CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.2717135

Available online at: http://www.iajps.com *Research Article*

ORAL VERSUS INTRAVENOUS ROUTE OF ANTIEMETIC MEDICATION: WHICH IS BETTER TO CONTROL ACUTE GASTROENTERITIS

[1]Dr Muhammad Usman Khan, [2]Dr Qurrat ul Aen Zafar, [3]Dr. Komal Nizam

[1]Shaikh Khalifa Bin Zayed Al-Nahyan Medical and Dental College, Lahore, [2]DHQ Hospital, Jhang, [3]Services Hospital Lahore.

Article Received: March 2019 **Accepted:** April 2019 **Published:** May 2019

Abstract:

Acute gastroenteritis is very much common among diseases which causes mortality among under-developed countries. Seventy percent of the acute gastroenteritis episodes is because of viruses. An effective approach to treat the onset of acute gastroenteritis is oral rehydration therapy. It is also suggested and recommended as well as first-line management therapy. However, ORS is a simple solution which is underused. Underuse of oral rehydration therapy is explained through an onset of vomiting. Antiemetics are not suggested in regular routine for the treatment of acute gastroenteritis but they are still prescribed. Ondansetron is much-explored antiemetics which enhances the role of oral rehydration therapy compliance and it also reduces hospitalization. Recent studies produced few pieces of evidence; on the basis of these evidence the recommendation of antiemetics have largely shifted as per the new guidelines.

Keywords: *Vomiting, Gastroenteritis, Antiemetic, Rotavirus, Ondansetron, Intravenous Therapy, Oral Rehydration Therapy and Guideline.*

Corresponding author:

Dr. Muhammad Usman Khan,

Shaikh Khalifa Bin Zayed Al-Nahyan Medical and Dental College, Lahore.

QR code

Please cite this article in press Muhammad Usman Khan et al., ***Oral Versus Intravenous Route Of Antiemetic Medication: Which Is Better To Control Acute Gastroenteritis.,*** *Indo Am. J. P. Sci, 2019; 06(05).*

INTRODUCTION:

Gastroenteritis refers to an inflammation of gastrointestinal tract mucous membranes and it has the features of vomiting and diarrhoea commonly reported in children [1]. Globally, every year about 3 – 5 billion children get affected by Gastroenteritis with 12% of mortality rate [2]. Health system suffers from the onset of Gastroenteritis. Acute gastroenteritis causes increased hospitalization and visits to healthcare professionals. Hospitalization is higher among under-developed countries. Every year nine out of one thousand are hospitalized in the USA every year with an average age of under five years [4]. However, hospitalization in China is more than any other country as 26 out of 1000 are hospitalized every year [5]. Better state of children is due to better dietary habits of the children in developed countries. Hospitalization decision does not simply rely on the clinical setting but it is also affected through social factors. Most important etiological factors relate to viruses which cause 70% of acute gastroenteritis episodes [6]. Etiological agents have identified more than twenty viruses [7]. About 30% – 70% hospitalization is because of rotavirus all over the world; whereas, 4% – 24% due to acute gastroenteritis [8]. Rotavirus is a prototypical virus as it commonly causes gastroenteritis among children ultimately requiring intravenous fluid. Physician visits and hospitalization is mostly associated with rotavirus [9]. Gastroenteritis leads to an increased economic burden on the healthcare system of any country. An author reported disease severity among children having fever and vomiting (63%), vomiting and diarrhoea (21%), fever and diarrhoea (7%), fever and vomiting (4%), fever (3%) and vomiting (2%) [10]. Vomiting is among the most common features of acute gastroenteritis which requires intravenous therapy [11].

Comparison of oral rehydration and intravenous therapy:

Almost every paediatrics association recommends the use of oral rehydration therapy as the first choice of treatment to manage acute gastroenteritis except severely affected cases of dehydration [12]. Various randomized trials also explain the effectiveness of oral rehydration therapy for mild to moderate dehydrated cases. No clinical difference was reported in these trials in the use of both strategies. Less hospitalization was reported among those who were treated with oral hydration therapy than intravenous therapy. Moreover, intravenous therapy also accompanies phlebitis risk which is not linked with oral rehydration. ORS is an achievement of 20th-century medical advances which is unanimously supported by various paediatrics associations. While judging the effectiveness of both therapies the top priority of acute gastroenteritis treatment goes to oral rehydration therapy. Cost and safety are also hot issues as oral rehydration therapy are successful in the community management of children. Oral rehydration therapy saves money and reduces hospital stay.

