International Research Journal of Pharmacy and Medical Sciences
ISSN (Online): 2581-3277

The Nutritional and Clinical Impacts of Using Non-Selective Beta-Blockers with Enteral and Parenteral Nutritional Formulas in Hospitalized Patients with Severe Wasting Syndromes

Yara Khalid Abu Taleb; Ph[1], "Moh'd Nour" Mahmoud Bani Younes; Ph[1], Jaafar Abd Alrahman Abu Abeeleh; Ph[1]
[1]Clinical Pharmacy Department/King Hussein Medical Hospital/ Royal Medical Services/Jordan
Address correspondence to: "Moh'd Nour" Bani Younes, Clinical Pharmacy Specialist, MSc Clinical Pharmacy, BCPS, BCCCP, BCNSP, BCACP, BCIDP, Chief of EN and TPN Unit, King Hussein Medical Hospital, King Abdullah II St 230, Amman 11733, Jordanian Royal Medical Services, e-mail: panasomycine[AT]Hotmail[DOT]com

Abstract— Objective: *Hospitalization associated malnutrition is a type of stress condition that characterizes by hypermetabolism. Such hypermetabolism is accompanied by increased lean body mass (LBM) catabolism and increased basal energy expenditure (BEE). The severity of this hyper-catabolism may be the primary determinant of severe wasting in hospitalized and critically ill patients. This hypermetabolic status can be mitigated partially through the beta-adrenergic receptors in which propranolol can mitigate this hyperdynamic and hypermetabolic status through its non-selective adrenergic antagonist. The aim of this study is to evaluate the clinical impacts of using propranolol as an anticatabolic agent in adjunctive to either enteral or parenteral nutrition provision.* ***Methods:*** *A retrospective analysis was conducted in our institution between April 2017 and April 2019. Discharged or dead patients were excluded if failed to complete at least 1 week after hospital admission. Our sample was stratified into two comparative groups. Group I (Malnourished hospitalized patients who were administered propranolol tab 40 mg TID as an anti-catabolic agent), Group II (Malnourished hospitalized patients who weren't administered propranolol tab). Independent Samples, One-Sample T-test, and Chi square test were used in our study.* ***Results:*** *The mean age of our 188 studied malnourished hospitalized patients was 58.94±10.37 years in which 131 patients (69.7%) of the eligible sample were males and 57 patients (30.3%) were females. Group I had significantly higher average albumin level (ALB_{avg}) than Group II (3.49±0.02 g/dl vs 3.25±0.06 g/dl) with Mean difference±SEM of +0.24±0.01 g/dl.* ***Conclusion****: Non-selective beta-blockade with propranolol improves survival in severe malnourished hospitalized patients without evidence of clinically significant hemodynamic compromise Significant higher ALB_{avg} accompanied with lower blood urea nitrogen (BUN) may indicate for propranolol anti-catabolic effect which may have a positive major and minor clinical impacts.*

Keywords— *Anticatabolic agents, Hypoalbumenia, Malnourished hospital patients, Propranolol.*

I. INTRODUCTION

Hospitalization associated malnutrition (HAM) is a type of stress condition that characterizes by hypermetabolism and hyperdynamic that are associated with substantially increasing in both basal metabolic rate (BMR) and resting energy expenditure (REE) in an attempt by the body to aid in the healing process, by allowing provision of amino acids and energy, mainly to the liver, in order to maintain gluconeogenesis and synthesis of acute-phase proteins needed for tissue repair and immunological response .[1-4] In critically and non-critically hospitalized individuals, high-protein breakdown and low-protein synthesis as a result of complex interactions between the neurohormones and several inflammatory mediators are the most relevant mechanisms altering protein metabolism.[2,3] Although initially beneficial, a prolonged adaptive metabolic response can lead to adverse outcomes such as the loss of total body protein mass[5] through muscle breakdown and results in a reduction in lean body mass (LBM)[6], leading to muscle wasting and Sarcopenia. As a result, hypermetabolism can lead to multiorgan dysfunction and even death. The duration and magnitude of the hypermetabolic response are major determinants of clinical outcomes of hospitalized patients with an increased risk of morbidity, mortality, and longer hospital length of stay (LOS).[3,4]

