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Original Article

Comparative effectiveness of six intravenous treatment protocols for hyperemesis gravidarum: A retrospective cohort study

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Abstract

Aim: To evaluate the real-world comparative effectiveness of six inpatient intravenous (IV) treatment protocols for hyperemesis gravidarum (HG), stratified by antiemetic strategy and IV B-complex vitamin supplementation.
Materials and Methods: We conducted a retrospective cohort study of women hospitalized for HG. Patients were classified into six treatment protocols according to IV antiemetic regimen (metoclopramide, ondansetron or no IV antiemetic) and IV B-complex vitamin use (yes/no). The primary outcome was early clinical response within 24-48 hours. Secondary outcomes included length of hospital stay (LOS), 14-day rehospitalization and treatment-related complications. Outcomes were compared across treatment protocols and according to B-complex exposure.
Results: A total of 1.120 women were included in the analysis. Crude outcomes differed across treatment protocols, with B-complex-containing regimens demonstrating higher rates of early clinical response and shorter LOS. When pooled by exposure, early clinical response occurred in 83.5% of patients receiving B-complex vitamins compared with 68.8% of those without supplementation, while mean LOS was 1.47 ± 0.50 days versus 2.62 ± 0.65 days, respectively (all $p < 0.001$). Rates of 14-day rehospitalization and treatment-related complications were comparable between groups. However, baseline clinical characteristics were largely similar across groups, and B-complex supplementation was not independently associated with early clinical response after adjustment for baseline severity and treatment-related factors in multivariable analyses.
Conclusion: In this large real-world inpatient cohort of women with HG, IV treatment protocols including B-complex vitamins were associated with more favorable short-term outcomes in unadjusted analyses; however, these associations were not clearly independent after accounting for clinical and treatment confounders. Nevertheless, B-complex supplementation should be considered a routine part of HG management, regardless of the antiemetic used, primarily for its role in neurological prophylaxis. These findings support efforts toward protocol standardization and suggest a more targeted, evidence-based approach to HG management.

Keywords: Hyperemesis gravidarum, intravenous therapy, metoclopramide, ondansetron, B-complex vitamins, length of hospital stay

INTRODUCTION

Hyperemesis gravidarum (HG) represents the most severe form of nausea and vomiting in pregnancy (NVP), a condition affecting most pregnant women to varying degrees. While mild or moderate NVP is common and generally resolves by the second trimester, HG is characterized by persistent vomiting, weight loss of at least 5% of pre-pregnancy body weight, ketonuria and electrolyte disturbances (1). Although it affects only 0.3-3% of pregnancies, HG has substantial clinical relevance due to its potential complications, including severe dehydration, Wernicke encephalopathy, hepatic dysfunction, thromboembolic events and, in rare cases, pregnancy termination (2). Beyond somatic morbidity, HG imposes a considerable psychological burden, contributing to anxiety, depression, negative pregnancy attitudes and impaired maternal-fetal bonding (3). Fetal risks such as low

birth weight, fetal growth restriction and preterm birth remain a matter of ongoing debate. Overall, HG adversely affects maternal well-being, pregnancy outcomes and healthcare utilization, often necessitating a multidisciplinary management approach (4).

Initial management of HG focuses on rapid volume resuscitation, correction of electrolyte abnormalities, nutritional support and symptom control. Intravenous (IV) therapy is typically the first-line intervention in acute care settings and aims to restore hemodynamic stability and improve tolerability of oral intake. Standard IV regimens usually include crystalloid fluids, electrolyte replacement, B-vitamin supplementation and antiemetics such as metoclopramide or ondansetron (5). However, the composition, dosing and duration of these IV protocols vary widely both across and within institutions, reflecting substantial practice heterogeneity (6). This variability has important implications for clinical outcomes and underscores the need for more standardized IV management strategies.

