15 days or more per month?” had 81% sensitivity and 85% specificity. A fourth question that asked about headache duration exceeding 3 months had 98% sensitivity but a specificity of only 18%. Therefore, this item was dropped for insufficient discrimination between medication overuse and other types of headache, Dr. Dousset said.

Participants included both men and women aged 18 years or older with a normal clinical examination. They had no primary headache type other than migraine. Mean age was significantly higher in the medication overuse headache cohort at 47 years, compared with a mean of 37 years in the migraine cohort. Both groups consisted mostly of women: 81% with medication overuse headache and 63% with migraine.

The self-questionnaire and neurologic diagnosis were performed independently on the same day. A nurse unaware of the neurologic diagnosis supervised patients but offered no help on the questionnaire. The neurologist was blinded to the results of the patient questionnaire.

“We have to ask the question about applicability [of the screening questionnaire] outside headache centers,” Dr. Dousset said. Although that is the focus of future research, she said she believes asking these two questions will prove an effective screening method for patients seen in a primary care setting as well.

A video interview with Dr. Dousset can be viewed by using the QR code, or by visiting [www.clinicalneurologynews.com](http://www.clinicalneurologynews.com).



## CUVPOSA™ (glycopyrrolate oral solution) R only Brief Summary of Prescribing Information

### CONTRAINDICATIONS

CUVPOSA is contraindicated in:

- Patients with medical conditions that preclude anticholinergic therapy (e.g., glaucoma, paralytic ileus, unstable cardiovascular status in acute hemorrhage, severe ulcerative colitis, toxic megacolon complicating ulcerative colitis, myasthenia gravis).
- Patients taking solid oral dosage forms of potassium chloride. The passage of potassium chloride tablets through the gastrointestinal (GI) tract may be arrested or delayed with coadministration of CUVPOSA.

### WARNINGS AND PRECAUTIONS

#### Constipation or Intestinal Pseudo-obstruction

Constipation is a common dose-limiting adverse reaction which sometimes leads to glycopyrrolate discontinuation [see Adverse Reactions (6.1)]. Assess patients for constipation, particularly within 4-5 days of initial dosing or after a dose increase. Intestinal pseudo-obstruction has been reported and may present as abdominal distention, pain, nausea or vomiting.

#### Incomplete Mechanical Intestinal Obstruction

Diarrhea may be an early symptom of incomplete mechanical intestinal obstruction, especially in patients with ileostomy or colostomy. If incomplete mechanical intestinal obstruction is suspected, discontinue treatment with CUVPOSA and evaluate for intestinal obstruction.

#### High Ambient Temperatures

In the presence of high ambient temperature, heat prostration (fever and heat stroke due to decreased sweating) can occur with use of anticholinergic drugs such as CUVPOSA. Advise parents/caregivers to avoid exposure of the patient to hot or very warm environmental temperatures.

#### Operating Machinery or an Automobile

CUVPOSA may produce drowsiness or blurred vision. As appropriate for a given age, warn the patient not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery, or performing hazardous work while taking CUVPOSA.

#### Anticholinergic Drug Effects

Use CUVPOSA with caution in patients with conditions that are exacerbated by anticholinergic drug effects including:

- Autonomic neuropathy
- Renal disease
- Ulcerative colitis – Large doses may suppress intestinal motility to the point of producing a paralytic ileus and for this reason may precipitate or aggravate “toxic megacolon,” a serious complication of the disease.
- Hyperthyroidism
- Coronary heart disease, congestive heart failure, cardiac tachyarrhythmias, tachycardia, and hypertension
- Hiatal hernia associated with reflux esophagitis, since anticholinergic drugs may aggravate this condition

### ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling:

- Constipation or intestinal pseudo-obstruction [see Warnings and Precautions (5.1)]
- Incomplete mechanical intestinal obstruction [see Warnings and Precautions (5.2)]

The most common adverse reactions reported with CUVPOSA are dry mouth, vomiting, constipation, flushing, and nasal congestion.

#### Clinical Trials Experience

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 trials of another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to CUVPOSA in 151 subjects, including 20 subjects who participated in a 8-week placebo-controlled study (Study 1) and 137 subjects who participated in a 24-week open-label study (six subjects who received CUVPOSA in the placebo-controlled study and 131 new subjects).

Table 2 presents adverse reactions reported by ≥ 15% of CUVPOSA-treated subjects from the placebo-controlled clinical trial.

CUVPOSA (N=20) n (%)	Placebo (N=18) n (%)	
Dry Mouth	8 (40%)	2 (11%)
Vomiting	8 (40%)	2 (11%)
Constipation	7 (35%)	4 (22%)
Flushing	6 (30%)	3 (17%)
Nasal Congestion	6 (30%)	2 (11%)
Headache	3 (15%)	1 (6%)
Sinusitis	3 (15%)	1 (6%)
Upper Respiratory Tract Infection	3 (15%)	0
Urinary Retention	3 (15%)	0

Table 2: Adverse Reactions Occurring in ≥ 15% of CUVPOSA-Treated Subjects and at a Greater Frequency than Placebo in Study 1

The following adverse reactions occurred at a rate of <2% of patients receiving CUVPOSA in the open-label study.

