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Review Article

Clinical Pharmacology of Ranitidine in Infants and Children

Gian Maria Pacifici*

Department of Pharmacology, University of Pisa, Italy

Abstract

Histamine H2 receptor antagonists inhibit acid production by reversibly competing with histamine for binding to H2 receptors on the basolateral membrane of parietal cells. Four H2 receptor antagonists are available: cimetidine, ranitidine, famotidine, and nizatidine. The major therapeutic indications for H2 receptor antagonists are to promote healing of gastric and duodenal ulcers, to treat uncomplicated gastroesophageal reflux disease, and to prevent the occurrence of stress ulcers. The H2 receptor antagonists generally are well tolerated with a low incidence of adverse-effects. Ranitidine may be administered orally or intravenously and following oral dosing it is rapidly absorbed. In newborns, the oral dose of ranitidine is 2 mg/kg thrice-daily and in older infants it is 2 to 4 mg/kg twice-daily. In children, the ranitidine dose varies according to the child age. Ranitidine causes different effects in infants and children. Ranitidine is converted into ranitidine N-oxide, ranitidine S-oxide, and desmethyl ranitidine, and the former metabolite is the major metabolite. The pharmacokinetics of ranitidine have been studied in infants and children and the elimination half-life is 2.79 hours in infants and 2.03 hours in children. Ranitidine interacts with drugs and the treatment of infants and children with ranitidine has been extensively studied. Ranitidine freely crosses the human placenta and migrates into the breast-milk in significant amounts. The aim of this study is to review the ranitidine dosing, effects, pharmacokinetics, and treatment in infants and children, and ranitidine metabolism, drug interaction, placental transfer and migration into the breast-milk.

***Corresponding author**

Gian Maria Pacifici, Department of Pharmacology, University of Pisa, Associate professor of Pharmacology, via Sant'Andrea 32, 56127 Pisa, Italy, Email: pacifici44@tiscali.it

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- Children

INTRODUCTION

Histamine H_2 Receptor antagonists

The arrival of selective histamine H_2 receptor antagonists was a landmarked in the treatment of acid-peptic disease. Before the availability of the H_2 receptor antagonists, the standard care was simply neutralization in the stomach lumen generally with inadequate results. The long history of safety and efficacy with the H_2 receptor antagonists led to their availability without a prescription. Increasingly, however, the proton pump inhibitors are replacing the H_2 receptor antagonists in clinical practice [1].

Mechanism of action of histamine H_2 receptor antagonists: The histamine H_2 receptor antagonists inhibit acid production by reversibly competing with histamine for binding to H_2 receptors on the basolateral membrane of parietal cells. Four different H_2 receptor antagonists, which differ mainly in their pharmacokinetics and propensity to cause drug interactions, are available in the USA: cimetidine, ranitidine, famotidine, and nizatidine. These drugs are less potent than the proton pump inhibitors but still suppress 24-hour gastric acid secretion by about 70%. Suppression of basal and nocturnal acid secretion is about 70%; because suppression of nocturnal acid secretion is important in the healing of duodenal ulcers, evening dosing of an H_2 receptor antagonist is adequate therapy in most cases. There is little evidence for the use of H_2 receptor antagonists for the treatment of blending ulcers, and they are no longer recommended for this purpose. All four H_2 receptor antagonists are available as prescription and over-the-counter formulations for oral administration. Intravenous and intramuscular preparations of cimetidine, ranitidine, and famotidine are also available for use in critically ill patients [1].

Therapeutic uses of histamine H_2 receptor antagonists: The major therapeutic indications for H_2 receptor antagonists are to promote healing of gastric and duodenal ulcers, to treat uncomplicated gastroesophageal reflux disease, and to prevent the occurrence of stress ulcers. The H_2 receptor antagonists generally are well tolerated, with a low (< 3%) incidence of adverse-effects. Side-effects are minor and include diarrhoea, headache, drowsiness, fatigue, muscular pain, and constipation. Less-common adverse-effects include those affecting the central nervous system (confusion, delirium, hallucinations, slurred speech, and headaches), which occur primarily with intravenous administration of the drugs or in elderly subjects. Several reports have associated H_2 receptor antagonists with various blood disorders, including thrombocytopenia. H_2 receptors antagonists cross the placenta and are excreted in breast-milk. Although no

major teratogenic risk have been associated with these drugs, caution is warranted when they are used in pregnancy. All agents that inhibit gastric acid secretion may alter the rate of absorption and subsequent bioavailability of the H_2 receptor antagonists [1].