Although guidelines recommend a stepwise pharmacologic approach beginning with hydration and lifestyle measures, progressing to antihistamines, dopamine antagonists, 5-HT_3 receptor antagonists and finally corticosteroids (1,7), real-world practice often diverges from this sequence. In many emergency and day-care settings, women with HG are treated immediately with IV fluids, antiemetics and intermittent vitamin supplementation, irrespective of prior oral therapy attempts (8). Notably, a large proportion of these women show substantial improvement with initial IV therapy alone, without requiring escalation to more intensive pharmacologic interventions (9). This pattern suggests that IV supportive care is highly effective for a specific subgroup of HG patients who respond rapidly to hydration and early antiemetic therapy.

Despite the central role of IV therapy in HG management, comparative real-world data evaluating different IV protocols are scarce. This evidence gap is particularly evident for women who respond adequately to IV therapy alone, leaving clinicians without a clear evidence-based framework for selecting the most effective and efficient IV regimen.

B-vitamin supplementation exemplifies this uncertainty. Thiamine deficiency is the primary risk factor for Wernicke encephalopathy in HG, and inclusion of B-complex vitamins in IV regimens is widely accepted as a preventive strategy (10). However, evidence supporting B-complex supplementation beyond neurological protection—specifically its effect on short-term symptomatic recovery—remains limited. Few studies have compared otherwise similar antiemetic-based IV regimens with versus without B-complex supplementation in terms of early clinical response, length of stay or readmission (11). While B-vitamins are unquestionably essential to prevent neurological complications, their independent contribution to accelerating clinical recovery is unclear.

Uncertainty also persists regarding the optimal choice of antiemetic therapy. Metoclopramide has long been used effectively for NVP and HG, despite the risk of extrapyramidal side effects (1,12). Ondansetron is increasingly prescribed for more severe symptoms or in cases refractory to first-line agents, although ongoing concerns about potential associations with congenital anomalies continue to influence prescribing behavior (13). Because both agents are commonly incorporated into IV protocols, clarifying their comparative short-term effectiveness in women who improve with IV therapy alone is clinically relevant.

Many women hospitalized with HG experience rapid improvement within 24-72 hours of IV therapy and are discharged without requiring further escalation (14). This subgroup represents a distinct and clinically important population in whom direct comparison of IV treatment strategies is both feasible and informative. Yet, few multicenter studies have systematically evaluated IV fluids alone versus combinations with metoclopramide, ondansetron or B-complex vitamins, particularly in relation to early symptom resolution, length of stay, rehospitalization and adverse events (15).

To address these gaps, we conducted a multicenter retrospective cohort study comparing the clinical effectiveness and safety of six commonly used IV treatment protocols—combinations of crystalloid fluids, metoclopramide, ondansetron and B-complex vitamins—among women hospitalized with HG who achieved clinical improvement with IV therapy alone. We hypothesized that any apparent association between B-complex supplementation and faster symptom improvement might reflect baseline severity or treatment selection rather than a direct pharmacologic effect. By providing real-world comparative data in this clinically relevant subgroup, our study aims to inform more rational, standardized and evidence-based IV management strategies for HG.

MATERIALS AND METHODS

Study Design and Setting

This multicenter retrospective cohort study compared the clinical effectiveness and safety of six IV treatment protocols used in the management of HG. The study was conducted at two tertiary referral hospitals with high-volume obstetric services, each managing approximately 30.000-40.000 deliveries annually.

Ethics Statement

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Harran University Clinical Research Ethics Committee (Approval No: HRÜ/25.14.04; Session No: 14; Date: 01 September 2025). Due to the retrospective study design and the use of anonymized patient data, the requirement for written informed consent was waived by the Ethics Committee.

Study Population

Consecutive pregnant women hospitalized with HG between 2015 and 2025 were screened for eligibility. Cases were identified using ICD-coded diagnoses, electronic medical records, and inpatient charts.

Inclusion Criteria

Patients were included if they met all of the following criteria:

1. Gestational age ≤ 20 weeks at admission,
2. Clinical diagnosis of HG, defined by:
   - Persistent nausea and ≥ 3-5 vomiting episodes per day
   - ≥ 5% pre-pregnancy weight loss
   - Ketonuria and/or electrolyte imbalance,
3. Receipt of IV therapy during the first hospitalization (no tube feeding or parenteral nutrition),
4. Documented clinical improvement with restored oral intake (classified as responsive to IV therapy),
5. Availability of complete medical and laboratory data.