The prevalence of malnutrition among hospitalized patients is as high as 50%.[7] Although appropriate nutrition can limit protein catabolism, it does not stop the loss of protein mass occurring in acute severe illness.[5] The hypermetabolic status is primarily mediated by catecholamines.[8] Propagation of catecholamine signaling is mainly through the beta-adrenergic receptors.[9] Propranolol, a nonselective beta-adrenergic receptor antagonist, holds promise for the mitigation of catecholamines' actions and thus, significantly reducing the hyperdynamic and hypermetabolic state. Administration of propranolol for 2 weeks to decrease heart rate by 15% augments net protein balance in muscle by enhancing the availability of free amino acids for muscle protein synthesis, it also decreases the loss in LBM and lowers resting energy expenditure.[10] The role of propranolol has been extensively studied in specific groups of population with proven efficacy in burned, septic and trauma patients[10,11-13], but there are only a few studies to show the

Yara Khalid Abu Taleb; Ph, "Moh'd Nour" Mahmoud Bani Younes; Ph, and Jaafar Abd Alrahman Abu Abeeleh; Ph, "The Nutritional and Clinical Impacts of Using Non-Selective Beta-Blockers with Enteral and Parenteral Nutritional Formulas in Hospitalized Patients with Severe Wasting Syndromes," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 3, Issue 1, pp. 28-31, 2019.

effect of adjunctive propranolol therapy in malnourished hospitalized adults who are already on enteral nutrition (EN) or parenteral nutrition (PN). The aim of this study is to evaluate the clinical impacts of using propranolol as anticatabolic agent in malnourished hypoalbumenic critically ill patients in adjunctive to EN or PN provision regarding average albumin level (ALB_{avg}), average c-reactive protein to ALB ratio ($CRP:ALB_{avg}$), percentage changes in blood urea nitrogen (%ΔBUN), hemodynamics differences, and major clinical outcomes of hospital length of stay (LOS) and overall 28-day hospital mortality.

II. Material and Methods

This is a single-center observational retrospective study conducted in the departments of King Hussein Medical Center (KHMC) at Royal Medical Services (RMS) in Jordan between April 2017 and April 2019. This study was approved by our Institutional Review Board (IRB), and a requirement for consent was waived owing to its retrospective design. In this study, 188 eligible malnourished hospitalized patients who were already on EN, PN, or both, admitted to our KHMH wards including ICU via the emergency deparment (ED) or directly via other hospitals with any medical or surgical problem. Totally, 1485 hospitalized patients were excluded because they either discharged or died before completed at least 1 week after admission (1055 participants) or because the required data couldn't be recruited (430 participants). Patients' demographics, anthropometrics, hemodynamic parameters, nutritional indices, overall hospital LOS, and overall 28-day hospital mortality were recorded retrospectively through our institutional electronic medical records (Hakeem).

Our sample was stratified into two groups: Group I (Malnourished hospitalized patients who were administered propranolol tab 40 mg TID as an anti-catabolic agent), Group II (Malnourished hospitalized patients who weren't administered propranolol tab). All patients' continuous variables were analyzed using independent samples T-test and expressed as Mean±SD for Group I and Group II and as Mean difference±SEM between Group I and Group II. One sample T-test was used to express the variables as Mean±SD for total malnourished hospitalized patients. Total patients, Group I, and Group II groups' categorical data were expressed as numbers with percentages by using Chi Square test. Statistical analysis was performed using IBM SPSS version 25 (IBM Corp., Armonk, NY, USA), and P-values ≤ 0.05 were considered to be statistically significant.

III. Results

The mean age of our 188 studied malnourished hospitalized patients was 58.94±10.37 years in which 131 patients (69.7%) of the eligible sample were males and 57 patients (30.3%) were females. Malnourished hospitalized patients who were administered Propranolol tab 40 mg three times daily (TID) as an anti-catabolic agent (Group I) had significantly higher ALB_{avg} than malnourished hospitalized patients who were not administered Propranolol (Group II) (3.49±0.02 g/dl vs 3.25±0.06 g/dl) with Mean difference±SEM of +0.24±0.01 g/dl. Though there were insignificant differences between the two groups regarding CRP_{avg}, the $CRP:ALB_{avg}$ was significantly lower in Group I compared with Group II (7.25±1.51 vs 7.66±1.57) with Mean difference±SEM of -0.41±0.04. All nutritional indices of TCI_{avg}, PD_{avg}, and $H.ALB_{avg}$ were significantly lower in Group I compared with Group II (1122.6±210.9 Cal/day, 4.21±0.60 g/100 Cal, and 19.67±1.80 g/day vs 1291.6±243.6 Cal/day, 4.42±0.93 g/100 Cal, and 21.23±3.61 g/day) with Mean differences±SEMs of -168.9±33.3 Cal/day, -0.21±0.11 g/100 Cal, and -1.57±0.42 g/day, respectively. Group I had significantly lower BUN_1 and %ΔBUN than in Group II (14.09±1.89 mg/dl and 16.66%±33.07% vs 20.64±3.14 mg/dl and 40.06%±54.73%) with Mean differences±SEMs of -6.55±0.38 mg/dl and -23.40%±6.65%, respectively.

