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The Clinical Impacts Of Using Crushed Erythromycin Tablet Versus Intravenous Metclopramide As A Prokinetic Agents In Ventilated Critically Illness Patients Who Are Intolerant To Enteral Nutrition Formulas.

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Abstract

Background: Prokinetics like metoclopramide and erythromycin are commonly used in critically ill patients, mainly to aid in early enteral feeding, which is now recognized as one of the fundamentals of critical care practice.

Objectives: The objective of this study is to test the positive impacts differences between using erythromycin as crushed tablet through nasogastric (NG) tube (Group I) in comparison with using metoclopramide 10 mg intravenously (Group II) thrice daily over 1 week regarding lowering gastric residual volume (GRV) in mechanically ventilated critically ill patients who are intolerant to standard enteral nutritional formulas.

Materials and Methods: We will perform a retrospective analysis of patients admitted to the adult intensive care unit (ICU) between April 2017 and Sep 2018 who were their first week data can be obtained and weren't discharged, extubated, or died before completed 1 week. Independent T-test will be conducted to determine the mean±SD and mean differences±SEM between Group I and II.

Results: The mean overall age was 57.50±9.02 years, and 89 subjects (71.2%) were male. Group I had a significantly higher ΔGRV_{1-7} than Group II (-90.95±13.05 ml vs -66.59±6.26 ml, respectively) with mean difference of -24.36±1.80 ml. The overall 28-day ICU mortality rate was significantly lower in Group I than in Group II (45.76% vs 54.55%, respectively) with RRR of -16.11% and NNT of 12.

Conclusion: Crushed erythromycin tablet is more effective than metoclopramide IV in reducing GRV and increasing feeding tolerance that may improve nutritional status, reduce bacterial translocation, hospital and ICU stay, and overall mortality.

Keywords: Critical care, Gastric residual volume, Malnutrition, Mortality, Prokinetic.

Introduction

Critical illness trigger hypercatabolism of nutritional reserves and a resultant depletion of lean body mass (LBM) and hypoalbuminemia result in a poor prognosis and mortality. Enteral nutrition, thus, becomes vital in maintaining enterocytes integrity and hence minimizes enteric gram negative bacteria translocation, in addition to its nutritional role in providing an appropriate protein density to critically ill patients. However, most critically ill mechanically ventilated patients have delayed gastric emptying attributed to multifactorial insults, especially the

commonly used of opioids as an anlagosedative [1] which increases gastric residual volume (GRV) and subsequently may increase risk of aspiration pneumonia. One of unique strategy to facilitate early enteral feeding is to use prokinetics agents like either erythromycin or metoclopramide or both in refractory cases. Gastrokinetics are now commonly used in critically ill patients as one of the fundamentals of critical care practice. Erythromycin has been used for decades as gastrokinetic agent at sub-antimicrobial doses due to its capability to increase contractile force and accelerate intraluminal transit [2]. Up to our knowledge, there was no study compared metoclopramide intravenous (IV) with crushed erythromycin tablet in mechanically ventilated critically ill patients. The primary objective of this study was to test the positive impacts differences between using erythromycin at standard prokinetics dose (250 mg thrice daily) as crushed tablet through nasogastric (NG) tube (Group I) in comparison to metoclopramide 10 mg IV thrice daily (Group II) over first week of intensive care unit (ICU) admission regarding changes in GRV from day 1 to day 3 (phase I), from day 4 to day 7 (phase II), and an overall changes over first week (Δ $GRV_{1-3,}$ $\Delta GRV_{4-7,}$ and $\Delta GRV_{1-7,}$ respectively) in relative to baseline GRV (GRV_0) in mechanically ventilated critically ill patients who are intolerant to standard enteral nutritional formulas (ENFs) that are available in our ICU (e.g., Ensure® and Resource® Optimum). The percentage of GRV reduction during phase I ($\%\Delta GRV_{1-3}$) and phase II ($\%\Delta GRV_{4-7}$), ICU and hospital stay days, and overall 28-day ICU mortality were the secondary outcomes studied.