Exclusion Criteria

Patients were excluded if any of the following were present:

1. Alternative causes of nausea and vomiting (e.g., molar pregnancy, multiple gestation, thyrotoxicosis, gastrointestinal disease, renal or hepatic failure),
2. Acute systemic illness or infection not primarily attributable to HG,
3. Requirement for enteral feeding, total parenteral nutrition, or intensive care unit admission (non-response to initial IV therapy),
4. Missing essential clinical or treatment data,
5. More than one hospitalization for HG within the same pregnancy (only the first admission was included).

Treatment Groups and IV Therapy Protocols

All patients received crystalloid fluids (0.9% saline or Ringer's lactate) and electrolyte correction as needed. Based on the use of antiemetics and B-complex vitamins, patients were categorized into six IV treatment groups:

- **Group 1 (n = 188):** metoclopramide without B-complex
- **Group 2 (n = 191):** metoclopramide plus B-complex
- **Group 3 (n = 170):** ondansetron without B-complex
- **Group 4 (n = 184):** ondansetron plus B-complex
- **Group 5 (n = 197):** no antiemetic, no B-complex
- **Group 6 (n = 190):** B-complex without antiemetic

In groups receiving B-complex, the standard regimen consisted of thiamine 100 mg, riboflavin 2 mg, pyridoxine 2 mg and nicotinamide 20 mg. These dosages and the choice of B-vitamin supplementation were based on the Royal College of Obstetricians and Gynaecologists (RCOG) Green-top Guidelines for the management of hyperemesis gravidarum and established institutional protocols. All IV medication regimens followed these standardized protocols and were verified from medication administration records. Detailed group characteristics are presented in Table 2.

Data Collection and Variables

Data were extracted using a standardized electronic case report form and included demographic, clinical, laboratory, and treatment-related variables.

Demographic and obstetric variables included maternal age, body mass index (BMI), gravidity, parity, and gestational age at admission.

Clinical and laboratory variables included vomiting frequency (episodes per 24 hours), percentage of weight loss, vital signs, ketonuria grade (semi-quantitative scale 0-4+), serum electrolytes, and renal and liver function tests.

Treatment-related variables included the type and volume of IV fluids, antiemetic use (drug, dose, and frequency), B-complex vitamin use, electrolyte supplementation, and other supportive therapies administered during the index hospitalization.

Outcome Measures

Primary Outcomes

1. Early clinical response, defined as cessation of vomiting, documented improvement of nausea (based on physician assessment), and the ability to tolerate oral fluids for at least 6 consecutive hours within 24-48 hours of treatment initiation.
2. Length of hospital stay (LOS) in days, calculated from admission to discharge.
3. Rehospitalization for HG within 14 days after discharge.

Secondary Outcomes

Secondary outcomes included treatment-related adverse events and time to correction of electrolyte abnormalities.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics, version 29 (IBM Corp., Armonk, NY, USA). A two-sided p-value < 0.05 was considered statistically significant. The distribution of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed continuous variables were summarized as mean ± standard deviation (SD) and compared using the independent-samples t-test or one-way analysis of variance (ANOVA), as appropriate. Non-normally distributed continuous variables were presented as median and interquartile range (IQR) and compared using the Mann-Whitney U test or Kruskal-Wallis test. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test or Fisher's exact test. Post hoc pairwise comparisons for ANOVA were performed using Tukey's honestly significant difference (HSD) test, while post hoc comparisons for categorical variables following chi-square tests were conducted using the Z-test with Bonferroni adjustment.

For multivariable analyses, logistic regression models were used to evaluate factors associated with early clinical response, and linear regression models were used to assess predictors of LOS. Covariates were selected for inclusion in the multivariable

models based on clinical relevance and prior evidence from existing literature, ensuring that clinically important confounders were accounted for regardless of univariate significance. Model selection was guided by the Akaike Information Criterion (AIC) to balance model fit and parsimony. Sensitivity analyses were performed using complete-case analysis and by stratifying outcomes according to the participating institution to explore the robustness and consistency of the findings.

