CISAPRIDE

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Cisapride acts in a manner similar to the physiological mechanism of the gastrointestinal tract with minimal side effects. The drug is considered to enhance the physiological release of acetylcholine from the post ganglionic nerve endings in the myenteric plexus in the gas- * trointestinal smooth muscles(l). It has no anti-dopaminergic effects like metclopromide and domperidone. A comparative analysis of action of prokinetic drugs is shown in *Table I.* There is also some evidence that cisapride acts as both agonist and antagonist of serotonin; the significance of this is not known(l).

Cisapride increases the lower esophageal sphincter tone and amplitude of esophageal contractions and decreases the time of exposure of esophagus to a pH less then 4(2). In the stomach it shortens the gastric emptying time, both for solids and liquids(3). In small and large intestine it enhances the transit(4). There is no effect on gastrin, insulin and prolactin secretion(4).

Pharmacokinetics

Cisapride is rapidly absorbed orally and food enhances its absorption. The peak concentrations in the blood are achieved in 1 to 2 hrs. It is metabolised in liver into non-cisapride. Cisparide has a half-life of 7 to 10 hrs and its metabolite is excreted equally through the liver and kidney. Cisapride is excreted in milk in small amounts (0.1% of dose given to the mother)(l,4).

Adverse Reactions

Cisapride is well tolerated with few side effects. They are mainly gastrointestinal in form of abdominal crams, diarrhea and borborygmi. Headache, fatigue and dizziness may occur. The increased acetylcholine may lead to a theoretical increase in the acid secretion in stomach which has however, not been shown in *vivo.* Reports of convulsions and extrapyramidal reactions are rare. In cases of overdosage, the patients experience retching, borborygmi, excessive passage of flatus and stool and urinary frequency for 2 hrs. There were no neurological, cardiovascular, respiratory, biochemical or hematological effects. Treatment consisted of gastric lavage and supportive measures(l,5).

Uses

Cisapride is used in motility disorders including gastroesophageal reflux(l,5-7), dyspepsia(8), chronic constipation(1), and pseudo-obstruction(9).

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TABLE I– *Comparitive Analysis of Prokinetic Drugs*

	Cisapride	Metclopramide	Domperidone
Mechanism of action	Increase release of Ach from nerve endings	Inhibits action of dopamine; cholinergic action on esophagus	Inhibits action of dopamine
Site of action	Entire GI tract	Esophagus & stomach	Esophagus & stomach
Increased LES tone	+++	+++	++
Anti-dopaminergic action	None	Yes	Yes
Prolactin levels	No change	Increased	Increased
GI side effects	++	+	+
Other side effects	None	++	+

Ach= Actylcholine; GI= Gastrointestinal; LES= Lower esophageal sphincter.

Gastroesophageal Reflux (GER)

In preterms of ≤32 weeks gestation, the esophageal peristalsis and the lower esophageal sphincter tone is poor. They have more chances of GER which manifests as regurgitation of feeds, apneic spells, failure to thrive, aspiration pneumonia, wheeze, neck retraction and sudden infant death syndrome. In older children GER presents as recurrent pneumonias, esophagitis, vomiting and chronic bronchopulmonary disease. GER in preterms increases a risk of mortality, but spontaneous cure occurs with increasing age.

Cisapride may benefit infants and children with GER by increasing the lower esophageal sphincter tone, decreasing the gastric transit, reducing the number of refluxes longer than 5 minutes and reducing the esophageal clearance time(2). Cisparide is effective in non-ulcer dyspepsia(8), which occurs primarily due to delayed gastric emptying and manifests as belching and early satiety. Chronic constipation in children with impacted stools or encopresis, responds to treatment with cisapride which normalizes the colonic motility. Cisparide is also found to be effective in pseudo-obstruction due to degenerative visceral myopathies and neuropathies(9).

Drug Interactions

Atropine-like drugs antagonise the effects of cisapride. Cisapride reduces the bioavailability of the drugs which are absorbed from the stomach and increases those of drugs absorbed from small intestine(l). Cisapride prolongs prothombin time if given with anticoagulants. Cisapride is contraindicated in cases of gastrointestinal hemorrhage, perforation and mechanical obstruction of the gut(l).

Route of Administration, Dose and Preparations

The preparations are shown in Table II. The drug is administered orally 0.15 to 0.3 mg/kg/d in 3 to 4 divided dosages given 15 to 30 minutes before feeds/meals. It should be given for a minimum of 4 to 6 wks in cases of GER and 6 mos to 1 yr in cases of constipation.

TABLE II – *Prepations of Cisapride*

Trade Name	Company	Tablets (mg)	Rate (Rs) (10 tabs)	Suspension (ml)	Rate (Rs)
Ciza	INTAS	10	38.00	60	29.80
Cisapid	Kopran	10	31.90	60	33.00
Motilax	USV	10	36.99	60	29.00
Unipride	Torrent	10	39.90	-	-
Cisapro	Zeita	10	32.00	30	19.80
Cispel	Panacea	10	32.00	60	24.00
Esorid	Sun	10	38.00	-	-
Pulsid	Max	5 & 10	16.00 & 29.50	60	29.80
Syspride	Systopic	10	38.00	0	0

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