Subjects and Methods

This was a single-center observational retrospective study conducted in the department of adult ICU of King Hussein Medical Center (KHMC) at Royal Medical Services (RMS) in Jordan. This study was approved by our Institutional Review Board (IRB), and a requirement for consent was waived owing to its retrospective design. This study included a cohort of mechanically ventilated critically ill patients intolerant to standard enteral nutritional formulas (GRV_0 > 150 ml for 2 consecutive checking) admitted via the emergency department (ED) or via other hospital wards with any medical or surgical problem. Flow chart of critically ill patient's selection and data collection process is fully illustrated in Figure 1. Feeding protocol of critically ill patients in our institution is fully described in Fig 2.

All patient's continuous variables was expressed as mean± standard deviation by using the independent samples T-test while categorical and ordinal variables was expressed as numbers with percentages by using χ^2 test or as median (interquartile range) by using Mann-Whitney U test, respectively. Analysis values were compared for the two tested groups (Group I and Group II) across phase I, phase II, and overall 1st week of ICU admission. Mean differences between Group I and Group II was expressed as mean±standard error of mean. Relative risk reduction (RRR), absolute risk reduction (ARR), and number needed to treat with crushed erythromycin tablet over metoclopramide IV to save life of one critically ill patient was also calculated. Statistical analyses were performed using IBM SPSS ver. 25 (IBM Corp., Armonk, NY, USA) and P-values $\leq$0.05 were considered statistically significant.

Results

The mean overall age was 57.50±9.02 years, and 89 subjects (71.2%) were male. The overall 28-day ICU mortality rate was significantly lower in Group I than in Group II (45.76% vs 54.55%, respectively) with RRR of -16.11% and NNT of 12. Although Group II had a significantly higher GRV_0 than Group I ((205.57±19.33 ml vs 193.73±16.07 ml, respectively) that led to

significantly lower GIT tolerance and ENFs intake (577.71±77.33 ml/day vs 625.02±64.15 ml/day), Group I had a significantly higher ΔGRV_{1-7} than Group II (-90.95±13.05 ml vs -66.59±6.26 ml, respectively) with mean difference of -24.36±1.80 ml. There were contrary results between two tested groups during phase I and phase II regarding ΔGRV. In phase I, Group I had a significantly higher ΔGRV_{1-3} than Group II (-73.46±12.66 ml vs-46.85±4.43 ml, respectively) with mean difference of -26.61±1.66 ml while in phase II, Group II had a significantly higher ΔGRV_{4-7} than Group I (-21.44±1.96 ml vs -12.42±0.59 ml, respectively) with mean difference of +9.02±0.27 ml. The correlation between GRV and days of prokinetic administration are described in Figure 3.

Theoretically, if GRV is increased enteral feeding tolerance is decreased and vice versa. We demonstrated in this study this relationship is correct. Enteral feeding tolerance was assessed in this study indirectly by ENF volume inputs in ml per day (ENF vol). ENF vol $_{1-3}$. ENF vol $_{4-7}$, and ENF vol $_{1-7}$ were significantly higher in Group I than Group II (918.69±17.51 ml/day vs 765.01±59.71 ml/day, 1041.74±13.03 ml/day vs 903.20±46.72 ml/day, and 978.23±15.58 ml/day vs 835.15 ± 52.52 ml/day. There were insignificant differences between Group I and Group II regarding both ICU and hospital stay days (12.39±3.22 vs 11.42±3.20 and 20.42±8.43 vs 21.42±9.01, respectively). Comparative analysis between Group I and Group II of the study's critically ill patients are fully presented in Table 1.