RESULTS

A total of 1.120 women admitted with hyperemesis gravidarum were included in the analysis. The patient flow and allocation to treatment groups are depicted in the flowchart (Figure 1).

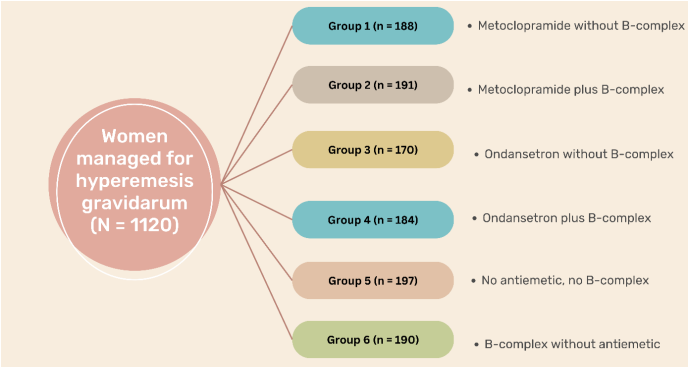

Figure 1. Flow diagram of patient allocation into the six intravenous treatment groups

Baseline Clinical Characteristics

Baseline characteristics of the study population are summarized in Table 1. The mean maternal age was 27.5 ± 5.2 years, the mean gestational age at admission was 10.0 ± 3.4 weeks, and the mean BMI was 24.1 ± 3.5 kg/m². On average, women reported 9.5 ± 2.9 vomiting episodes during the 24 hours prior to admission and had experienced a mean weight loss of 7.1 ± 1.1%. Ketonuria was present in all 1.120 patients (100.0%) at the time of admission, indicating a clinically severe study cohort.

Comparative analysis between women who received B-complex supplementation and those who did not demonstrated well-balanced groups at baseline. No statistically significant differences were observed in maternal age (27.5 ± 5.3 vs. 27.5 ± 5.1 years, p = 0.578), gestational age at admission (10.0 ± 3.5 vs. 10.1 ± 3.3 weeks, p = 0.217), BMI (24.1 ± 3.6 vs. 24.1 ± 3.4 kg/m², p = 0.962), percentage weight loss (7.1 ± 1.2% vs. 7.0 ± 1.0%, p = 0.387), or vomiting frequency (9.5 ± 3.0 vs. 9.6 ± 2.8 episodes per day, p = 0.826). Similarly, obstetric history variables, including gravida (2.5 ± 1.2 vs. 2.4 ± 1.0, p = 0.058) and parity (1.1 ± 1.3 vs. 1.1 ± 1.1, p = 0.510), did not differ significantly between the two groups. Overall, these findings indicate that the study groups were well-balanced with respect to all measured baseline demographic, obstetric, and clinical characteristics.

Table 1. Baseline clinical characteristics

Variable	Mean ± SD	p-value
Age (years)	27.5 ± 5.2	0.578
Gestational age at admission (weeks)	10.0 ± 3.4	0.217
Gravida (n)	2.5 ± 1.1	**0.058**
Parity (n)	1.1 ± 1.2	0.51
BMI (kg/m²)	24.1 ± 3.5	**0.962**
Weight loss (%)	7.1 ± 1.1	0.387
Vomiting episodes in last 24 h (n/day)	9.5 ± 2.9	0.826

*Data are shown as mean (SD). p-values represent comparisons between women receiving and not receiving B-complex supplementation (Welch's t-test for continuous variables; chi-square test for categorical variables)

Treatment Groups and Crude Clinical Outcomes

The distribution of patients across treatment groups is presented in Table 2. Patients were categorized into six groups according to IV antiemetic regimen and B-complex use: Group 1 (metoclopramide only, n = 188), Group 2 (metoclopramide + B-complex, n = 191), Group 3 (ondansetron only, n = 170), Group 4 (ondansetron + B-complex, n = 184), Group 5 (no IV antiemetic, no B-complex, n = 197) and Group 6 (no IV antiemetic + B-complex, n = 190). Overall, 555 women (49.6%) did not receive B-complex whereas 565 (50.4%) received B-complex supplementation.