THERAPEUTIC USE OF RANITIDINE IN INFANTS AND CHILDREN

Ranitidine is used to treat symptomatic oesophagitis, gastritis, and peptic ulceration. A proton pump inhibitor such as omeprazole, esomeprazole, or lansoprazole may sometimes be more effective [2]. Ranitidine is used for the prevention and treatment of stress ulcers, and gastrointestinal haemorrhage aggravated by gastric acid secretion. Ranitidine inhibits gastric acid secretion by histamine H_2-receptor antagonism. In infants, the peak serum concentration of ranitidine occurs 1 to 3 hours after oral administration and it is not influenced by food. The bioavailability of ranitidine is quite variable. Hepatic metabolism predominates after oral absorption, with 30% excreted unchanged drug in the urine. In contrast, 70% of an intravenous dose of ranitidine is excreted unchanged in the urine. The elimination half-life in infants is 3 to 7 hours, and is prolonged in preterm infants and patients with renal and hepatic insufficiency. The use of H_2 receptor antagonists has been associated with an increased risk for late-onset bacterial and fungal sepsis. Routine gastric acid suppression in infants should be avoided. Elevation in hepatic enzymes, leukopenia, and bradycardia has been reported in adult patients. Ranitidine is incompatible to amphotericin B, pentobarbital, and phenobarbital [3].

ABSORPTION, DISTRIBUTION, METABOLISM AND ELIMINATION OF HISTAMINE H_2 RECEPTOR ANTAGONISTS

The H_2 receptor antagonists are rapidly absorbed after oral administration, with peak serum concentrations within 1 to 3 hours. The absorption may be enhanced by food or decreased by antacids but these effects are unimportant clinically. Therapeutic levels are achieved rapidly after intravenous dosing and are maintained for 4 to 5 hours (cimetidine), 6 to 8 hours (ranitidine), or 10 to12 hours (famotidine). The elimination half-life values of these agents after oral administration in adults range from 1 to 3.5 hours and only a small fraction of these drugs is protein bound. The kidneys excrete these drugs and their metabolites by filtration and renal tabular secretion, and it is important to reduce drug dose in patients with decreased creatinine clearance. Neither haemodialysis nor peritoneal dialysis clears significant amounts of these drugs. Hepatic metabolism accounts for a small fraction of clearance (from 10% to about 35%), but liver disease per se is generally not an indication for dose adjustment [1] (Figure 1).

LITERATURE SEARCH

The literature search was performed electronically using PubMed database as search engine and the following key words were used: “ranitidine dosing infants, children“, ranitidine effects infants, children”, “ranitidine adverse-effects infants, children”, “ranitidine metabolism”, “ranitidine pharmacokinetics infants, children”, “ranitidine drug interactions”, “ranitidine treatment infants, children”, “ranitidine placental transfer”, and “ranitidine breast-milk”. In addition, the books: The Pharmacological Basis of Therapeutics [1], Neonatal Formulary [2], NEOFAX® by Young and Mangum [3], and The British National Formulary for Children [4] have been consulted.

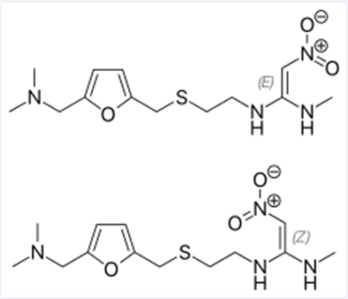

Figure 1 Molecular structure of ranitidine enantiomers (molecular weight = 314.404 grams/mole).