Discussion

Only a few studies evaluated the differences between erythromycin and metoclopramide in mechanically ventilated critically ill patients. But what is unique in our study is that we compare the crushed form of erythromycin tablet with metoclopramide IV. After crushing erythromycin tablet, we reconstituted it with 10 ml water for infusion through NG tube TID for 1st week of ICU admission. Due to hypercatabolism and high prevalence of GIT intolerance of stress critically ill patients, an appropriate early enteral nutritional support may enhance nutritional status, decrease sepsis related gastrointestinal bacterial translocation, and decrease overall LOS and mortality [3-6]. ENFs intolerance manifests mostly as increased GRV and abdominal distention which results in poor enteral intakes and wasting complications [7]. So, it becomes of our priority to solve the feeding intolerance in critically ill patients as soon as possible. Better gastric emptying with a resultant improvement in ENFs tolerance had been reported with use of either erythromycin or metoclopramide in critically ill patients [8-10]. American Society for Parenteral and EN (ASPEN) and European Society for Parenteral and EN (ESPEN) recommend the use of either metoclopramide or erythromycin in critically ill patients with feeding intolerance [11-12]. In our study, using crushed erythromycin tablet TID for 1st week of ICU admission resulted in significantly decreasing in baseline GRV by -90.95±13.05 ml, in which -80.34%±2.56% occurred during first 3 days of ICU admission (Phase I) and -19.66%±2.56% occurred during next four days of ICU admission (Phase II). Also, GRV was reduced significantly in patients who were taken metoclopramide IV TID but with a lower ΔGRV_{1-7} and % ΔGRV_{1-3} (-66.59±6.26 ml and -70.34%±0.00%, respectively) and higher % ΔGRV_{4-7} (-29.66%±0.00%). These results suggest that tachyphylaxis occurs slightly quicker with erythromycin than metoclopramide but erythromycin maintains the desired effects in reducing GRVs overall the tested period with higher overall efficacy in increasing enteral nutritional inputs. In other word, erythromycin prokinetic undergoes an exponential like pattern while metoclopramide prokinetic undergoes linear like pattern.

Similar to the findings of Nguyen et al [13] this study found that erythromycin was more effective than metoclopramide at reducing GRV from baseline to 24 hour (-35.06±2.18 ml, P=0.000), achieved a higher rate of feeding tolerance, and the efficacy for both prokinetics declined during the 7-day study. In summary, crushed form of erythromycin tablet to be infused through NG tube in mechanically ventilated critically patients is more effective than metoclopramide IV in reducing GRV and increasing both the GIT and ENFs tolerance. Improving feeding tolerance may improve nutritional status of ICU patients and may reduce GIT bacterial translocation related sepsis, hospital and ICU LOS, and overall mortality. This study is limited by its retrospective design, using single-center data, including only mechanically ventilated ICU patients. Nonetheless, our center is an experienced and high-volume unit, so our data may be useful in other centers. A larger, multisite, and prospective study is needed to control for multiple confounders.