Crude clinical outcomes across these six treatment groups are summarized in Table 3. The mean ± SD LOS showed marked variation, ranging from 1.47 ± 0.50 days in the B-complex groups (Groups 2, 4 and 6) to 2.46 ± 0.50 to 2.83 ± 0.82 days in the corresponding non-B-complex groups (Groups 1, 3 and 5), with a highly significant overall difference across groups (p < 0.001). Early clinical response rates also differed

substantially: in B-complex groups, early response ranged from 78.4% to 88.0% whereas in non-B-complex groups it ranged from 64.0% to 72.9% (overall $p < 0.001$). These crude patterns are illustrated in Figure 2 for early clinical response and Figure 3 for LOS.

In contrast, there were no statistically significant differences across treatment groups in 14-day rehospitalization ($p = 0.055$) or treatment-related complications ($p = 0.148$) although numerically rehospitalization and complication rates tended to be slightly lower in several B-complex groups.

Table 2. Treatment groups and allocation

Group	N	IV antiemetic	B-complex supplementation
1	188	Metoclopramide	No
2	191	Metoclopramide	Yes
3	170	Ondansetron	No
4	184	Ondansetron	Yes
5	197	None	No
6	190	None	Yes

*Note. Groups were defined by intravenous (IV) antiemetic regimen and B-complex supplementation status

Table 3. Clinical outcomes across treatment groups

Treatment Group	N	LOS (Mean ± SD)	Early clinical response n (%)	Rehospitalization n (%)	Treatment-related complications n (%)
1	188	2.53 ± 0.50	137 (72.9)	20 (10.6)	22 (11.7)
2	191	1.47 ± 0.50	168 (88.0)	8 (4.2)	12 (6.3)
3	170	2.46 ± 0.50	119 (70.0)	10 (5.9)	13 (7.6)
4	184	1.47 ± 0.50	155 (84.2)	16 (8.7)	14 (7.6)
5	197	2.83 ± 0.82	126 (64.0)	13 (6.6)	9 (4.6)
6	190	1.48 ± 0.50	149 (78.4)	7 (3.7)	12 (6.3)
p value		< 0.001	< 0.001	0.055	0.148

*Note. LOS: Length of hospital stay. p-values for LOS were calculated using one-way ANOVA. P-values for categorical outcomes (early clinical response, rehospitalization and treatment-related complications) were determined using Chi-square tests. Following the Chi-square tests, post hoc comparisons were performed using Bonferroni correction to maintain statistical rigor

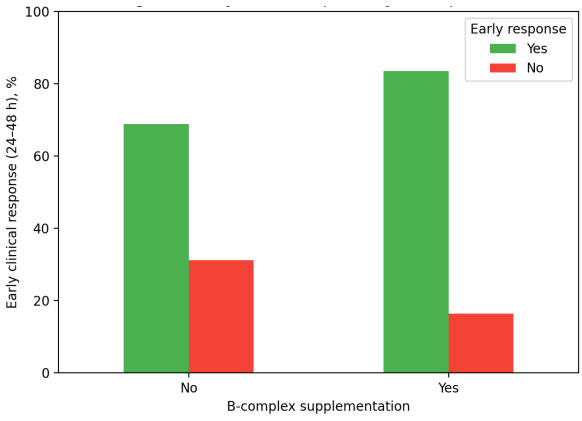

Figure 2. Early clinical response rates within 24-48 hours according to B-complex supplementation. Response rates were significantly higher in patients receiving B-complex compared with the non-supplemented group

