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ORIGINAL ARTICLE

Evaluation of Terlipressin's Therapeutic Efficacy and Safety Profile in the Management of Intestinal Paralysis Among End-stage Liver Disease Patients

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ABSTRACT

Background: Intestinal paralysis is a common yet under-recognized complication in patients with end-stage liver disease (ESLD), leading to increased morbidity and hospital stay.

Objective: To evaluate the therapeutic efficacy and safety profile of Terlipressin in the management of intestinal paralysis among ESLD patients.

Methods: This prospective, observational study was conducted at Department of Gastroenterology Muhammad Teaching Hospital Peshawar during august 2021 to January 2023. A total of 52 adult patients (aged ≥18 years) with a confirmed diagnosis of end-stage liver disease and clinical features suggestive of intestinal paralysis were enrolled in the study. All patients received intravenous Terlipressin at a dose of 1 mg every 6 hours. The treatment duration ranged from 48 to 96 hours, adjusted based on individual clinical responses. The drug was administered under inpatient care with continuous monitoring of hemodynamic and renal parameters.

Results: The mean time to return of bowel sounds was 27.4 ± 9.2 hours, and spontaneous bowel movement occurred within 48 hours in 84.6% of patients. Abdominal distension resolved in 88.5%, and 78.8% tolerated oral intake by Day 4. Significant reductions were observed in abdominal girth ($p < 0.001$) and serum creatinine ($p = 0.042$), with a modest drop in serum sodium ($p = 0.032$). Minor adverse effects occurred in 17.3% of patients, with no major ischemic or cardiac events. Clinical success was achieved in 92.3% of cases without the need for surgical intervention.

Conclusion: It is concluded that Terlipressin offers a promising and safe therapeutic option for managing intestinal paralysis in ESLD patients. Its use is associated with early symptom resolution and improved clinical outcomes, warranting further investigation in larger, controlled trials.

Keywords: End Stage Liver Disease, Intestinal Paralysis, Terlipressin

INTRODUCTION

Intestinal paralysis, also referred to as intestinal pseudo-obstruction or adynamic ileus, is a frequently overlooked but clinically significant complication among patients with end-stage liver disease (ESLD). Choose functional impairment of gastrointestinal motility when no physical blockages exist and you will have intestinal paralysis. Patients with this condition face abdominal distension while experiencing bloating together with nausea alongside delayed bowel movements[1]. These patients develop worse portal hypertension and experience reduced nutritional capacity as well as reduced lifestyle quality. The decompensated liver function of ESLD drives multiple factors comprising abnormal autonomic regulation, blood vessel dilatation in the digestive system swollen intestinal walls, and elevated inflammatory cytokines and nitric oxide levels[2]. The treatment of intestinal paralysis through liver failure presents various challenges because the approach mainly focuses on supporting patients. The therapeutic use of prokinetic agents (e.g., erythromycin, neostigmine) and nasogastric decompression together with electrolyte balance adjustments provides inconsistent temporary resolution of the issue[3]. These treatments fail to tackle the source of intestinal dysmotility caused by the hemodynamic and inflammatory changes that occur in cirrhosis. The necessity for pharmacological measures that change the fundamental causes of the condition exceeds the requirement for symptomatic treatment methods[4]. This synthetic vasopressin analog Terlipressin shows multiple important effects for treating the hemodynamic complications that occur in advanced liver disease. By binding V1 receptors of vascular smooth muscle Terlipressin causes strong splanchnic vasoconstriction which shifts blood flow to optimize renal perfusion and strengthen systemic vascular resistance[5]. Its mechanisms of action have led to its adoption for treating the two critical ESLD complications which are hepatorenal syndrome and acute variceal haemorrhage[6]. New preclinical and clinical study data reveal Terlipressin has positive effects on intestinal movement through its ability to reduce blood congestion in the mesenteric area and relieve wall tissue swelling and normalize smooth muscle tension regulation by nitric oxide[7]. The secondary effects of Terlipressin make the drug suitable for treating intestinal paralysis. When used for treating paralytic ileus Terlipressin works by curing splanchnic vasodilation problems along with enhancing intestinal perfusion pressure which results in restored peristalsis functions[8]. Through its anti-inflammatory actions, Terlipressin demonstrates the capability to modify the intestinal barrier function which may decrease the potential risks of bacterial translocation experienced by spontaneous bacterial peritonitis (SBP)-prone patients with cirrhosis[9]. Research on Terlipressin's effectiveness for managing intestinal paralysis exists but it remains weak and scattered throughout studies. The research contains few direct assessments of Terlipressin's effects on bowel motility measurements and its capacity to dissolve ileus in liver disease patients with esophageal varices[10]. This population faces significant security risks because Terlipressin treatment can trigger heart-related adverse effects and lead to low sodium levels and tissue damage while putting these patients at risk for complications of swelling[11].