References

1. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) JPEN J Parenter Enteral Nutr. 2009;33:277–316.
2. Ramirez B, Richter JE. Review article: promotility drugs in the treatment of gastro-oesophageal reflux disease. Aliment Pharmacol Ther 1993; 7: 5–20.
3. Krakau K, Omne-Pontén M, Karlsson T, Borg J. Metabolism and nutrition in patients with moderate and severe traumatic brain injury: A systematic review. Brain Inj. 2006;20:345–67.
4. Perel P, Yanagawa T, Bunn F, Roberts I, Wentz R, Pierro A. Nutritional support for head-injured patients. Cochrane Database Syst Rev. 2006;18:CD001530.
5. Norton JA, Ott LG, McClain C, Adams L, Dempsey RJ, Haack D, et al. Intolerance to enteral feeding in the brain-injured patient. J Neurosurg. 1988;68:62–6.
6. Acosta Escribano JA, Carrasco Moreno R, Fernández Vivas M, Navarro Polo JN, Más Serrano P, Sánchez Payá J, et al. Gastric enteral intolerance in mechanically ventilated patients with traumatic cerebral lesion. Nutr Hosp. 2001;16:262–7.
7. Mentec H, Dupont H, Bocchetti M, Cani P, Ponche F, Bleichner G. Upper digestive intolerance during enteral nutrition in critically ill patients: Frequency, risk factors, and complications. Crit Care Med. 2001;29:1955–61.
8. Berne JD, Norwood SH, McAuley CE, Vallina VL, Villareal D, Weston J, et al. Erythromycin reduces delayed gastric emptying in critically ill trauma patients: A randomized, controlled trial. J Trauma. 2002;53:422–5.
9. Nguyen NQ, Chapman MJ, Fraser RJ, Bryant LK, Holloway RH. Erythromycin is more effective than metoclopramide in the treatment of feed intolerance in critical illness. Crit Care Med. 2007;35:483–9.
10. Dickerson RN, Mitchell JN, Morgan LM, Maish GO, 3rd, Croce MA, Minard G, et al. Disparate response to metoclopramide therapy for gastric feeding intolerance in trauma patients with and without traumatic brain injury. JPEN J Parenter Enteral Nutr. 2009;33:646–55.
11. McClave SA, Martindale RG, Vanek VW, McCarthy M, Roberts P, Taylor B, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) JPEN J Parenter Enteral Nutr. 2009;33:277–316.

12.Kreymann KG, Berger MM, Deutz NE, Hiesmayr M, Jolliet P, Kazandjiev G, et al. ESPEN guidelines on enteral nutrition: Intensive care. Clin Nutr. 2006;25:210–23.