Why oral rehydration therapy is underused?

Such reasons are not fully known as there are variables involved factors such as a physician, patients, environment and parental concerns. In most of the cases, physicians were not fully aware of the AAP guidelines of treating moderate and mild dehydration. Intravenous therapy is likely chosen when the OPD is crowded and waiting time is more than expected, parental concerns about actual dehydration level and severity level of the dehydration. In the case of diarrhoea, 8% of physicians opt for the intravenous therapy. Patients no taking water is another reason for 98% of intravenous therapy along with an onset of vomiting.

The pathophysiology of vomiting and antiemetic medications mechanism:

Vomiting can be correlated with retching and nausea [13]. It is a state in which stomach contents expel through the mouth in a violent and unpleasant way. The vomiting centre located at lateral reticular medulla oblongata integrates and controls vomiting. It is close to other centres which regulate vasomotor, respiration and other autonomic functions which can also be helpful in the act of vomiting. Emetic stimuli may directly be received from vomiting centre or it may arrive from chemoreceptor trigger zone. The chemoreceptor trigger zone is exposed to bloodstream and cerebrospinal fluid. Psychological stress like fear can act on the limbic system and cerebral cortex through vomiting centre can induce vomiting. The vestibular system stimulates vomiting as a result of motion sickness, its impulses come from inner ear labyrinth to vomiting centre. However, vomiting mechanism of gastroenteritis is still unknown. A strong relation is also made with the peripheral stimuli that arise from the gastrointestinal tract primarily via serotonin stimulation or vagus nerve (5-hydroxytryptamine 3 (5HT3) receptors) located in the gut [14]. The objective of antiemetic therapy is to depress the vomiting centre, chemoreceptor centre, inhibition of chemoreceptor zone pulses receiving at vomiting centre and inhibition of peripheral receptors pulses to the vomiting centre. All areas involved in the pathogenesis of vomiting are full of dopaminergic, serotoninergic, muscarinic and histaminic receptors [15].

ANTIEMETIC MEDICATIONS (SEROTONIN 5HT3 RECEPTOR ANTAGONISTS)

Ondansetron:

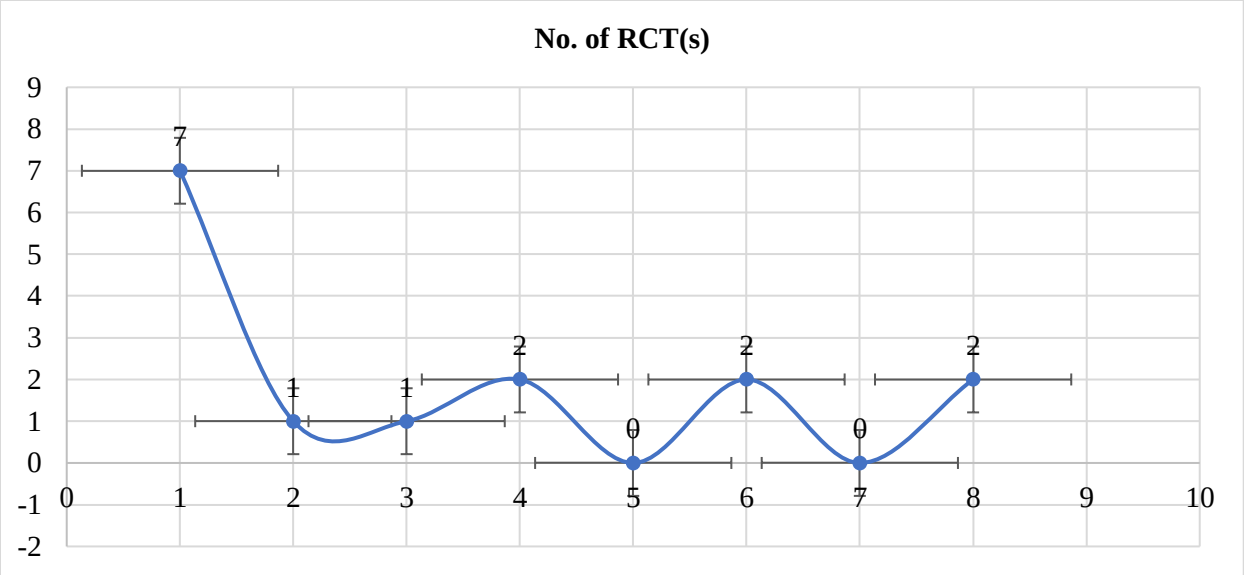
Ondansetron is a derivative of carbazole and best-known serotonin (5HT3) receptor antagonists which are available as a medication since 1991. It blocks the receptors at sympathetic nerves and vagus with the help of chemoreceptor trigger zones. Ondansetron possesses no antidopaminergic features and effective against migraine induced vomiting, acetaminophen poisoning and procedural sedation. It produces positive outcomes to control vomiting in gastroenteritis. Various authors have also reviewed it for emesis cessation, hospital admission, intravenous rehydration fluid, medications adverse effects and care resumption. Ondansetron profile for safety is fine in the management of gastroenteritis with a repeated side effect of diarrhoea [16]. Bryson reported similar adverse events of ondansetron as of placebo. There were no signs of sedation or extrapyramidal reactions. Few trials also report headache, constipation and fatigue as common adverse effects. The tolerability of Ondansetron is very good and carried low potential. Gastrointestinal tract completely absorbs it and it is also metabolized as well. It recommended dose varies according to the weight of the children which varies from 0.1 to 0.15 mg to 4 mg maximum. A single dose is sufficient for the management of gastrointestinal vomiting.