RESULTS

Administration schedules of ranitidine to infants and children

Administration to infants [2]:

Oral administration:

Newborns: Give: 2 mg/kg thrice-daily. The dose may be increased to a maximum of 3 mg/kg thrice-daily. Variable first-pass metabolism affects uptake in the term infant.

Infants aged 1 to 6 months: Start at 1 mg/kg thrice-daily. The dose may be increased to 3 mg/kg thrice-daily

Infants aged 7 to 12 months: Give: 2 to 4 mg/kg twice-daily.

Intermittent intravenous administration:

Newborns: Give: 500 µg/kg given slowly intravenously twice-daily will usually keep the gastric pH above 4 in infants < 32 weeks of gestation in the first week of life. Term infants may need 1 (or even 1.5) mg/kg 4 times-daily or thrice-daily. Rapid administration can rarely cause an arrhythmia.

Infants aged 1 to 6 months. Give: 1 mg/kg 4 times-daily or thrice-daily.

Continuous intravenous infusion:

This administration is rarely used (or necessary). Give: 1.5 mg/kg loading dose, followed by a maintenance infusion of 50 µg/kg per hour. Half of this dose is more than adequate in the very preterm infant soon after birth.

Administration to children [4]:

Oral administration for benign ulceration and duodenal ulcerations:

Children aged 1 to 5 months. Give: 1 mg/kg thrice-daily (maximum per dose 3 mg/kg thrice-daily).

Children aged 6 months to 2 years. Give: 2 to 4 mg/kg twice-daily.

Children aged 3 to 11 years. Give: 2 to 4 mg/kg twice-daily (maximum per dose = 150 mg).

Intravenous prophylaxis of stress ulceration:

Children aged 1 month to 11 years. Give: 1 mg/kg 4 times-daily or thrice-daily (maximum per dose = 50 mg), the dose may be given as an intermittent infusion at a rate of 25 mg per hour.

Children aged 12 to 17 years. Give: 50 mg thrice-daily, the dose to be diluted to 20 ml, and given over at least 2 min, and then (by mouth) give 150 mg twice-daily, the dose may be given when oral feeding commences.

Oral treatment of reflux oesophagitis and other conditions where gastric acid reduction is beneficial

Children aged 1 to 5 months. Give: 1 mg/kg thrice-daily (maximum per dose = 3 mg/kg thrice-daily).

Children aged 6 months to 2 years. Give: 2 to 4 mg/kg twice-daily.

Children aged 3 to 11 years. Give: 2 to 4 mg/kg twice-daily (maximum per dose = 150 mg); increase the dose to 5 mg/kg twice-daily (maximum per dose = 300 mg); the dose may be increased for severe gastroesophageal disease.

Children aged 12 to 17 years. Give: 150 mg twice-daily, alternatively 300 mg once-daily, the dose should be taken at night, and then increase the dose if necessary to 300 mg twice-daily for up to 12 weeks in moderate to severe gastroesophageal reflux disease, alternatively increase the dose if necessary to 150 mg 4 times-daily for up to 12 weeks in moderate to severe gastroesophageal reflux disease.

Treatment of reflux oesophagitis and other conditions where gastric acid reduction is beneficial by slow intravenous injection

Children. Give: 1 mg/kg 4 times-daily or thrice-daily (maximum per dose = 50 mg), the dose may be given as an intermittent infusion at a rate of 25 mg per hour.