Objective: To evaluate the therapeutic efficacy and safety profile of Terlipressin in the management of intestinal paralysis among ESLD patients.

METHODOLOGY

This prospective, observational study was conducted at Department of Gastroenterology Muhammad Teaching Hospital Peshawar during august 2021 to January 2023. A total of 52 adult patients (aged ≥18 years) with a confirmed diagnosis of end-stage liver disease and clinical features suggestive of intestinal paralysis were enrolled in the study.

Inclusion Criteria:

- Adult patients (≥18 years) with documented ESLD.
- Clinical signs and symptoms of intestinal paralysis (e.g., absence of bowel sounds, abdominal distension, delayed or absent bowel movements for >48 hours).
- Radiological evidence of dilated, non-obstructed bowel loops on abdominal imaging (X-ray or CT scan).
- No mechanical obstruction as confirmed by imaging and clinical examination.
- Hemodynamically stable for Terlipressin administration.

Exclusion Criteria:

- Presence of mechanical intestinal obstruction or acute abdomen requiring surgical intervention.
- Severe cardiovascular disease or peripheral vascular disease contraindicating vasopressor use.
- Ongoing septic shock or uncontrolled infection.
- Pregnancy or lactation.
- Known hypersensitivity to vasopressin analogs.
- Patients with a history of bowel ischemia or prior bowel surgery altering normal motility.

Data Collection: All patients received intravenous Terlipressin at a dose of 1 mg every 6 hours. The treatment duration ranged from 48 to 96 hours, adjusted based on individual clinical responses. The drug was administered under inpatient care with continuous monitoring of hemodynamic and renal parameters. Supportive treatment included bowel rest, nasogastric decompression when indicated, correction of fluid and electrolyte imbalances, and avoidance of enteral feeding during the initial 24–48 hours. This standardization of supportive care allowed for clearer attribution of therapeutic outcomes to Terlipressin. Patients were monitored closely for changes in bowel function and systemic response. The primary efficacy endpoints included the time to return of bowel sounds, time to first bowel movement or passage of flatus, and resolution of abdominal distension. Additional markers of clinical improvement included tolerance of oral intake within five days and changes in abdominal girth. Radiological reassessment was performed in selected cases to observe resolution of bowel dilation. Secondary endpoints included total hospital stay and recurrence of symptoms within 14 days post-therapy. Safety evaluation included routine assessment of renal function through serum creatinine and urine output, serum sodium levels to monitor for hyponatremia, and continuous monitoring for adverse effects such as ischemia (e.g., digital cyanosis, chest pain), arrhythmias, or any new organ dysfunction. Clinical and laboratory data were collected using structured case report forms and entered into a secure electronic database.

Statistical Analysis: Data were analyzed using SPSS v17. Continuous variables such as time to symptom resolution and laboratory values were expressed as means with standard deviations or medians with interquartile ranges, depending on data distribution. A p-value less than 0.05 was considered statistically significant.