All tested hemodynamics of SBP_{avg}, DBP_{avg}, MAP_{avg}, and HR_{avg} were significantly lower in Group I than in Group II (105.45±10.07 mmHg, 64.52±7.49 mmHg, 78.39±9.40 mmHg, and 75.64±9.94 bpm vs 110.24±9.92 mmHg, 71.14±5.81 mmHg, 85.30±8.21 mmHg, and 79.92±10.85 bpm) with Mean differences±SEMs of -4.79±1.46 mmHg, -6.63±0.98 mmHg, -6.91±1.29 mmHg, and -4.29±1.52 bpm, respectively. Regarding major clinical outcomes of LOS and mortality, patients in Group I had significantly lower hospital LOS and overall 28-day mortality than in patients of Group II (11.73±3.15 days and 10 (10.99%) vs 14.09±5.76 days and 26 (26.80%), respectively) with hospital LOS Mean difference±SEM of -2.37±0.68 days. The demographics, anthropometrics, nutritional indices, hemodynamics, and major clinical outcomes of all, Group I, and Group II hypoalbumenic malnourished hospitalized patients are fully presented in Table 1.

IV. Discussion

This study demonstrates that non-selective beta-blockade with propranolol improves survival in malnourished hospitalized patients without evidence of clinically significant hemodynamic compromise. Furthermore, for the first time the anti-catabolic effect of propranolol and its effectiveness on the general population of malnourished hospitalized patients who received ENF were studied, without limiting the study to a specific group of hospitalized patients. The measured overall anthropometrics of our malnourished hospitalized subjects of study were 74.05±10.23 kg and 25.90±3.97 kg/m^2 for actual body weight (ABW) and body mass index (BMI), respectively. There is an established correlation between CRP level, which is a positive acute phase reactant, and ALB. Both Inflammation and malnutrition reduce ALB concentration by decreasing its rate of synthesis, while inflammation alone is associated with a higher fractional catabolic rate (FCR) and, when extreme, increased escape of albumin from the intravascular compartment, while the rate of synthesis of ALB is inversely related to the CRP.[14]

Moreover, many studies stated that Albumin remains a useful tool in evaluating nutrition and predicting the patient's risk for morbidity.[15] Therefore, these two markers were used to give an indication of the anti-catabolic effect of Propranolol. In our study, the difference in CRP levels between the two groups was statistically insignificant, while

Yara Khalid Abu Taleb; Ph, "Moh'd Nour" Mahmoud Bani Younes; Ph, and Jaafar Abd Alrahman Abu Abeeleh; Ph, "The Nutritional and Clinical Impacts of Using Non-Selective Beta-Blockers with Enteral and Parenteral Nutritional Formulas in Hospitalized Patients with Severe Wasting Syndromes," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 3, Issue 1, pp. 28-31, 2019.

the differences in ALB levels and CRP: ALB ratio were significant, (3.49±0.02 g/dl vs 3.25±0.06 g/dl) and (7.25±1.51 vs 7.66±1.57) with Mean difference±SEM of (+0.24±0.01 g/dl) and (-0.41±0.04), respectively. Our explanation for the significant differences in ALB levels is the anti-catabolic effect of Propranolol. Confirmed by the lower %ΔBUN in Group I (the intervention group) compared with Group II, (16.66%±33.07%) vs (40.06%±54.73%), respectively. Hemodynamic differences between the two groups were statistically significant due to the anti-adrenergic effects of Propranolol, but were clinically acceptable, with SBP_{avg}, DBP_{avg}, MAP_{avg}, and HR_{avg} were significantly lower in Group I. Hospital LOS and overall 28-day mortality among patients were significantly lower in Group I than in Group II (11.73±3.15 days and 10 (10.99%) vs 14.09±5.76 days and 26 (26.80%), respectively) with hospital LOS Mean difference±SEM of -2.37±0.68 days. These major clinical outcomes are consistent with the outcomes of other previous studies.[3,4]

In summary, significant higher ALB_{avg} accompanied with lower blood urea nitrogen (BUN) in Group I compared with Group II may indicate for Propranolol anti-catabolic effect which may have a positive major and minor clinical impacts in malnourished critically ill patients. This study is limited by its retrospective design, using single-center data. 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.