Other antiemetic medications:

Other antiemetic medications include dimenhydrinate, Promethazine, Metoclopramide, Droperidol, Domperidone, Domperidone, Prochlorperazine, Trimethobenzamide and Dexamethasone.

Table: Detailed analysis of various drugs

Drug	No. of RCT(s)	Route/dose	Consideration
Ondansetron	7	PO: 2 mg for Bw 8–15 kg 4 mg for Bw 15–30 kg 8 mg for Bw .30 kg iv: 0.1–0.15 mg/kg Bw	Minimal adverse effects, with good evidence for reduced admission and intravenous therapy
Dimenhydrinate	1	PO/PR/iM/iv: 1.25 mg/kg Bw	Sedative effect
Promethazine	1	PO/PR/iM/iv: 0.25-1 mg/kg Bw	FDA black box warning
Metoclopramide	2	PO/iM/iv: 0.1 mg/kg Bw	High frequency of extra-pyramidal reaction
Droperidol	0	iM/iv: 0.05–0.06 mg/kg Bw	FDA black box warning
Domperidone	2	PO: 0.3–0.6 mg/kg Bw PR: ,2 yr: 10 mg, 2–6yr: 30 mg, .6 yr: 60 mg	No iv as increase cardiac arrhythmias
Prochlorperazine	0	PO: 0.1–0.2 mg/kg Bw PR: 0.1–0.2 mg/kg Bw iM: 0.15 mg/kg Bw	Not recommended if ,2y/iv dosing not recommended in pediatric patients
Trimethobenzamide	2	PO: 4–5 mg/kg Bw PR: 4–5 mg/kg Bw	PR form was removed from the manufacture/iM/iv routes not recommended in pediatric patients



Few are discussed in detail below:

Dimenhydrinate:
Dimenhydrinate blocks H-I receptors, muscarinic-cholinergic receptors in vomiting centre and vestibular. It can be used conveniently via rectal, oral, intravenous or intramuscular routes with a recommended dose of 1.25 to 50 mg [17]. It also treats postoperative nausea, vomiting, radiation sickness, motion sickness and labyrinthine function disorder. It is more expensive than ondansetron. The major concern of dimenhydrinate is its sedative effect which can risk the oral rehydration fluids intake which can even enhance the dehydration level.

Promethazine:
Promethazine has activities like anti-dopaminergic and anticholinergic and it is derived from phenothiazines. It is used for the management of motion sickness, vomiting and postoperative nausea. It can be used conveniently via rectal, oral, intravenous or intramuscular routes with a recommended dose of 0.25 to 25 mg. It is absorbed easily and also among less expensive medications. It poses serious adverse outcomes such as oversedation, respiratory depression, hallucinations, agitation, dystonic reactions and seizures [18]. It is suggested not to prescribe to those children already taking other drugs having respiratory depressant effects as these effects may further aggravate.

Metoclopramide:
Metoclopramide is a derivative of chlorinated procainamide that acts as a D-2 receptor antagonist. It also possesses peripheral and central actions which increase vomiting and nausea by lowering impulses to gastric sphincter tone, chemoreceptor trigger zone, increases gastric emptying, stimulates gastric motility and small transit time of intestine. It also prevents chemotherapy-induced vomiting, vomiting, postoperative nausea and pregnancy-related vomiting and nausea [19]. Its severe effects include seizures, methemoglobinemia, neuroleptic malignant syndrome, gynecomastia and hemoglobinemia.