RESULTS

Data were collected from 52 patients, with a predominance of males (65.4%). The mean age of the participants was 54.2 years (±9.8), and the average MELD score was 23.7 (±4.5), reflecting advanced hepatic dysfunction. At baseline, the mean serum creatinine was 1.6 mg/dL (±0.3), and serum sodium averaged 131.2 mmol/L (±3.6), indicating mild hyponatremia. Clinical signs of intestinal paralysis were prominent, with 88.5% of patients presenting with absent bowel sounds and all patients (100%) experiencing no passage of stool or flatus for more than 48 hours.

The average time to return of bowel sounds was 27.4 ± 9.2 hours, and the first passage of flatus occurred at 35.6 ± 11.1 hours. A spontaneous bowel movement within 48 hours was achieved by 84.6% of patients, while 88.5% experienced resolution of abdominal distension by Day 3. Additionally, 78.8% of patients tolerated oral intake by Day 4. There was a significant reduction in abdominal girth (4.3 ± 1.7 cm, $p < 0.001$), and radiologic improvement in bowel dilation was observed in 85.7% of reassessed cases. The mean duration of hospital stay following treatment was 6.2 ± 2.1 days.

Table 1: Baseline Characteristics of the Study Population (N = 52)

Parameter	Value
Total patients	52
Male (%)	34 (65.4%)
Female (%)	18 (34.6%)
Mean age (years)	54.2 ± 9.8
Mean MELD score	23.7 ± 4.5
Baseline serum creatinine (mg/dL)	1.6 ± 0.3
Baseline serum sodium (mmol/L)	131.2 ± 3.6
Absent bowel sounds (%)	88.5%
No flatus/stool for >48 hours (%)	100%

Table 2: Therapeutic Efficacy Outcomes Following Terlipressin Administration

Outcome Measure	Result
Time to return of bowel sounds (hours)	27.4 ± 9.2
Time to first passage of flatus (hours)	35.6 ± 11.1
Spontaneous bowel movement within 48 hours	44 (84.6%)
Resolution of abdominal distension by Day 3	46 (88.5%)
Oral intake tolerated by Day 4	41 (78.8%)
Reduction in abdominal girth (cm)	4.3 ± 1.7 ($p <$ 0.001)
Radiologic improvement in bowel dilation (n = 28)	24 (85.7%)
Mean duration of hospital stay (days)	6.2 ± 2.1

Serum creatinine levels decreased from 1.6 ± 0.3 mg/dL to 1.4 ± 0.2 mg/dL ($p = 0.042$), reflecting enhanced renal perfusion. Although serum sodium levels declined slightly from 131.2 ± 3.6 mmol/L to 128.5 ± 4.1 mmol/L ($p = 0.032$), this change remained clinically manageable. Additionally, mean arterial pressure increased from 72.5 ± 6.4 mmHg to 78.9 ± 5.8 mmHg ($p = 0.018$), and daily urine output rose significantly from 980 ± 240 mL to 1280 ± 310 mL ($p = 0.027$), both indicating improved hemodynamic stability.

Table 3: Biochemical Parameters Before and After Terlipressin Treatment (N = 52)

Parameter	Baseline	Post-Treatment	p-Value
Serum Creatinine (mg/dL)	1.6 ± 0.3	1.4 ± 0.2	0.042
Serum Sodium (mmol/L)	131.2 ± 3.6	128.5 ± 4.1	0.032
Mean Arterial Pressure (mmHg)	72.5 ± 6.4	78.9 ± 5.8	0.018
Urine Output (mL/day)	980 ± 240	1280 ± 310	0.027

The progression of symptom resolution following Terlipressin administration showed consistent and steady clinical improvement over five days. By day 1, 28.8% of patients had regained bowel sounds, 13.5% had passed flatus or stool, and none had resumed oral intake. On day 2, 65.4% showed bowel sounds, 48.1% achieved bowel movement, and 23.1% tolerated oral intake. By day 3, 86.5% had bowel sounds, 78.8% had bowel movements, and 57.7% had resumed oral intake.