TABLE 1. The demographics, anthropometrics, nutritional indices, hemodynamics, and major clinical outcomes of all, Group I, and Group II malnourished hospitalized patients.

Variable		Total (N=188)	(Group I) (N=91) Mean±SD	Group II, (N=97) Mean±SD	Mean difference±SEM	P-Value
Age (Yrs)		58.94±10.37	59.82±10.22	58.11±10.50	1.71±1.51	0.259 (NS)
Gender	Female	57 (30.3%)	27 (29.7%)	30 (30.9%)		0.489 (NS)
	Male	131 (69.7%)	64 (70.3%)	67 (69.1%)		
BW (Kg)		74.05±10.23	76.52±10.51	71.73±9.45	4.79±1.46	0.001 (S)
BMI (Kg/m^2)		25.90±3.97	26.97±3.91	24.89±3.79	2.08±0.56	0.000 (S)
CRP_{avg} (mg/dl)		25.11±4.67	25.30±5.05	24.91±4.53	0.39±0.61	0.091 (NS)
$H.ALB_{avg}$ (g/day)		20.48±2.98	19.67±1.80	21.23±3.61	-1.57±0.42	0.000 (S)
TCI_{avg} (Cal/kg/day)		17.63±3.12	16.20±2.63	18.96±2.96	-2.76±0.41	0.000 (S)
TCI_{avg} (Cal/day)		1209.8±242.9	1122.6±210.9	1291.6±243.6	-168.9±33.3	0.000 (S)
PD_{avg} (g/100 Cal)		4.32±0.79	4.21±0.60	4.42±0.93	-0.21±0.11	0.031 (S)
ALB_{avg} (g/dl)		3.37±0.05	3.49±0.02	3.25±0.06	0.24±0.01	0.000 (S)
$CRP:ALB_{avg}$ (X:1)		7.45±1.54	7.25±1.51	7.66±1.57	-0.41±0.04	0.000 (S)
BUN_0		14.87±5.27	12.90±3.89	16.71±5.74	-3.81±0.72	0.000 (S)
BUN_1		17.47±4.19	14.09±1.89	20.64±3.14	-6.55±0.38	0.000 (S)
%ΔBUN		28.73%±46.92%	16.66%±33.07%	40.06%±54.73%	-23.40%±6.65%	0.001 (S)
SBP_{avg}		107.77±10.26	105.45±10.07	110.24±9.92	-4.79±1.46	0.001 (S)
DBP_{avg}		67.72±7.49	64.52±7.49	71.14±5.81	-6.63±0.98	0.000 (S)
MAP_{avg}		81.73±9.47	78.39±9.40	85.30±8.21	-6.91±1.29	0.000 (S)
HR_{avg}		77.85±10.61	75.64±9.94	79.92±10.85	-4.29±1.52	0.005 (S)
Hospital LOS		12.91±4.45	11.73±3.15	14.09±5.76	-2.37±0.68	0.000 (S)
Overall 28-day Survival		152 (80.85%)	81 (89.01%)	71 (73.19%)		0.000 (S)
Overall 28-day Mortality		36 (19.15%)	10 (10.99%)	26 (26.80%)		

Values are presented as Mean±SD by using independent T-test and one sample T-test or as number (%)by using Chi-square test.
Group I: Malnourished hospitalized patients who were administered Propranolol tab 40 mg TID as an anti-catabolic agent.
Group I: Malnourished hospitalized patients who weren't administered Propranolol tab.

Yrs: Years.
Kg: Kilogram.
BW: Actual body weight.
BMI: Body mass index.
S: Significant (P-Value <0.05).
NS: Nonsignificant (P-Value >0.05).
N: Number of study's patients.
TCR: Total calories requirement.
PD: Protein density.
Δ: Changes occurred after an intervention.
ALB: Albumin level.
H.ALB: Human albumin 20%.
0: Baseline before the intervention was commenced.
1: 1 week after the intervention was commenced.
Avg: Average value of the tested variable over 1 week.
BUN: Blood urea nitrogen.
CRP: C-reactive protein.
CRP:ALB ratio: C-reactive protein to albumin level ratio.
SBP: Systolic blood pressure.
DBP: Diastolic blood pressure.
MAP: Mean arterial pressure.
HR: Heart rate.
Bpm: Beat per minute.
LOS: Length of stay.

