ATROPINE, HYOSCYAMINE, METHENAMINE, METHYLENE BLUE, PHENYL SALICYLATE, AND BENZOIC ACID b (Systemic)

Indications

Accepted

Irritative voiding, symptoms of (treatment)¾Indicated for the relief of local symptoms, such as inflammation, hypermotility, and pain, which accompany lower urinary tract infections. 1, 8

Diagnostic procedure-induced symptoms, urinary (treatment)¾Indicated for the relief of urinary tract symptoms caused by diagnostic procedures. 1

Precautions to Consider

Cross-sensitivity and/or related problems

Patients sensitive to other belladonna alkaloids or other salicylates may be sensitive to this medication also. 1

Pregnancy/Reproduction

Pregnancy¾Atropine, hyoscyamine, and methenamine cross the placenta. Studies have not been done in humans. 1

Studies have not been done in animals.

FDA Pregnancy Category C. 1

Breast-feeding

Methenamine 3 and traces of atropine and hyoscyamine are distributed into breast milk. However problems in humans have not been documented. 1, 3

Pediatrics

No information is available on the relationship of age to the effects of this combination in pediatric patients. However, it is known that infants and young children are especially susceptible to the toxic effects of the belladonna alkaloids. 1

Close supervision is recommended for infants and children with spastic paralysis or brain damage since an increased response to anticholinergics has been reported in these patients and dosage adjustments are often required.

When anticholinergics are given to children where the environmental temperature is high, there is risk of a rapid increase in body temperature because of these medications' suppression of sweat gland activity.

A paradoxical reaction characterized by hyperexcitability may occur in children taking large doses of anticholinergics.

Geriatrics

No information is available on the relationship of age to the effects of this combination in geriatric patients. However, it is known that geriatric patients may respond to the usual doses of the belladonna alkaloids with excitement, agitation, drowsiness, or confusion. 1, 3 Also, geriatric patients are especially susceptible to anticholinergic side effects, such as constipation, dryness of mouth, and urinary retention (especially in males). 3

In addition, caution is recommended when anticholinergics are given to geriatric patients, because of the danger of precipitating undiagnosed glaucoma.

Memory may become severely impaired in geriatric patients, especially those who already have memory problems, with the continued use of atropine and hyoscyamine since these medications block the action of acetylcholine, which is responsible for many functions of the brain, including memory functions. 7, 11

Dental

Prolonged use of belladonna alkaloids may decrease or inhibit salivary flow, thus contributing to the development of caries, periodontal disease, oral candidiasis, and discomfort. 4

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

Only specific interactions between this combination medication and other oral medications have been identified in this monograph. However, because of atropine's and hyoscyamine's effects on gastrointestinal motility and gastric emptying, absorption of other oral medications may be decreased during concurrent use with this combination medication. 1

>> Alkalizers, urinary, such as: 1, 15, 17

Antacids, calcium- and/or magnesium-containing

Carbonic anhydrase inhibitors 3

Citrates

Sodium bicarbonate or 3, 8

>> Diuretics, thiazide 13, 14

(may cause the urine to become alkaline, thereby reducing the effectiveness of methenamine by inhibiting its conversion to formaldehyde; concurrent use is not recommended 15, 17)

>> Anticholinergics, other, or other medications with anticholinergic action (See Appendix II)

(concurrent use of these medications may intensify anticholinergic effects of atropine and hyoscyamine; patients should be advised to report occurrence of gastrointestinal problems promptly since paralytic ileus may occur with concurrent therapy 1, 15, 22)

>> Antacids or

>> Antidiarrheals, adsorbent

(simultaneous use of these medications with this combination medication may reduce absorption of atropine and hyoscyamine, resulting in decreased therapeutic effectiveness; doses of these medications should be spaced 2 to 3 hours apart from doses of atropine and hyoscyamine 1, 26, 27)

(concurrent use of this combination medication with antacids, especially calcium carbonate-, magnesium-, or sodium bicarbonate-containing, may cause the urine to become alkaline, thereby reducing the effectiveness of methenamine by inhibiting its conversion to formaldehyde; simultaneous use may reduce absorption of atropine and hyoscyamine, resulting in decreased therapeutic effectiveness 1, 16, 17)

>> Ketoconazole

(atropine and hyoscyamine may cause increased gastrointestinal pH; concurrent administration of ketoconazole with atropine and hyoscyamine may result in a marked reduction in absorption of ketoconazole; patients should be advised to take this combination at least 2 hours after ketoconazole 1, 18)

Metoclopramide

(concurrent use of metoclopramide with atropine and hyoscyamine may antagonize the effects of metoclopramide on gastrointestinal motility 19, 21)

Monoamine oxidase (MAO) inhibitors, including furazolidone, procarbazine, and selegiline

(concurrent use may result in intensified anticholinergic side effects because of these medications' secondary anticholinergic activities; also, concurrent use of MAO inhibitors may block detoxification of anticholinergics, thus potentiating their action 1, 2, 20)

Opioid (narcotic) analgesics

(concurrent use of opioids with atropine and hyoscyamine may result in increased risk of severe constipation, which may lead to paralytic ileus, and/or urinary retention 1, 29, 30)

>> Potassium chloride, especially wax matrix preparations

(concurrent use with atropine and hyoscyamine may increase severity of potassium chloride-induced gastrointestinal lesions 23, 24, 25)

