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The Clinical Effects of Proactively Using Low Dose Versus Standard Dose Crushed Erythromycin Tablet on Early Enteral Nutrition in Mechanically Ventillated Critically Ill Patients

Hadeel Telfah, Hiyam Salem Al Haqeesh, Faisal Alnoimi, "Moh'd Nour" Bani Younes, Malik Ahed Alhyari, Laith Ahmad Abuhjeeleh
Pharmacists at Royal Medical Services, Amman, Jordan

Abstract— *Objectives: Feeding intolerance is a common problem in mechanically ventilated critical ill patients and it is usually manifested by elevation in gastric residual volume (GRV) prior to the next scheduled feeding. The objective of this study is to test the outcome differences between Group I (patients used Erythromycin at standard prokinetic dose of 250 mg TID) and Group II (patients used Erythromycin at low dose of 125 mg TID) in terms of GRVs and nutritional intakes. Methods: We conducted a retrospective study in our institution at King Hussein Medical Hospital (KHMH). Patients were excluded if he/she discharged or died before completed 1 week of admission and if GRV was below 100 ml or was exceeded 200 ml at any time during study. One sample and independent sample T-test were conducted to determine the Mean±SD of GRVs between Group I and Group II. Results: The mean overall age was 57.50±9.02 years. 89 subjects (71.2%) were male and 36 subjects (31.2%) were female. 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 nutritional 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. Conclusion: Crushed erythromycin crushed tablet (250 mg TID) was more effective than low dose erythromycin (125 mg TID) in reducing GRV from baseline and in increasing and maintaining nutritional status.*

Keywords— *Protein, Residual, Critical, Early, Prokinetic, Low and standard dose, Erythromycin.*

I. Introduction

Feeding intolerance is a common problem in mechanically ventilated critical ill patients and it is usually manifested by elevation in gastric residual volume (GRV) prior to the next scheduled feeding.[1-3] Delaying advancement of enteral feeding in these intolerated critically ill patients, often leads to inevitable use of parenteral nutrition to combat for the high nutritional requirements, which predisposes the mechanically ventilated patients to nosocomial infections, hepatic dysfunction, prolonged hospitalization, and many other complication.[4-8] Erythromycin, a macrolide antibiotic, acts as motilin analogue to stimulate gastric emptying and subsequently decrease GRV, is commonly used as a prokinetic agents either at low dose (125 mg thrice daily) or at standard dose (250 mg thrice daily) to maintain an adequate enteral feeding. Better gastric emptying with a resultant improvement in ENFs tolerance has been reported to improve all hospitalized patients morbidities and mortalities. The objective of this study is to test the outcome differences between Group I (patients used Erythromycin 250 mg TID as a proactively prokinetic) and Group II (patients used Erythromycin 125 mg TID as a proactively prokinetic) during first week of admission to our adult intensive care unit (ICU) in terms of average changes in GRVs and standard enteral feeding (EF) volume in mechanically ventilated critically ill patients who have GRV above 100 ml but below 200 ml.

II. Subjects And Methods

This was a single-center observational retrospective study conducted in our adult critical unit of 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 only mechanically ventilated critically ill patients on standard enteral nutritional formula in which the GRV ranged between 100 ml and 200 before and during study period. Flow chart of critically ill patient's selection and data collection process is fully illustrated in Figure 1. All patient's continuous variables was expressed as mean± standard deviation by using the one sample and independent two samples T-test while ordinal variables was expressed as numbers with percentages by using chi square test. Analysis values were compared for the two tested groups (Group I and Group II). Statistical analyses were performed using IBM SPSS ver. 25 (IBM Corp., Armonk, NY, USA) and P-values ≤0.05 were considered statistically significant.

III. Results

The mean overall age was 57.50±9.02 years. 89 subjects (71.2%) were male and 36 subjects (31.2%) were female. 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 -

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24.36±1.80 ml. 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) in which ENF vol $_{1-7}$ were significantly higher in Group I than Group II (978.23±15.58 ml/day vs 835.15 ± 52.52 ml/day. Comparative analysis between Group I and Group II of the study's critically ill patients are fully presented in Table 1.