Legends Figure and Table

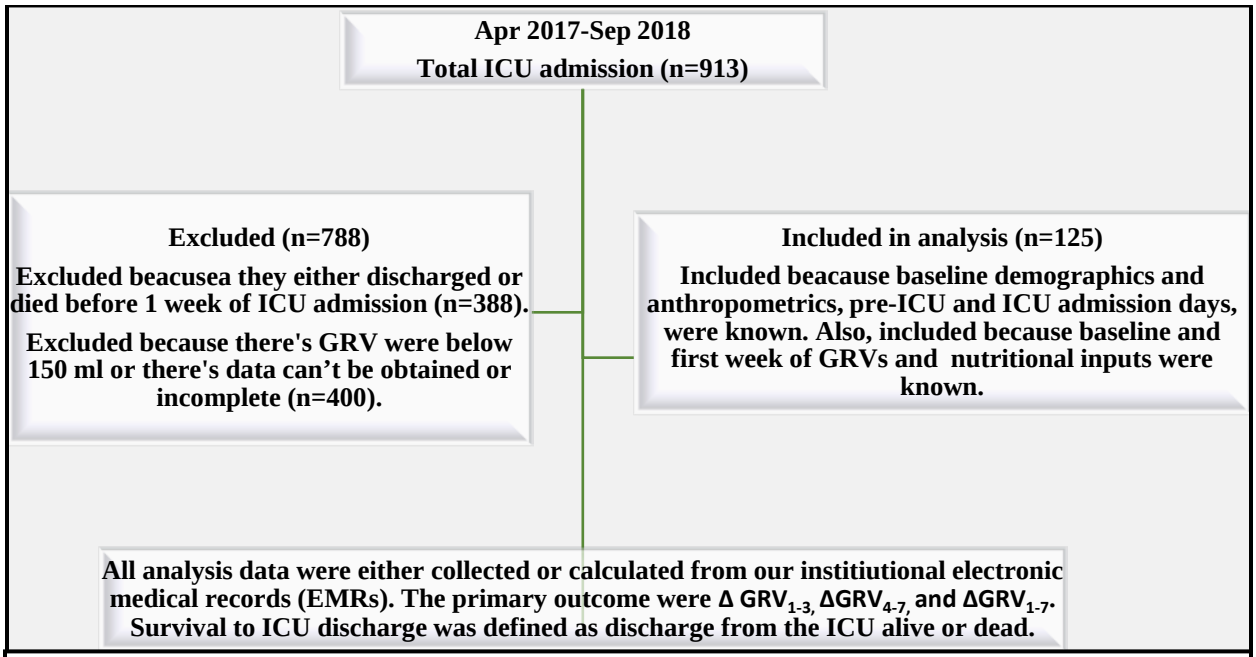

Fig 1. Flow chart of critically ill patient's selection and data collection process.
Apr: April. Sep: September.
GRVs: Gastric residual volumes. 1-3: Over first 3 days (Phase I).
4-7: From day 4 to day 7 (Phase II). 1-7: Overall 1st week of admission.
ICU: Intensive Care Unit. Δ: Changes.

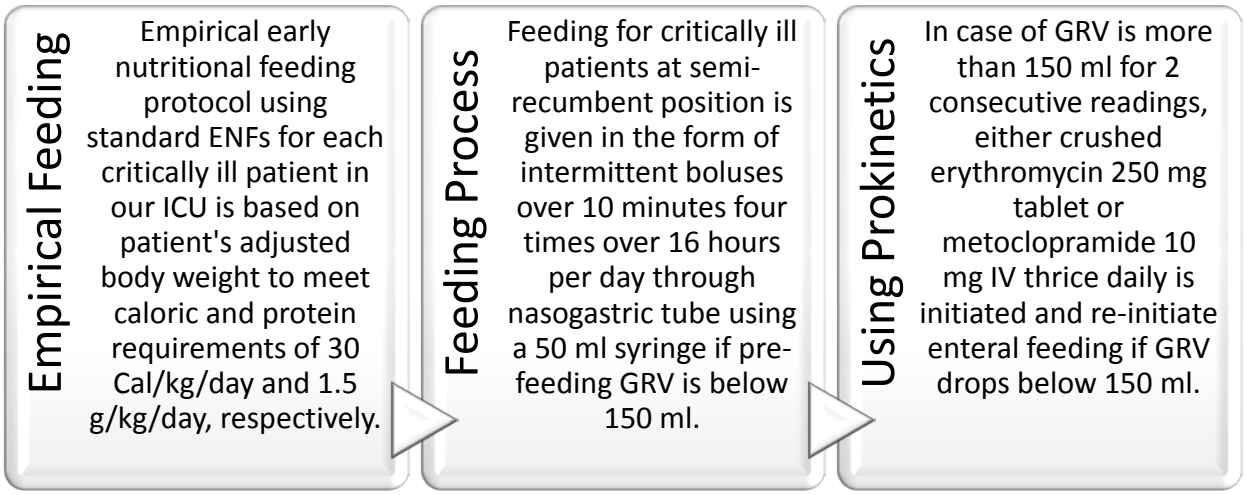

Fig 2. Feeding protocol of critically ill patients in our ICU of KHMH.ENFs: Enteral nutritional formulas. ICU: Intensive care unit. Cal: Kilocalories.GRV: Gastric residual volume. KHMH: King Hussein Medical Hospital. Kg: Kilogram.