**Gastrointestinal:** Abdominal distention, abdominal pain, stomach discomfort, chapped lips, flatulence, retching, dry tongue

**General Disorders:** Irritability, pain

**Infections:** Pneumonia, sinusitis, tracheostomy infection, upper respiratory tract infection, urinary tract infection

**Investigations:** Heart rate increased

**Metabolism and Nutrition:** Dehydration

**Nervous System:** Headache, convulsion, dysgeusia, nystagmus

**Psychiatric:** Agitation, restlessness, abnormal behavior, aggression, crying, impulse control disorder, moaning, mood altered

**Respiratory:** Increased viscosity of bronchial secretion, nasal congestion, nasal dryness

**Skin:** Dry skin, pruritus, rash

**Vascular:** Pallor

### Post-marketing Experience

The following adverse reactions have been identified during post-approval use of other formulations of glycopyrrolate for other indications. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Additional adverse reactions identified during post-approval use of glycopyrrolate tablets include: loss of taste and suppression of lactation.

### DRUG INTERACTIONS

#### Drugs Affected by Reduced GI Transit Time

Glycopyrrolate reduces GI transit time, which may result in altered release of certain drugs when formulated in delayed- or controlled-release dosage forms.

The passage of potassium chloride tablets through the GI tract may be arrested or delayed with coadministration of glycopyrrolate. Solid dosage forms of potassium chloride are contraindicated [see Contraindications (4)].

Digoxin administered as slow dissolution oral tablets may have increased serum levels and enhanced action when administered with glycopyrrolate. Monitor patients receiving slow dissolution digoxin for increased action if glycopyrrolate is coadministered regularly. Consider the use of other oral dosage forms of digoxin (e.g., elixir or capsules).

#### Amantadine

The anticholinergic effects of glycopyrrolate may be increased with concomitant administration of amantadine. Consider decreasing the dose of glycopyrrolate during coadministration of amantadine.

#### Drugs Whose Plasma Levels May be Increased by Glycopyrrolate

Coadministration of glycopyrrolate may result in increased levels of certain drugs.

Atenolol's bioavailability may be increased with coadministration of glycopyrrolate. A reduction in the atenolol dose may be needed.

Metformin plasma levels may be elevated with coadministration of glycopyrrolate, increasing metformin's pharmacologic and toxic effects. Monitor clinical response to metformin with concomitant glycopyrrolate administration; consider a dose reduction of metformin if warranted.

#### Drugs Whose Plasma Levels May be Decreased by Glycopyrrolate

Coadministration of glycopyrrolate may result in decreased levels of certain drugs.

Haloperidol's serum levels may be decreased when coadministered with glycopyrrolate, resulting in worsening of schizophrenic symptoms, and development of tardive dyskinesia. Closely monitor patients if coadministration cannot be avoided.

Levodopa's therapeutic effect may be reduced with glycopyrrolate administration. Consider increasing the dose of levodopa.

### USE IN SPECIFIC POPULATIONS

#### Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. Animal reproduction studies have not been conducted with glycopyrrolate. It is also not known whether glycopyrrolate can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. CUVPOSA should be given to a pregnant woman only if clearly needed.

#### Nursing Mothers

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

#### Pediatric Use

CUVPOSA was evaluated for chronic severe drooling in patients aged 3 to 16 years with neurologic conditions associated with problem drooling. CUVPOSA has not been studied in subjects under the age of 3 years.

#### Geriatric Use

Clinical studies of CUVPOSA did not include subjects aged 65 and over.

#### Renal Impairment

Because glycopyrrolate is largely renally eliminated, CUVPOSA should be used with caution in patients with renal impairment (see Clinical Pharmacology 12.3).

### OVERDOSAGE

Because glycopyrrolate is a quaternary amine which does not easily cross the blood-brain barrier, symptoms of glycopyrrolate overdosage are generally more peripheral in nature rather than central compared to other anticholinergic agents. In case of accidental overdose, therapy may include:

Maintaining an open airway, providing ventilation as necessary.

Managing any acute conditions such as hyperthermia, coma and or seizures as applicable, and managing any jerky myoclonic movements or choreoathetosis which may lead to rhabdomyolysis in some cases of anticholinergic overdosage.

Administering a quaternary ammonium anticholinesterase such as neostigmine to help alleviate peripheral anticholinergic effects such as anticholinergic induced ileus.

Administering activated charcoal orally as appropriate.

Manufactured by:  
Mikart, Inc.  
Atlanta, GA 30318

Manufactured for:  
**SHIONOGI INC.**  
Florham Park, NJ 07932

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