1.6.3 Patient information leaflet (PIL)

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For the use of Registered Medical Practitioner, Hospital or a Laboratory only.

SPASMODEX-10

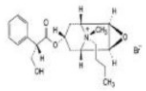
Hyoscine Butylbromide Tablets BP 10 mg

COMPOSITION

Each film coated tablet Contains:
Hyoscine Butylbromide BP 10 mg
Colour: Titanium Dioxide BP

DESCRIPTION

Hyoscine Butylbromide is Anticholinergic.it is a medication used to treat crampy abdominal pain, esophageal spasms, renal colic, and bladder spasms. Chemically it is known as (1R,2R,4S,5S,7s,9r)-9-Butyl-7-[[(2S)-3-hydroxy-2-phenylpropanoyl]oxy]-9-methyl-3- oxa-9-azoniatricyclo[3.3.1.02,4]nonane bromide. Its molecular formula a is C21H30BrNO4 & molecular Weight is 440.4.
Chemical Structure :



CLINICAL PHARMACOLOGY

Mechanism of Action

Hyoscine N-butylbromide is a competitive antagonist of the actions of acetylcholine and other muscarinic agonist. The drug is devoid of central nervous actions. The receptors affected by the drug are those of the peripheral structures that are either stimulated or inhibited by muscarine; such as exocrine glands and smooth and cardiac muscle. Cholinergic nerve stimulations are also inhibited but less readily than are responses to injected choline esters.
Depending on the dose, hyoscine N-butylbromide may inhibit the secretions of the respiratory tract, GIT, and sweat glands; it may reduce the motility and tone in the GIT, ureter, urinary bladder and biliary tract.

Pharmacokinetics

Absorption

As a quaternary ammonium compound, hyoscine butylbromide is highly polar and hence only partially absorbed following oral (8%) or rectal (3%) administration. After oral administration of single doses of hyoscine butylbromide in the range of 20 to 400 mg, mean peak plasma concentrations between 0.11 ng/mL and 2.04 ng/mL were found at approximately 2 hours. In the same dose range, the observed mean AUC0-tz-values varied from 0.37 to 10.7 ng h/mL. The median absolute bioavailabilities of different dosage forms, i.e. coated tablets, suppositories and oral solution, containing 100 mg of hyoscine butylbromide each were found to be less than 1%.

Distribution

Because of its high affinity for muscarinic receptors and nicotinic receptors, hyoscine butylbromide is mainly distributed on muscle cells of the abdominal and pelvic area as well as in the intramural ganglia of the abdominal organs. Plasma protein binding (albumin) of hyoscine butylbromide is approximately 4.4%. Animal studies demonstrate that hyoscine butylbromide does not pass the blood-brain barrier, but no clinical data to this effect is available. Hyoscine butylbromide (1mM) has been observed to interact with the choline transport (1.4 nM) in epithelial cells of human placenta *in vitro*.

Metabolism and elimination

Following oral administration of single doses in the range of 100 to 400 mg, the terminal elimination half-lives ranged from 6.2 to 10.6 hours. The main metabolic pathway is the hydrolytic cleavage of the ester bond. Orally administered hyoscine butylbromide is excreted in the faeces and in the urine. Studies in man show that 2 to 5% of radioactive doses is eliminated renally after oral, and 0.7 to 1.6% after rectal administration. Approximately 90% of recovered radioactivity can be found in the faeces after oral administration. The urinary excretion of hyoscine butylbromide is less than 0.1% of the dose. The mean apparent oral clearances after oral doses of 100 to 400 mg range from 881 to 1420 L/min, whereas the corresponding volumes of distribution for the same range vary from 6.13 to 11.3 x 105 L, probably due to very low systemic availability. The metabolites excreted via the renal route bind poorly to the muscarinic receptors and are therefore not considered to contribute to the effect of the hyoscine butylbromide.

INDICATIONS

Hyoscine Butylbromide is indicated in the treatment of spasm and hypermotility of the GIT, biliary and renal colic, and in spasmodic dysmenorrhea. It may also be used in patients with gastric or duodenal ulcer.

DOSAGE & ADMINISTRATION

Adults: 2 tablets four times daily. For the symptomatic relief of Irritable Bowel Syndrome, the recommended starting dose is 1 tablet three times daily, this can be increased up to 2 tablets four times daily if necessary.

Children 6 - 12 years: 1 tablet three times daily.
No specific information on the use of this product in the elderly is available. Clinical trials have included patients over 65 years and no adverse reactions specific to this age group have been reported.
Hyosc-10 Tablets should not be taken on a continuous daily basis or for extended periods without investigating the cause of abdominal pain.