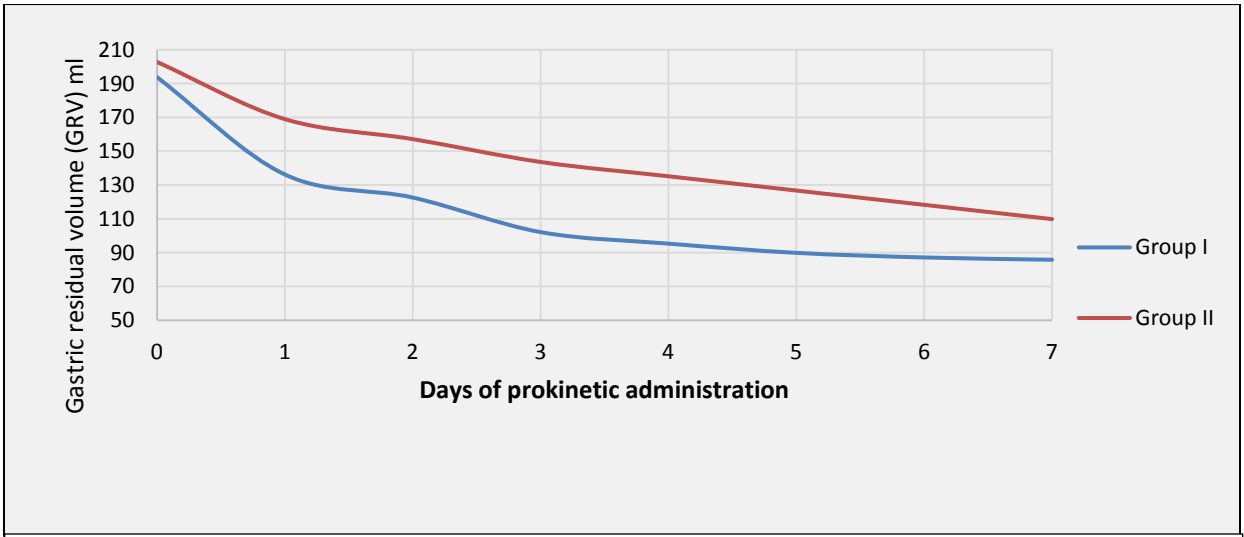

Fig 3. Correlation between GRV and days of prokinetic administration between Group I and Group II.
Group I: Critically ill patients who were taken crushed erythromycin tablet TID.
Group II: Critically ill patients who were taken metoclopramide IV TID.

Table 1. Comparison analysis between Group I and Group II of the study's critically ill patients.

Variables		Overall (N=125)	Group I (N= 59)	Group II (N= 66)	Group I vs II	P-Value
Age (Yrs)		57.50±9.02	56.86±9.77	58.06±8.33	-1.19±1.62	0.461(NS)
Gender	Male	89 (71.2%)	42 (71.19%)	47 (71.21%)		0.606 (NS)
	Female	36 (31.2%)	17 (28.81%)	19 (28.79%)		
Day(s) Pre-ICU admission (day(s))		9.08±8.79	8.03±8.54	10.02±8.96	-1.98±1.57	0.210 (NS)
ICU Stay day(s)		11.88±3.23	12.39±3.22	11.42±3.20	+0.97±0.58	0.096 (NS)
Hospital Stay day(s)		20.95±8.72	20.42±8.43	21.42±9.01	-1.00±1.57	0.524 (NS)
Overall 28-day ICU Mortality	Survivors	62 (49.6%)	32 (54.24%)	30 (45.45%)	RRR→ -16.11%	0.000 (S)
	Non Survivors	63 (50.4%)	27 (45.76%)	36 (54.55%)	ARR→ 8.79% NNT→ 12	
BW	BW_0 (Kg)	74.60±11.59	73.10±10.91	75.95±12.11	-2.85±2.07	0.170 (NS)
	BW_7 (Kg)	77.58±11.57	76.49±10.95	78.57±12.09	-2.08±2.07	0.318 (NS)
BMI	BMI_0 (Kg/m²)	27.57±4.19	26.67±4.23	28.37±4.01	-1.69±0.74	0.023 (NS)