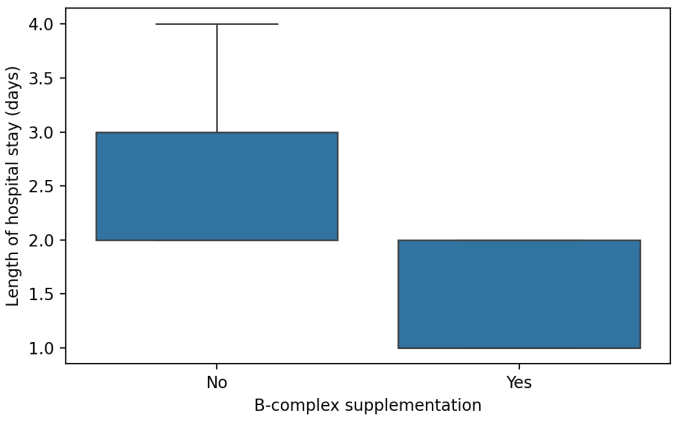

Figure 3. Boxplot comparing length of hospital stay (LOS) between patients with and without B-complex supplementation. LOS was significantly shorter in the B-complex group compared with the non-supplemented group ($p < 0.001$)

Clinical Outcomes According to B-Complex Vitamin Use

The impact of B-complex supplementation on clinical outcomes was evaluated by pooling data across all antiemetic regimens (Table 4). Women who received IV B-complex vitamins (n = 565) demonstrated a significantly higher rate of early clinical response within 24-48 hours compared with those who did not receive supplementation (n = 555) (83.5% vs. 68.8%; odds ratio 2.27, 95% confidence interval (CI) 1.71 – 3.01; p < 0.001).

Hospitalization outcomes also differed significantly between the two groups. The mean ± SD LOS was markedly shorter in the B-complex group (1.47 ± 0.50 days) than in the non-supplemented group (2.62 ± 0.65 days; mean difference (MD) -1.15 days, 95% CI -1.22 to -1.08; p < 0.001). This finding was consistent with the median LOS which was 1 day (IQR 1 – 2) in the B-complex group compared with 3 days (IQR 2-3) in patients who did not receive B-complex supplementation (p < 0.001).

In contrast, no significant differences were observed in safety or longer-term recovery outcomes. Rehospitalization within 14 days occurred in 5.5% of women in the B-complex group and 7.7% of those without supplementation (p = 0.16). Similarly, treatment-related complication rates were comparable between the İV groups (6.7% vs. 7.9%; p = 0.51). Overall, these results indicate that adjunctive IV B-complex vitamin therapy is associated with more rapid clinical improvement and a significantly shorter LOS without a significant effect on rehospitalization or complication rates.

Table 4. Clinical outcomes stratified by B-complex supplementation

Outcome	B-complex (n = 565)	No B-complex (n = 555)	Effect estimate (95% CI)	p-value
Early clinical response, n (%)	472 (83.5)	382 (68.8)	OR 2.27 (1.71 – 3.01)	< 0.001
LOS (mean ± SD), days	1.47 ± 0.50	2.62 ± 0.65	MD -1.15 (-1.22 to -1.08)	< 0.001
LOS [median (IQR)], days	1 (1-2)	3 (2-3)	—	< 0.001
Rehospitalization within 14 days, n (%)	31 (5.5)	43 (7.7)	—	0.160
Treatment-related complications, n (%)	38 (6.7)	44 (7.9)	—	0.510

*CI: confidence interval, IQR: interquartile range, LOS: length of hospital stay, MD: mean difference, OR: odds ratio; Categorical variables are compared using the Chi-square test; Continuous variables are compared using the unpaired t-test (for means) and Mann-Whitney U test (for medians); Effect estimates are crude (unadjusted)

Characteristics According to Early Clinical Response

Of the 1.120 women included in the analysis, 854 (76.3%) were classified as responders and 266 (23.7%) as non-responders. Comparative analyses demonstrated no statistically significant differences between the two groups with respect to baseline demographic and clinical characteristics. Specifically, maternal age, gestational age at admission, gravida, parity, BMI, pre-admission weight loss and frequency of vomiting episodes were comparable between responders and non-responders (all p > 0.05).

Similarly, treatment-related variables did not differ significantly according to response status. These included the severity of ketonuria at admission, the type and volume of IV fluids administered and the antiemetic regimens used (all p > 0.05). The proportion of women receiving B-complex vitamin supplementation was also similar between the two groups (p = 0.78). In addition, the mean ± SD LOS did not differ significantly between responders and non-responders (2.3 ± 0.9 vs. 2.4 ± 1.0 days, p = 0.68). Overall, these findings indicate that baseline patient characteristics and initial treatment modalities were not the primary determinants of early clinical response in this cohort.