Effects of ranitidine in infants and children

Ranitidine administration is associated with an increased risk of necrotizing enterocolitis in preterm infants. H_2-blockers use should be only administered in very strictly selected cases after careful consideration of the risk-benefit ratio [5]. An infusion of 0.0625 mg/kg per hour of ranitidine is sufficient to increase and maintain gastric pH above 4 [6]. Oral ranitidine is more effective than probiotics in reducing stool frequency and normalizing stool consistency in toddler's diarrhoea [7]. Proton pump inhibitors or histamine H_2 receptor antagonists may be used to treat children with gastroesophageal reflux disease [8]. Ranitidine increases gastric fluid pH significantly compared to control (P-value < 0.05) in children [9]. Oral ranitidine at doses of 2 to 3.5 mg/kg is effective in decreasing gastric acidity in children [10]. The administration of ranitidine plus quince syrup is useful to improve paediatric gastroesophageal reflux disease in children [11]. Ranitidine or omeprazole treats gastroesophageal reflux disease in infants [12]. An infusion of 0.1 mg/kg per hour of ranitidine increases the gastric pH over 5.3 in children [13]. Ranitidine is comparable or superior to most other antiulcer agents in the treatment and prevention of a variety of gastrointestinal disorders associated with gastric acid secretion in children [14].

Adverse-effects of ranitidine in infants and children [4]

General adverse-effects

Adverse-effects rare or very rare

Bone marrow depression, bradycardia, breast conditions, dyskinesia, nephritis acute interstitial, pancreatitis acute, and vision blurred.

Adverse-effects which frequency is not known

Dyspnoea

Specific adverse-effects

Adverse-effects rare or very rare with parenteral use

Anaphylactic shock, and cardiac arrest.

Metabolism of ranitidine

Rat and human liver microsomes oxidized ranitidine to its N-oxide for 66 to 76%, S-oxide for 13 to 18%, and desmethyl ranitidine for 12 to 16% [15] (Figure 2, Figure 3 and Figure 4).

Ranitidine N-oxide, ranitidine S-oxide and desmethyl ranitidine have been recovered in the urine of four volunteers [16].

Pharmacokinetics of ranitidine in preterm and term infants

Asseff et al. [17], studied the pharmacokinetics of ranitidine in 30 preterm and 20 term infants and ranitidine was intravenously administered at a dose of 3 mg/kg once-daily (Table 1 and Table 2).

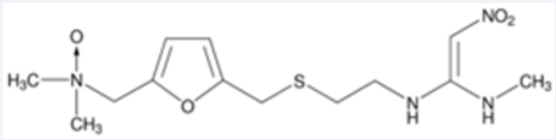

Figure 2 Ranitidine N-oxide molecular structure (molecular weight = 330.41 grams/mole).

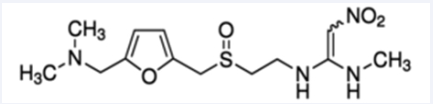

Figure 3 Ranitidine S-oxide molecular structure (molecular weight = 330.41 grams/mole).

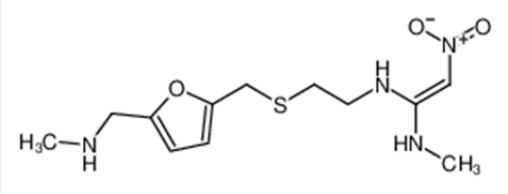

Figure 4 Desmethyl ranitidine molecular structure (molecular weight = 300.38 grams/mole).

This table shows that ranitidine rapidly distributes following intravenous administration as the distribution half-life is 0.3899 hours, ranitidine is rapidly eliminated as the elimination half-life is 2.79 hours, ranitidine rapidly diffuses from the central to peripheral compartment as K_{12} is 0.5395

h^{-1}, the diffusion-rate from the peripheral compartment to the central compartment (K_{21}) is 1.76 h^{-1} suggesting that ranitidine slowly diffuses from the peripheral to central compartment, the distribution volume of ranitidine is similar to the water volume, and there is a remarkable interindividual variability of the pharmacokinetics.

Orenstein et al. [18], investigated the pharmacokinetics of ranitidine in children with gastroesophageal reflux disease and a single oral dose of 75 mg ranitidine was administered (Table 3 and Table 4).

This table shows that ranitidine is rapidly absorbed after oral administration as Tmax is 2.5 hours, the elimination half-life is similar to that obtained in infants (for comparison to infants see

Table 1: Demographic characteristics of infants included in the study, by Asseff et al. [17].