	BMI_7 (Kg/m²)	28.68±4.19	27.92±4.29	29.35±4.01	-1.44±0.74	0.055 (NS)
% ΔBW_{0-7}		+4.11%±1.04%	+4.75%±1.01%	+3.54%±0.67%	+1.21%±0.15%	0.000 (S)
GRV (ml)	GRV_0 (ml)	199.98±18.76	193.73±16.07	205.57±19.33	-11.85±3.20	0.000 (S)
	ENF Vol_0 (ml/day)	600.04±74.98	625.02±64.15	577.71±77.33	+47.32± 12.79	0.000 (S)
	GRV_1 (ml)	154.76±21.36	136.25±4.94	171.31±16.11	-35.06±2.18	0.000 (S)
	GRV_2 (ml)	141.98±21.56	122.61±4.45	159.29±14.98	-36.68±2.03	0.000 (S)
	GRV_3 (ml)	125.04±24.03	102.14±3.76	145.52±13.68	-43.38±1.84	0.000 (S)
	GRV_{1-3} (ml)	140.60±22.32	120.29±4.38	158.76±14.96	-38.47±2.02	0.000 (S)
	ΔGRV_{1-3} (ml)	-59.41±16.22	-73.46±12.66	-46.85±4.43	-26.61± 1.66	0.000 (S)
	ENF Vol_{1-3} (ml/day)	837.54±89.14	918.69±17.51	765.01±59.71	+153.68±8.07	0.000 (S)
	GRV_4 (ml)	117.36±23.02	95.34±3.49	137.05±12.91	-41.71±1.74	0.000 (S)
	GRV_5 (ml)	110.28±21.32	89.93±3.33	128.47±12.07	-38.54±1.63	0.000 (S)
	GRV_6 (ml)	104.50±18.44	87.24±3.25	119.94±11.25	-32.70±1.52	0.000 (S)
	GRV_7 (ml)	99.32±15.04	85.83±3.14	111.38±10.48	-25.55±1.42	0.000 (S)
	GRV_{4-7} (ml)	107.88±19.47	89.56±3.23	124.26±11.69	-34.69±1.57	0.000 (S)
	ΔGRV_{4-7} (ml)	-17.18±4.754	-12.42±0.59	-21.44±1.96	+9.02±0.27	0.000 (S)
	ENF Vol_{4-7} (ml/day)	837.54±89.14	1041.74±13.03	903.20±46.72	+138.54±6.29	0.000 (S)
	GRV_{1-7} (ml)	121.90±20.63	102.76±3.76	139.02±13.02	-36.25±1.76	0.000 (S)
	ΔGRV_{1-7} (ml)	-78.09±15.79	-90.95±13.05	-66.59±6.26	-24.36±1.80	0.000 (S)
	% ΔGRV_{1-3}	-75.06%±5.31%	-80.34%±2.56%	-70.34%±0.00%	-9.99%±0.31%	0.000 (S)
	% ΔGRV_{4-7}	-24.94% 5.31%	-19.66%±2.56%	-29.66%±0.00%	+9.99%±0.33%	0.000 (S)
	ENF Vol_{1-7} (ml/day)	912.43±82.59	978.23±15.58	835.15±52.52	+145.03±7.05	0.000 (S)
Norepinephrine Rate (mcg/min)		5.78±2.43	6.58±1.39	5.08±2.91	+1.50±0.42	0.000 (S)
$SOFA_{1-7}$ (0-25)		2 (1-3)	2 (1-3)	2 (1-3)	0 (0-3)	0.613 (NS)

Values are presented as Mean±SD or number (%) or Median (Range) or Mean diff ±SEM.

Yrs: Years.

BW: Actual body weight at admission.

BMI: Body mass index at admission.

ARR: Absolute risk reduction.

Group I: Critically ill patients who were taken crushed erythromycin tablet.

Group II: Critically ill patients who were taken metoclopramide IV.

0: Baseline at admission.

1-3: First three days of admission (Phase I).

4-7: Next four days of admission (Phase II).

1-7: First week of ICU admission (duration of our study).

ICU: Intensive care unit.

SD: Standard deviation.

SEM: Standard error of mean.

RRR: Relative risk of mortality reduction.

NNT: Number to treat with crushed erythromycin tablet over metoclopramide to save life of one critically ill patient.

SOFA: Sequential organ failure assessment.

GRV: Gastric residual volume.

ENF: Enteral nutritional formula.

Δ: Changes.