Droperidol: Droperidol is applied for the maintenance of tranquilization or sedation to reduce vomiting and nausea and anti-anxiety activity. Droperidol is a potent D-2 receptor antagonist with the weaker activity of antihistamine and anticholinergic. It acts in the peripheral and central way. Studies prove it as a postoperative antiemetic agent. The anti-nausea effect is good with reduced antiemetic effect with a recommended dose of 0.05 mg – 0.06 mg which can be managed intravenously and intramuscularly. Droperidol is not suggested for children under two years of age due to efficacy and safety.

Domperidone:
Domperidone is known as D-2 receptor antagonist which can accelerate emptying time of gastric and also acts on chemoreceptor trigger zone. It also treats postoperative vomiting and nausea. Presently, it is available suppository and oral administration due to cardiac arrhythmias caused by higher dose through intravenous route. Its suggested dose starts from a minimum of 0.3 mg – 0.6 mg and up to a maximum of 25 mg. Its adverse effects include cardiac arrest and

ventricular arrhythmias. Its penetration into the nervous system is poor so it does not cause any significant adverse effect.

SHIFTING PHARMACOEPIDEMIOLOGY OF ANTIEMETIC MEDICATIONS:

Pfeil investigated the antiemetic medications pattern among children (0 – 9) years of age who were diagnosed with gastroenteritis infection back in 2005 [20]. The author investigated distribution and percentage of acute gastroenteritis among patients selected from different regions. Every patient was prescribed with dopaminergic or antihistamines receptor antagonists. Most of the German patients were prescribed with dimenhydrinate. Various backgrounds prescribed different drugs such as promethazine, dopamine receptor antagonist and ondansetron. Different countries showed the contrasting prescription pattern for different drugs. Moreover, ondansetron's therapeutic efficacy is relatively current. Physicians are starting the prescription of ondansetron to avoid hospitalization and intravenous therapy for children diagnosed with gastroenteritis associated vomiting [21]. Back in 2009, antiemetics use among children of one to ten years of age was also reported in the emergencies [22]. Other surveys also reflect the use of ondansetron to treat acute gastritis in OPDs and emergencies [23 – 25]. With the availability of generic formula, the use of ondansetron will further increase.

BASICS OF GOOD TREATMENT OF ACUTE GASTROENTERITIS:

At present, the importance of oral rehydration therapy as key management of acute gastroenteritis cannot be negated as it is still the first choice of most of the physicians. Literature review shows that ondansetron reduces vomiting and increases the chances of success. It also reduces the onset of intravenous therapy and oral rehydration therapy compliance along with reduces stay at the hospital.

No formal research has been carried out to study the medication and hospitalization cost. Ondansetron likely reduces both hospitalization and medication cost for acute gastroenteritis patients. No sedative effects are there and the safety profile is also good. Increased episodes of diarrhoea are the only drawback. Oral rehydration therapy refers to the management of disease at home which offers comfort for patient and parents. For vomiting, an only a single dose of ondansetron is sufficient. The oral dose is preferred than the intravenous route due to comfort and ease [26]. Antiemetics may pose potent value for severe vomiting episodes; however, it is not clearly stated in the given guidelines in order to select various types of antiemetics. Essential pillars of a suitable treatment program for the management of acute gastroenteritis include oral rehydration, hypotonic ORS, rapid oral rehydration (3 – 4 hours), rapid normal feeding, not to use special or diluted formula, all-time breastfeeding continuation and ORS supplementation. Moreover, selected patients may receive antiemetic medications as an essential medical intervention.

REFERENCES:

1. Parashar UD, Alexander JP, Glass RI. Prevention of rotavirus gastroenteritis among infants and children. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 2006;55(RR-12):1–13.
2. Malek MA, Curns AT, Holman RC, et al. Diarrhea- and rotavirus-associated hospitalizations among children less than 5 years of age: the United States, 1997 and 2000. Paediatrics. 2006;117(6):1887–1892.
3. Lee BP, Azimi PH, Staat MA, et al. Nonmedical costs associated with rotavirus disease requiring hospitalization. Pediatr Infect Dis J.2005;24(11):984–988.
4. Chang HG, Glass RI, Smith PF, Cicirello HG, Holman RC, Morse DL. Disease burden and risk factors for hospitalizations associated with rotavirus infection among children in New York State, 1989 through2000. Pediatr Infect Dis J. 2003;22(9):808–814.
5. Staat MA, Azimi PH, Berke T, et al. Clinical presentations of rotavirus infection among hospitalized children. Pediatr Infect Dis J.2002;21(3):221–227.
6. Reis EC, Goepp JG, Katz S, Santosham M. Barriers to the use of oral rehydration therapy. Paediatrics. 1994;93(5):708–711.
7. Fang ZY, Yang H, Zhang J, et al. Child rotavirus infection in association with acute gastroenteritis in two Chinese sentinel hospitals. Pediatr Int.2000;42(4):401–405.
8. Canadian Paediatric Society. Oral rehydration therapy and early refeeding in the management of childhood gastroenteritis. Paediatr Child Health. 2006;11(8):527–531.
9. Nelson EA, Tam JS, Bresee JS, et al. Estimates of rotavirus disease burden in Hong Kong: hospital-based surveillance. J Infect Dis 2005;(192Suppl 1): S71–S79.
10. Webb A, Starr M. Acute gastroenteritis in children. Aust Fam Physician.2005;34(4):227–231.

11. Wilhelmi I, Roman E, Sanchez-Fauquier A. Viruses causing gastroenteritis. Clin Microbiol Infect. 2003;9(4):247–262.
12. Rivest P, Proulx M, Lonergan G, Lebel MH, Bedard L. Hospitalizations for gastroenteritis: the role of rotavirus. Vaccine.2004;22(15–16):2013–2017.
13. Ehlken B, Laubereau B, Karmaus W, Petersen G, Rohwedder A, Forster J. Prospective population-based study on rotavirus disease in Germany. Acta Paediatr. 2002;91(7):769–775.
14. Parashar UD, Hummelman EG, Bresee JS, Miller MA, Glass RI. Global illness and deaths caused by rotavirus disease in children. Emerg Infect Dis. 2003;9(5):565–572.
15. Parashar UD, Gibson CJ, Bresse JS, Glass RI. Rotavirus and severe childhood diarrhoea. Emerg Infect Dis. 2006;12(2):304–6.
16. Leung AK, Kellner JD, Davies HD. Rotavirus gastroenteritis. Adv Ther.2005;22(5):476–487.
17. Andreas MS, Cardoso DD, Fernandes SM, et al. Adenovirus, calici virus and astrovirus detection in faecal samples of hospitalized children with acute gastroenteritis from Campo Grande, MS, Brazil. Mem Inst Oswaldo Cruz. 2008;103(7):741–744.
18. Caracciolo S, Minini C, Colombrita D, Foresti I, Avolio M, Tosti G, et al. Detection of sporadic cases of Norovirus infection in hospitalized children in Italy. New Microbiol. 2007;30(1):49–52.
19. Fodha I, Chouikha A, Dewar J, Trabelsi A, Boujaafar N, Steele AD. Prevalence of adenovirus antigens in children presenting with acute diarrhoea. Med Trop (Mars). 2007;67(3):256–258.
20. Jakab F, Peterfai J, Meleg E, Banyai K, Mitchell DK, Szucs G. Comparison of clinical characteristics between astrovirus and rotavirus infections diagnosed from 1997 to 2002 in Hungary. Acta Paediatr.2005;94(6):667–671.
21. Kapikian AZ. Viral gastroenteritis. JAMA. 1993;269(5):627–630.
22. Elliott EJ. Acute gastroenteritis in children. BMJ. 2007;334(7583):35–40.
23. by-Payne J, Elliott E. Gastroenteritis in children. Clin Evid.2004;12:443–454.
24. King CK, Glass R, Bresee JS, Duggan C. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. MMWR Recomm Rep. 2003;52(RR-16):1–16.
25. Santosham M. Oral rehydration therapy: reverse transfer of technology. Arch Pediatr Adolesc Med. 2002;156(12):1177–1179.
26. Glass RI, Kilgore PE, Holman RC, et al. The epidemiology of rotavirus diarrhoea in the United States: surveillance and estimates of disease burden. J Infect Dis. 1996;174(Suppl 1): S5–S11.
27. Ryan MJ, Ramsay M, Brown D, Gay NJ, Farrington CP, Wall PG. Hospital admissions are attributable to rotavirus infection in England and Wales. J Infect Dis. 1996;(174 Suppl 1): S12–S18.
28. Carlin JB, Chondros P, Masendycz P, Bugg H, Bishop RF, Barnes GL. Rotavirus infection and rates of hospitalization for acute gastroenteritis in young children in Australia, 1993–1996. Med J Aust.1998;169(5):252–256.