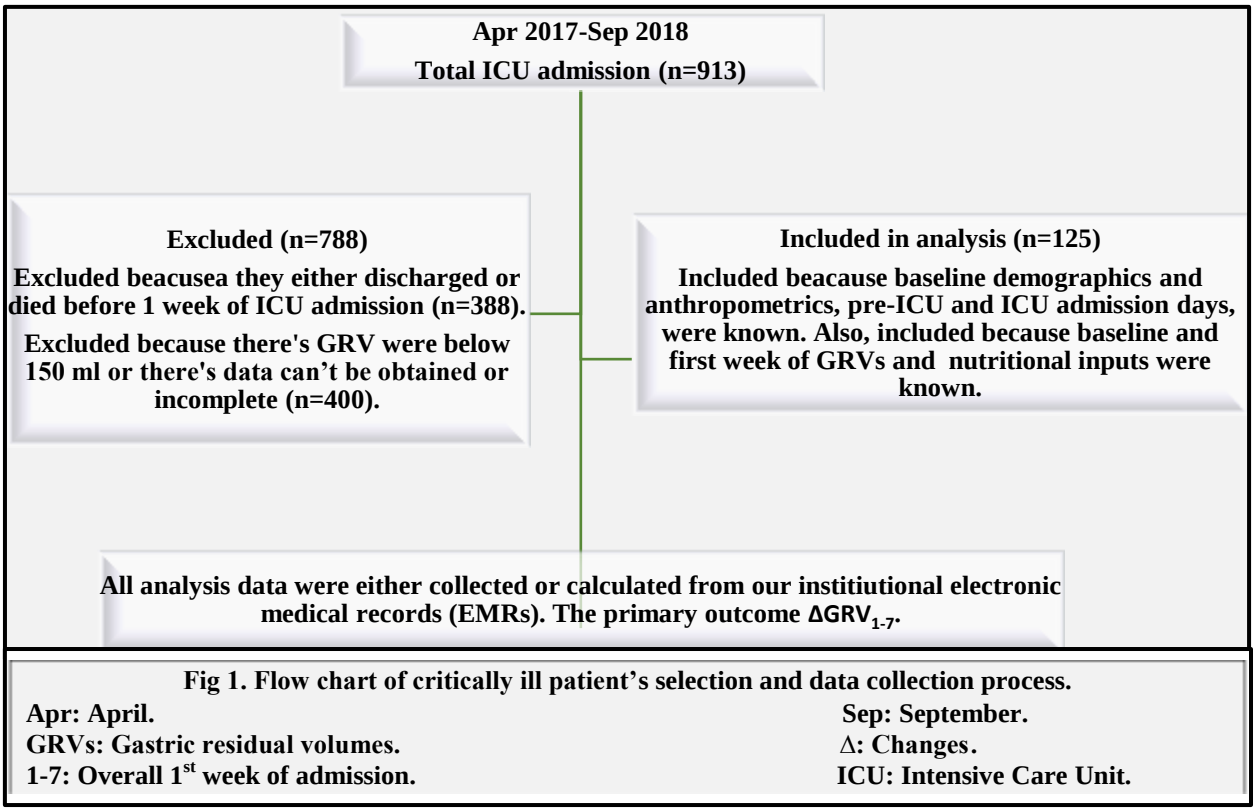

Fig 1. Flow chart of critically ill patient's selection and data collection process.
Apr: April. **Sep: September.**
GRVs: Gastric residual volumes. **Δ: Changes.**
1-7: Overall 1st week of admission. **ICU: Intensive Care Unit.**

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%)		
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_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_{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)
	$ENF\ Vol_{1-7}$ (ml/day)	912.43±82.59	978.23±15.58	835.15±52.52	+145.03±7.05	0.000 (S)

Values are presented as Mean±SD using one sample and independent sample T-test or are presented as number (%) by using chi square test.

Group I: Critically ill patients who were taken crushed erythromycin 250 mg TID Group II: Critically ill patients who were taken crushed erythromycin 125 mg TID.
0: Baseline at admission.
1-7: First week of ICU admission (duration of our study).

ICU: Intensive care unit.
SD: Standard deviation.
GRV: Gastric residual volume.
ENF: Enteral nutritional formula.
Δ: Changes.

IV. Discussion

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 cachexia in stress critically ill patients, maintaining an adequate nutritional intake is of our priority to maintain positive nutritional status and decreasing risk of aspiration

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pneumonia.[9-10] American Society for Parenteral and EN (ASPEN) and European Society for Parenteral and EN (ESPEN) prefer the use of erythromycin over metoclopramide in critically ill patients with feeding intolerance. In our study, using crushed erythromycin tablet 250 mg TID for 1st week of ICU admission resulted in significantly decreasing in baseline GRV by -90.95±13.05 ml. Also, GRV was reduced significantly in patients who were taken the lower dose of erythromycin (125 mg TID) but with a lower ΔGRV_{1-7} (-66.59±6.26 ml). In this study, we found that standard dose of erythromycin crushed tablet (250 mg TID) was more effective than low dose erythromycin (125 mg TID) in reducing GRV from baseline and in increasing and maintaining nutritional status. This study is limited by its retrospective design, using single-center data, including only mechanically ventilated ICU patients. A larger, multisite, and prospective study is needed to control for multiple confounders.

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