>> Sulfonamides

(in acid urine, methenamine breaks down into formaldehyde, which may form an insoluble precipitate with certain sulfonamides and may also increase the danger of crystalluria; concurrent use is not recommended 1, 8, 15, 16)

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):

With diagnostic test results

Catecholamine determinations, urinary and 3

17-hydroxycorticosteroid (17-OHCS) determinations, urinary and 8

Vanillylmandelic acid (VMA), urinary 8

(methenamine may cause a false increase 3)

Estriol determinations, urinary and 8

5-Hydroxy indoleacetic acid (5-HIAA) determinations, urinary 8

(methenamine may cause a false decrease)

>> Gastric acid secretion test

(atropine and hyoscyamine may antagonize the effect of pentagastrin and histamine in the evaluation of gastic acid secretory function; 33 administration of this combination is not recommended during the 24 hours preceding the test)

>> Phenolsulfonphthalein (PSP) excretion test

(methylene blue may cause a false positive 34)

Radionuclide gastric emptying studies

(atropine and hyoscyamine may result in delayed gastric emptying 10, 12)

Urinary free formaldehyde and

Urine pH

(methylene blue may interfere with analysis)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).

Risk-benefit should be considered when the following medical problems exist 1, 8

Brain damage, in children 28

(CNS effects may be exacerbated by atropine and hyoscyamine)

>> Cardiac disease, especially cardiac arrhythmias, congestive heart failure, coronary heart disease, mitral stenosis 1 or

>> Hemorrhage, acute, with tachycardia or 38

Hyperthyroidism or 1

Tachycardia 35

(increase in heart rate caused by atropine and hyoscyamine may be undesirable 1, 12, 15, 16)

Dehydration, severe or

Renal function impairment

(inadequate concentrations of this combination medicine may be achieved in urine; 3 salts of methenamine may precipitate, causing crystalluria in patients with low urine output 8)

>> Esophagitis, reflux 37

(decrease in esophageal and gastric motility 39 and relaxation of lower esophageal sphincter caused by atropine and hyoscyamine may promote gastric retention by delaying gastric emptying and may increase gastroesophageal reflux through an incompetent sphincter)

Fever

(may be increased through suppression of sweat gland activity caused by atropine and hyoscyamine 37)

>> Gastrointestinal tract obstructive disease 1

(decrease in motility and tone caused by atropine and hyoscyamine may result in obstruction and gastric retention)

>> Glaucoma, angle-closure, or predisposition to

(mydriatic effect caused by atropine and hyoscyamine may result in increased intraocular pressure and may precipitate an acute attack of angle-closure glaucoma 15, 16)

>> Glaucoma, open-angle

(mydriatic effect of atropine and hyoscyamine may cause a slight increase in intraocular pressure; glaucoma therapy may need to be adjusted 15, 16)

Glucose-6-phosphate dehydrogenase (G6PD) deficiency

(use of methylene blue may induce hemolysis 6)

Hepatic function impairment

(decreased metabolism of atropine and hyoscyamine; methenamine may facilitate ammonia production in the intestinal tract 8)

>> Hernia, hiatal, associated with reflux esophagitis

(atropine and hyoscyamine may aggravate condition 38)

Hypertension 38

(atropine and hyoscyamine may aggravate condition)

>> Intestinal atony in the elderly or debilitated patient or 37

>> Paralytic ileus 37

(atropine and hyoscyamine may result in obstruction)

Lung disease, chronic, especially in infants, small children, and debilitated patients

(reduction in bronchial secretion 39 caused by atropine and hyoscyamine can lead to inspissation and formation of bronchial plugs 37)

>> Myasthenia gravis 1

(condition may be aggravated because of inhibition of acetylcholine action 16)

Neuropathy, autonomic 38

(urinary retention and cycloplegia may be aggravated by atropine and hyoscyamine)

>> Prostatic hypertrophy, nonobstructive or

>> Urinary retention or 1

>> Uropathy, obstructive, such as bladder neck obstruction due to prostatic hypertrophy 1

(urinary retention may be precipitated or aggravated by atropine and hyoscyamine 12, 15)

Sensitivity to any of the medications in this combination

Spastic paralysis, in children 38

(response to atropine and hyoscyamine may be increased)

Toxemia of pregnancy 38

(hypertension may be aggravated by atropine and hyoscyamine)

Ulcerative colitis 38

(large doses of atropine and hyoscyamine may suppress intestinal motility, possibly causing paralytic ileus; also, use may precipitate or aggravate toxic megacolon)

Xerostomia

(prolonged use of atropine and hyoscyamine may further reduce limited salivary flow 37)

Caution in use is also recommended in patients over 40 years of age because of the danger of precipitating undiagnosed glaucoma. 12

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; >> = major clinical significance):

Intraocular pressure determinations

(recommended at periodic intervals because atropine and hyoscyamine may increase the intraocular pressure by producing mydriasis 35)

Urine pH

(monitoring recommended before start of treatment and throughout therapy since the effectiveness of methenamine is increased if a pH of 5.5 or below is maintained. 8 To check urine pH, phenaphthazine paper, which has a pH range of 4.5 to 7.5, may be used. However, the presence of methylene blue may interfere with urinary pH determination)