Table 4: Timeline of Symptom Resolution Over 5 Days

Day	Patients with Bowel Sounds (%)	Patients with Flatus/Bowel Movement (%)	Patients Resuming Oral Intake (%)
Day 1	15 (28.8%)	7 (13.5%)	0
Day 2	34 (65.4%)	25 (48.1%)	12 (23.1%)
Day 3	45 (86.5%)	41 (78.8%)	30 (57.7%)
Day 4	50 (96.1%)	48 (92.3%)	41 (78.8%)
Day 5	52 (100%)	52 (100%)	50 (96.1%)

DISCUSSION

The present study demonstrates that Terlipressin administration in patients with end-stage liver disease (ESLD) and intestinal

paralysis is associated with significant improvements in gastrointestinal motility and clinical outcomes, with an acceptable safety profile. Medical documentation reveals that 84% of patients recovered bowel sounds after 27.4 hours and develope bowel movements at 35.6 hours under Terlipressin therapy. Research evidence supports Terlipressin's mechanism whereby arterial constriction in the spleen improves blood flow to the intestine and decreases bowel tissue swelling. Cirrhosis patients develop excessive vasodilator production specifically nitric oxide which causes mesenteric congestion to slow down intestinal motility [12]. Terlipressin reversed vasodilation in the patients which probably contributed to the improvement of peristaltic functions. On Day 3 medical clinics observed distension resolution in 88.5% of patients and 80% of patients started eating orally by Day 4. The functional improvements revealed themselves through reduced hospital stays together with surgery-free outcomes that reached 92.3% of patients [13]. The study outcomes demonstrate that using Terlipressin as a bridge treatment might reduce the requirement for high-risk invasive procedures within patients who exhibit both bleeding disorders and weak nutritional status [14].

Most patients demonstrated a low incidence of security problems while receiving Terlipressin treatment. 17.3% of patients recorded small adverse events that encompassed digital cyanosis and abdominal cramping combined with transient bradycardia but these side effects resolved independently without medical intervention [15]. The safe administration of Terlipressin for non-variceal bleeding control was confirmed through the absence of bowel ischemia or arrhythmias when patients received proper medical observation [16]. The biochemical analysis showed Terlipressin improved serum creatinine values and mean arterial pressure levels despite modest findings because they supported previous research on hemodynamic effects. Although significant, the decline in sodium serum concentration presented acceptable clinical management because only two patients required dosage changes or medication stoppage because of moderate hyponatremia [17]. The diversity of cirrhosis etiologies represented in this cohort predominantly alcoholic and HCV-related suggests that Terlipressin's efficacy is likely independent of the underlying liver disease etiology. This is critical for generalizing the findings to broader clinical populations [18]. Despite these encouraging outcomes, several limitations should be acknowledged. The sample size, while sufficient for preliminary analysis, limits the generalizability of the findings. The study design was observational and lacked a control group, which precludes definitive causal conclusions. Additionally, longer-term outcomes such as recurrence rates and quality-of-life measures were not assessed beyond 14 days. Future randomized controlled trials are warranted to compare Terlipressin directly with other prokinetic agents or placebo in this patient population. Moreover, mechanistic studies exploring how Terlipressin modulates gut neurohormonal signaling in cirrhosis could enhance understanding of its therapeutic potential in gastrointestinal complications of ESLD.

CONCLUSION

It is concluded that Terlipressin is a safe and effective therapeutic agent in the management of intestinal paralysis among patients with end-stage liver disease. Its administration resulted in significant and timely improvements in gastrointestinal motility, resolution of clinical symptoms, and restoration of bowel function in the majority of patients. Moreover, its beneficial impact on hemodynamic stability and renal function supports its multifaceted role in managing decompensated cirrhosis-related complications.

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