REFERENCES

[1] Corish, C. A., & Kennedy, N. P. (2000). Protein–energy undernutrition in hospital in-patients. British Journal of Nutrition,83(6), 575-591.
[2] Flier, J. S., Underhill, L. H., & Wilmore, D. W. (1991). Catabolic Illness. New England Journal of Medicine,325(10), 695-702.
[3] Guadagni, M., & Biolo, G. (2009). Effects of inflammation and/or inactivity on the need for dietary protein. Current Opinion in Clinical Nutrition and Metabolic Care,12(6), 617-622.
[4] Baudouin, S. V., & Evans, T. W. (2003). Nutritional support in critical care. Clinics in Chest Medicine,24(4), 633-644.
[5] Genton, & Pichard. (2011). Protein Catabolism and Requirements in Severe Illness. International Journal for Vitamin and Nutrition Research,81(23), 143-152.

Yara Khalid Abu Taleb; Ph, "Moh'd Nour" Mahmoud Bani Younes; Ph, and Jaafar Abd Alrahman Abu Abeeleh; Ph, "The Nutritional and Clinical Impacts of Using Non-Selective Beta-Blockers with Enteral and Parenteral Nutritional Formulas in Hospitalized Patients with Severe Wasting Syndromes," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 3, Issue 1, pp. 28-31, 2019.

[6] Michie, H. R. (1996). Cytokines and the Acute Catabolic State. Acute Catabolic State Update in Intensive Care and Emergency Medicine,227-237.
[7] Hill, G., Pickford, I., Young, G., Schorah, C., Blackett, R., Burkinshaw, L.. Morgan, D. (1977). Malnutrition In Surgical Patients. The Lancet,309(8013), 689-692.
[8] Wilmore, D. W., & Aulick, L. H. (1978). Metabolic Changes in Burned Patients. Surgical Clinics of North America,58(6), 1173-1187.
[9] Herndon, D. N., Rodriguez, N. A., Diaz, E. C., Hegde, S., Jennings, K., Mlcak, R. P.. Finnerty, C. C. (2012). Long-Term Propranolol Use in Severely Burned Pediatric Patients. Annals of Surgery,256(3), 402-411.
[10] Herndon, D. N., Hart, D. W., Wolf, S. E., Chinkes, D. L., & Wolfe, R. R. (2001). Reversal of Catabolism by Beta-Blockade after Severe Burns. New England Journal of Medicine,345(17), 1223-1229.
[11] Norbury, W. B., Jeschke, M. G., & Herndon, D. N. (2007). Metabolism modulators in sepsis: Propranolol. Critical Care Medicine,35(Suppl).
[12] Lunawat, A., Vishwani, A., Datey, S., & Singh, V. (2015). Modulation of hypermetabolism in burn patient by administration of propranolol in the first two weeks and assessing its effect by using clinical and biochemical parameters. Indian Journal of Burns,23(1), 19.
[13] Wilson, J., Higgins, D., Hutting, H., Serkova, N., Baird, C., Khailova, L., Wischmeyer, P. E. (2013). Early propranolol treatment induces lung heme-oxygenase-1, attenuates metabolic dysfunction, and improves survival following experimental sepsis. Critical Care,17(5).
[14] Don, B. R., & Kaysen, G. (2004). Poor Nutritional Status And Inflammation: Serum Albumin: Relationship to Inflammation and Nutrition. Seminars in Dialysis,17(6), 432-437.
[15] Gibbs, J. (1999). Preoperative Serum Albumin Level as a Predictor of Operative Mortality and Morbidity. Archives of Surgery,134(1), 36.

Yara Khalid Abu Taleb; Ph, "Moh'd Nour" Mahmoud Bani Younes; Ph, and Jaafar Abd Alrahman Abu Abeeleh; Ph, “The Nutritional and Clinical Impacts of Using Non-Selective Beta-Blockers with Enteral and Parenteral Nutritional Formulas in Hospitalized Patients with Severe Wasting Syndromes,” *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 3, Issue 1, pp. 28-31, 2019.