Biological characteristics	Females (N = 20)	Males (N = 30)	*P-value	Preterm infants (N = 30)	Term infants (N = 20)	*P-value
Gestational age (weeks)	34.2	38.5	0.103	33.6	38.3	0.0001
Mean±SD	±4.16	±2.7	---	±3.7	±0.9	---
Birth weight (grams)	2,331	2,680	0.715	2,362	3,001	0.008
Mean±SD	±677	±561	---	±563	±620	---
*Squire Chi Test (X^2)						

Table 2: Pharmacokinetic parameters of ranitidine which are obtained in 30 preterm infants and in 20 term infants. Figures are the mean±SD, by Asseff et al. [17].

Parameter	Value
$AUC_{0-\infty}$ (ng/ml/h)	1,689±563
Distribution half-life (h)	0.3899±0.129
Elimination half-life (h)	2.79±0.93
K_{12} (Velocity of transferase) h^{-1}	0.5395±0.176
K_{21} (Velocity of transferase) h^{-1}	1.76±0.58
Distribution volume (L/kg)	1.44±0.48
Total body clearance (ml/kg/h)	5.9±1.96

Table 3: Demographic characteristics of 19 children included in the study. Figures are the median and (range), by Orenstein et al. [18].

Parameter	Value
Age (years)	8.0 (4 – 11)
Male/female (%)	53/47
Height (cm)	133 (105 – 146)
Body-weight (kg)	30.5 (14.4 – 49.5)
Duration of reflux (months)	14.0 (2 – 112)

Table 4: Pharmacokinetic parameters of ranitidine which are obtained in 19 children with gastroesophageal reflux disease. Figures are the median and (range) by Orenstein et al. [18].

Parameter	Value
$AUC_{0-6\,h}$ (h*ng/ml)	1,450 (412 – 4,286)
$AUC_{0-\infty}$ (h*ng/ml)	1,813 (797 – 1,494)
Peak concentration (ng/ml)	477 (128 – 1,569)
TBC/F (ml/min)	690 (253 – 1,569)
TBC/F/kg (ml/min/kg)	24 (11- 46)
Tmax (h)	2.5 (0.5 – 5.0)
Elimination half-life (h)	2.03 (1.35 – 4.53)
DV/F (L)	125 (40 – 615)
DV/F/kg (L/kg)	4.0 (2.1 – 17.6)

table 2), and the distribution volume is larger than the water volume. This finding contrasts with the distribution volume obtained in infants who have a distribution volume similar to the water volume. In addition, there is a remarkable interindividual variability of the pharmacokinetic parametees.

Interaction of ranitidine with drugs

Intravenous trospium significantly lowers the mean absorption time and the oral bioavailability of ranitidine [19]. In therapeutic concentrations, ranitidine inhibits the disappearance-rate of fentanyl [20]. Ranitidine interacts with clopidogrel through adenylyl cyclase inhibition [21]. Steady-state serum phenytoin concentration increases 40% after the addition of ranitidine 150 mg [22]. Theophylline blood concentrations rise from 104 to 188 μM when theophylline is co-administered with ranitidine and theophylline concentrations returned to normal values with the discontinuation of ranitidine [23].

Treatment of infants and children with ranitidine

Ranitidine and omeprazole use in very-low-birth-weight preterm infants is not associated with an increased risk of infection, necrotising enterocolitis, and mortality [24]. Ranitidine therapy is associated with an increased risk of infections, necrotising enterocolitis, and fatal outcome in very-low-birth-weight preterm infants [25]. Histamine H_2 blocker use is associated with increased risk of death, necrotising enterocolitis, or sepsis in hospitalized very-low-birth-weight infants [26]. Preterm infants need significantly smaller doses of ranitidine than term infants to keep their intraluminal gastric pH over 4. The optimal dose of ranitidine for preterm infants is 0.5 mg/kg twice-daily and that for term infants is 1.5 mg/kg thrice-daily [27]. Pharmacologic management of gastroesophageal reflux disease includes a prokinetic agent such as metoclopramide or cisapride and a histamine-receptor type 2 antagonists such as cimetidine or ranitidine when esophagitis is suspected [28]. Histamine H_2 receptor antagonists and proton pump inhibitors are the principal medical therapies for gastroesophageal reflux disease in children [29]. Ranitidine dose recommendations are based on children weight. However, the dosing scheme should take into consideration both cardiac failure and surgery in order to avoid administration of higher or more frequent doses than necessary [30]. Esophagitis is common in children with cerebral palsy and histamine$_2$-receptor antagonists such as ranitidine is effective in the treatment of esophagitis in children [31]. Upper gastrointestinal haemorrhage is an important complication in critically ill children and prophylaxis with almagate, ranitidine, or sucralfate reduces the occurrence-rate of clinically important gastrointestinal haemorrhage in children [32].