DISCUSSION

In this large retrospective cohort of women hospitalized for HG, we evaluated the impact of IV B-complex supplementation on early clinical response and LOS. In crude analyses, women receiving B-complex appeared to have higher early response rates and shorter hospital stays. However, these apparent benefits disappeared entirely after adjustment for baseline characteristics. In multivariable models, B-complex showed no independent association with either early clinical response (adjusted OR 1.00; p = 0.96) or LOS (β 0.00 days; p = 0.98). These findings challenge the assumption that routine B-complex supplementation meaningfully accelerates short-term clinical recovery in HG.

Comparison with Previous Literature

IV hydration, electrolyte replacement and antiemetic therapy are widely regarded as the cornerstone of HG management (16). Numerous guidelines and observational studies strongly recommend thiamine and other B-vitamins, primarily to prevent Wernicke encephalopathy and related neurological complications in women with prolonged vomiting and inadequate intake (17). Our institutional IV B-complex dosage (100 mg thiamine, 2 mg riboflavin, 2 mg pyridoxine and 20 mg nicotinamide) was

determined in accordance with established clinical protocols and international recommendations such as those from the RCOG to ensure adequate neurological prophylaxis. However, these recommendations are largely extrapolated from pathophysiological reasoning and case series; robust data on short-term clinical endpoints such as time to symptom improvement, early response and duration of hospitalization remain limited (18).

By focusing specifically on clinical outcomes in women who improved with IV therapy alone, our study helps address this gap. We found that B-complex supplementation was not an independent determinant of LOS once potential confounders were taken into account. The striking crude differences in LOS—such as an apparent reduction of more than one day among B-complex recipients—may seem consistent with anecdotal impressions of benefit from earlier reports, but our adjusted findings suggest that much of this effect is likely attributable to selection bias and unmeasured differences in clinical presentation rather than a direct pharmacologic action of B-vitamins.

Interpretation of the Discrepancy Between Crude and Adjusted Outcomes

The marked divergence between crude and adjusted results is a notable aspect of our analysis. Despite well-balanced baseline characteristics between B-complex users and non-users, the substantial crude benefits observed for early clinical response and LOS were completely attenuated in the multivariable models. This pattern strongly suggests the presence of unmeasured selection factors. In routine practice, clinicians may be more inclined to prescribe B-complex to women who appear likely to improve rapidly or do not seem severely ill based on overall clinical impression, even if this is not fully captured by recorded variables. Such treatment allocation driven by clinical intuition rather than standardized severity scores naturally favors better outcomes in the B-complex group regardless of any true treatment effect (19).

The observation that none of the routinely measured demographic or severity parameters—such as age, BMI and vomiting frequency—were independently associated with early improvement further supports the hypothesis that the crude benefit of B-complex acted as a surrogate for broader supportive care delivered to patients whose underlying illness trajectory was already more favorable (3,20). Furthermore, in our study, the rehospitalization rate ($p = 0.055$) approached the threshold for statistical significance. While this did not reach the formal alpha level of 0.05, the observed numerical trend suggests that standardized IV protocols might influence readmission risks. This near-significant finding highlights the importance of future prospective trials with larger sample sizes to further investigate the impact of specific vitamin and antiemetic combinations on long-term clinical stability and healthcare utilization.

Comparison of Antiemetic Regimens

Our analyses indicated that neither metoclopramide nor ondansetron had a significant independent effect on LOS after accounting for baseline characteristics. This is consistent with the notion that early response may depend more on timely and adequate supportive measures than on the specific choice of these two commonly used antiemetics (7,21). Our findings align with previous clinical trials suggesting that while both agents are effective in reducing emetic episodes, they often demonstrate comparable efficacy regarding overall clinical recovery and duration of hospitalization in acute settings. These results are consistent with meta-analyses indicating that neither drug is clearly superior for symptom control in HG, emphasizing that clinical improvement may depend more on timely and adequate supportive measures than on the choice between these two specific antiemetics. While metoclopramide and ondansetron remain integral components of HG management, our results suggest that within the context of effective IV fluid and electrolyte replacement, their relative contribution to shortening hospital stay in women who improve with IV therapy alone may be limited. Future prospective studies are needed to explore whether specific subgroups derive differential benefit from one antiemetic over the other.