CONTRAINDICATIONS

Hyosc-10 Tablets should not be administered to patients with myasthenia gravis, megacolon and narrow angle glaucoma. In addition, they should not be given to patients with a known hypersensitivity to hyoscine butylbromide or any other component of the product.

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WARNINGS AND PRECAUTIONS

In case severe, unexplained abdominal pain persists or worsens, or occurs together with symptoms like fever, nausea, vomiting, changes in bowel movements, abdominal tenderness, decreased blood pressure, fainting, or blood in stool, medical advice should immediately be sought.
Hyosc-10 Tablets should be used with caution in conditions characterised by tachycardia such as thyrotoxicosis, cardiac insufficiency or failure and in cardiac surgery where it may further accelerate the heart rate. Due to the risk of anticholinergic complications, caution should be used in patients susceptible to intestinal or urinary outlet obstructions.
Because of the possibility that anticholinergics may reduce sweating, Hyosc-10 should be administered with caution to patients with pyrexia.
Elevation of intraocular pressure may be produced by the administration of anticholinergic agents such as hyoscine butylbromide in patients with undiagnosed and therefore untreated narrow angle glaucoma. Therefore, patients should seek urgent ophthalmological advice in case they should develop a painful, red eye with loss of vision whilst or after taking hyoscine butylbromide.

Fertility, pregnancy and lactation

Pregnancy

There are limited data from the use of hyoscine butylbromide in pregnant women. Animal studies are insufficient with respect to reproductive toxicity . As a precautionary measure Hyosc-10 is not recommended during pregnancy.

Lactation

There is insufficient information on the excretion of hyoscine butylbromide and its metabolites in human milk. A risk to the breastfeeding child cannot be excluded. Use of Hyosc-10 during breastfeeding is not recommended.

Fertility

No studies on the effects on human fertility have been conducted.

INTERACTIONS WITH OTHER MEDICAMENTS

The anticholinergic effect of drugs such as tri- and tetracyclic antidepressants, antihistamines, quinidine, amantadine, antipsychotics (e.g. butyrophenones, phenothiazines), disopyramide and other anticholinergics (e.g. tiotropium, ipratropium, atropine-like compounds) may be intensified by Hyosc-10.
Concomitant treatment with dopamine antagonists such as metoclopramide may result in diminution of the effects of both drugs on the gastrointestinal tract. The tachycardic effects of beta-adrenergic agents may be enhanced by hyoscine butylbromide.

ADVERSE EFFECTS

Many of the listed undesirable effects can be assigned to the anticholinergic properties of hyoscine butylbromide.
Adverse events have been ranked under headings of frequency using the following convention:
Very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1000, <1/100); rare (≥ 1/10000, <1/1000); very rare (<1/10000); not known – cannot be estimated from the available data.
Immune system disorders
Uncommon: skin reactions (e.g. urticaria, pruritus)
Not known*: anaphylactic shock , anaphylactic reactions, dyspnoea, rash, erythema, other hypersensitivity
Cardiac disorders
Uncommon: tachycardia
Gastrointestinal disorders:
Uncommon: dry mouth
Skin and subcutaneous tissue disorders
Uncommon: dyshidrosis
Renal and urinary disorders
Rare: urinary retention

OVERDOSE AND TREATMENT

Symptoms

Serious signs of poisoning following acute overdosage have not been observed in man. In the case of overdosage, anticholinergic effects such as urinary retention, dry mouth, reddening of the skin, tachycardia, inhibition of gastrointestinal motility and transient visual disturbances may occur, and Cheynes-Stokes respiration has been reported.

Treatment

In the case of oral poisoning, gastric lavage with medicinal charcoal should be followed by magnesium sulfate (15%). Symptoms of Hyosc-10 overdosage respond to parasympathomimetics. For patients with glaucoma, pilocarpine should be given locally. Cardiovascular complications should be treated according to usual therapeutic principles. In case of respiratory paralysis, intubation and artificial respiration. Catheterisation may be required for urinary retention.
In addition, appropriate supportive measures should be administered as required.

PRESENTATION

Blister Pack of 10 x 10 Tablets

STORAGE :

Store below 30°C. Protect from light & Moisture.
Keep Medicine out of reach of children

Manufactured For / Fabriqué pour:
Pharma Life Science Ltd.
P.O. Box 38148-00623,
Nairobi Kenya.

Manufactured By / Fabriqué Par:
Skybiotech Life Sciences Private Limited.
Factory: Gut No:5, Gevrai Tanda Paithan Road Aurangabad 431002 (M.S.) India.