Transfer of ranitidine across the human placenta

In literature there is only one study on the placental transfer of ranitidine and it has been reported by Lalic-Popovic et al. [33]. Ranitidine umbilical cord (arterial and venous) concentrations are similar to the maternal concentrations indicating that ranitidine freely crosses the human placenta.

Migration of ranitidine into the breast-milk

Six women with established lactation were 6 to 10 days postpartum and were given a single oral dose of 150 mg of ranitidine. The average breast-milk concentrations of ranitidine are 1.28, 1.42, and 1.02 μg/ml at 2, 4, and 8 hours, respectively, after the dose; however, there is a great interpatient variability in both peak concentrations and the time of the peak [34]. After 5 oral doses of ranitidine 150 mg twice-daily to a 54-day postpartum woman, the highest measured breast-milk concentration of ranitidine occurs 5.5 hours after the 5th dose and it is 2.6 μg/ml [35].

DISCUSSION

The arrival of selective histamine H_2 receptor antagonists was a landmarked in the treatment of acid-peptic disease. Histamine H_2 receptor antagonists inhibit acid production by reversibly competing with histamine for binding to H_2 receptors on the basolateral membrane of parietal cells. Four H_2 receptor antagonists are available and they are: cimetidine, ranitidine, famotidine, and nizatidine. The major therapeutic indications for H_2 receptor antagonists are to promote healing of gastric and duodenal ulcers, to treat uncomplicated gastroesophageal reflux disease, and to prevent the occurrence of stress ulcers. The H_2 receptor antagonists are rapidly absorbed after oral administration with peak serum concentrations within 1 to 3 hours. Therapeutic concentrations of H_2 receptor antagonists are achieved rapidly after intravenous dosing and are maintained for 4 to 5 years (cimetidine), 6 to 8 hours (ranitidine), or 10 to 12 hours (famotidine) [1]. Ranitidine is used to treat symptomatic oesophagitis, gastritis, and peptic ulceration. A proton pump inhibitor such as omeprazole, esomeprazole, or lansoprazole may sometimes be more effective [2]. Ranitidine inhibits gastric acid secretion by histamine H_2 antagonism. In infants, the peak serum concentration of ranitidine occurs 1 to 3 hours after oral administration and it is not influenced by food and the bioavailability of ranitidine is quite variable [3]. Ranitidine may be administered orally or intravenously. In newborns, the oral dose of ranitidine is 2 mg/kg thrice-daily and in older infants it is 2 to 4 mg/kg twice-daily. In newborns, the intravenous dose is 500 μg/kg twice-daily and in older infants it is 1 mg/kg 4 times-daily [2]. In children, the oral and the intravenous dose vary according to the child age [4]. Ranitidine causes different effects in infants and children [5-14]. Ranitidine is associated with an increased risk of necrotizing enterocolitis in preterm infants and H_2-blockers should be administered in very strictly cases after consideration of the risk-benefit ratio [5], a ranitidine infusion of 0.0625 mg/kg per hour increases and maintains a gastric pH above 4 in children [6], oral ranitidine administered to toddlers with diarrhoea normalizes stool consistency [7]. Proton pump inhibitors or histamine H_2 receptor antagonists treat gastroesophageal reflux disease in children [8]. Ranitidine increases the gastric fluid pH in children [9], oral ranitidine, at doses of 2 to 3.5 mg/kg, decreases gastric acidity in children [10], ranitidine plus quince treats paediatric gastroesophageal reflux disease in children [11], ranitidine or omeprazole treats gastroesophageal reflux disease in children [12], an infusion of 0.1 mg/kg per hour of ranitidine increases the gastric pH over 5.3 in children [13], and ranitidine is comparable or superior to most other antiulcer agents in the treatment and prevention of gastrointestinal disorders associated with gastric acid secretion in children [14]. Ranitidine is metabolized into ranitidine N-oxide, ranitidine S-oxide, and desmethyl ranitidine [15,16], and ranitidine N-oxide is the