Limitations

This study has several important limitations inherent to its retrospective design. First, HG symptom severity and improvement were assessed using clinical judgment and oral tolerance rather than validated instruments such as the Pregnancy-Unique Quantification of Emesis (PUQE) score which may introduce observer bias and limit comparability with other studies (22). Second, detailed information on the exact timing of B-complex initiation and discontinuation, as well as precise transitions from IV to oral intake, was not consistently available and may have influenced LOS.

Third, our data reflect the experience of two tertiary referral hospitals which may limit generalizability to settings with different patient demographics, health system structures or institutional protocols. Although management strategies were largely comparable across the two participating centers, some variation is inevitable. Furthermore, because this was a retrospective analysis, the choice of intravenous treatment was likely determined by physician preference. This introduces the potential for confounding by indication as clinicians might have reserved certain protocols for patients perceived to have a different clinical trajectory. Finally, as with all observational studies, residual confounding by unmeasured factors—such as psychosocial stress, pre-existing functional gastrointestinal symptoms or institutional bed-management pressures—cannot be fully excluded (23).

Future Research and Clinical Implications

Prospective studies with standardized assessment of B-vitamin status, randomized allocation of B-complex and systematic

evaluation of both neurological and short-term clinical outcomes are required to clarify the true benefit profile of B-vitamin supplementation in HG. Incorporating validated symptom scores and patient-reported outcomes into such trials would provide a more patient-centered understanding of treatment effects (24).

In parallel, large multicenter trials comparing different combinations of antiemetics and supportive interventions—including nutritional strategies, psychosocial support and multidisciplinary care models—could help explain how the substantial practice variation observed across institutions translates into real-world outcomes (25). Our findings may serve as hypothesis-generating data and help inform sample size calculations and outcome selection for these future investigations.

The marked reduction in the length of hospital stay observed in our crude analysis—decreasing from 2.62 ± 0.65 days to 1.47 ± 0.50 days with B-complex supplementation—highlights a significant area for clinical evaluation. While our multivariable model suggests these unadjusted benefits may be driven by selection factors rather than a direct therapeutic effect, the potential for improving hospital resource management through standardized protocols remains an important clinical consideration. If these findings regarding clinical efficiency can be validated in prospective, controlled settings, incorporating IV B-complex into standard HG protocols could potentially enhance healthcare efficiency. From a clinical perspective, the absence of an independent therapeutic effect of B-complex on LOS or early response in our cohort suggests that routine use of B-complex solely to accelerate recovery in women without clear risk factors for Wernicke encephalopathy requires careful justification. Instead, a more targeted strategy prioritizing high-risk patients for prophylactic thiamine and reserving routine B-complex supplementation for those with prolonged vomiting, poor nutritional status or other established risk markers may offer a more rational approach to the IV management of HG.

CONCLUSION

In summary, this large multicenter retrospective cohort study indicates that adding IV B-complex to standard supportive care for HG does not independently improve early clinical response or shorten LOS despite apparently favorable crude associations. Nevertheless, B-complex supplementation remains an essential component of HG management primarily for its role in neurological prophylaxis. Therefore, B-complex should be considered a routine part of HG treatment protocols, regardless of the specific antiemetic regimen used, to ensure comprehensive patient care and prevent long-term complications. These findings support a more targeted, evidence-based and patient-centered approach to HG management and underscore the need for high-quality prospective studies to refine current treatment algorithms.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that there is no financial support.

Ethical Approval
The study protocol received approval from the Harran University Clinical Research Ethics Committee (Date: September 01, 2025; Session No: 14; Approval No: HRÜ/25.14.04).

Informed Consent
Due to the retrospective study design and the use of anonymized patient data, the requirement for written informed consent was waived by the Ethics Committee.

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