major metabolite [15]. The pharmacokinetics of ranitidine have been studied in preterm and term infants and the elimination half-life and the distribution volume are 2.79 hours and 1.44 L/kg, respectively [17] and the pharmacokinetics of ranitidine have been studied in children with gastroesophageal reflux disease [18]. In these children, the elimination half-life and the distribution volume are 2.03 hours and 4.0 L/kg, respectively. Ranitidine interacts with drugs [19-23]. Trospium reduces the absorption time and the oral bioavailability of ranitidine [19], ranitidine inhibits the disappearance-rate of fentanyl [20], ranitidine interacts with clopidogrel through adenylyl cyclase inhibition [21], phenytoin serum concentration is increased after the addition of ranitidine [22], and ranitidine increases the blood concentration of theophylline [23]. The treatment of infants and children with ranitidine has been extensively studied [24-32]. Ranitidine and omeprazole do not increase the risk of infection, necrotising enterocolitis, and mortality in very-low-birth-weight infants [24], in contrast to this finding, ranitidine or histamine H_2 blockers increase the risk of infections, necrotising enterocolitis, and mortality in very-low-birth-weight infants [25, 26], preterm infants need smaller doses of ranitidine than term infants to increase the gastric pH [27], the treatment of gastroesophageal reflux disease includes a prokinetic agent such as metoclopramide or cisapride and a histamine-receptor type 2 antagonists such as cimetidine or ranitidine [28], histamine H_2 receptor antagonists and proton pump inhibitors are the principal therapies for the treatment of gastroesophageal reflux disease in children [29], ranitidine dose is based on the children weight but both cardiac failure and surgery should be considered to optimize ranitidine therapy [30], ranitidine is an effective treatment of esophagitis in children [31], the prophylaxis of upper gastrointestinal haemorrhage in children requires almagate, ranitidine, or sucralfate [32]. Ranitidine freely crosses the human placenta [33] and migrates into breast-milk in significant amounts [34,35].

In conclusion, ranitidine is a histamine H_2 receptor antagonist and it is used to promote healing of gastric and duodenal ulcers, to treat uncomplicated gastroesophageal reflux disease, and to prevent the occurrence of stress ulcers. Ranitidine may be administered orally or intravenously and following oral dosing ranitidine is rapidly absorbed. In newborns, the oral dose of ranitidine is 2 mg/kg thrice-daily and in older infants the oral dose of ranitidine is 2 to 4 mg/kg twice-daily. In children, the dose of ranitidine increases with the child age. Ranitidine causes different effects in infants and children, and ranitidine is converted into ranitidine N-oxide, ranitidine S-oxide, and desmethyl ranitidine and the former metabolite is the major metabolite. The pharmacokinetics of ranitidine have been studied in infants and children and the elimination half-life of ranitidine is 2.79 and 2.03 hours in infants and children, respectively. Ranitidine interacts with drugs, and the treatment of infants and children with ranitidine has been extensively studied. Ranitidine freely crosses the human placenta and migrates into the breast-milk in significant amounts. The aim of this study is to review the clinical pharmacology of ranitidine in infants and children.

CONFLICT OF INTERESTS

The authors declare no conflicts of financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employments, gifts, and honoraria.

This article is a review and drugs have not been administered to men or animals.

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