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Systematic Review

Octreotide versus Terlipressin as Adjuvant to Endoscopic Variceal Band Ligation in Bleeding Oesophageal Varices: A Systematic Review and Meta-Analysis

Ahmed A. Sadeq [1], Noha Abou Khater [2], Farah Ahmed Issa [2] and Ahmed Al-Rifai [3,*]

[1] Department of Pharmacy, Shaikh Shakhbout Medical City, Abu Dhabi P.O. Box 11001, United Arab Emirates; ahmed.sadeq@hud.ac.uk
[2] Department of Medicine, Shaikh Shakhbout Medical City, Abu Dhabi P.O. Box 11001, United Arab Emirates; abukhater.nuha@gmail.com (N.A.K.); farahissa95@hotmail.com (F.A.I.)
[3] Department of Gastroenterology and Hepatology, Sheikh Shakhbout Medical City, Abu Dhabi P.O. Box 11001, United Arab Emirates
* Correspondence: doctor.alrifai@gmail.com

Abstract: Background: Acute variceal bleeding (AVB) is a critical complication of portal hypertension, contributing significantly to mortality worldwide. Pharmacological interventions, including terlipressin and octreotide, have evolved to manage AVB, yet consensus on their comparative effectiveness remains elusive. This study conducts a comprehensive systematic review and meta-analysis of randomized control trials (RCTs) comparing terlipressin and octreotide in the management of AVB, aiming to provide insights into their relative benefits. Methods: This study included RCTs with head-to-head comparisons of terlipressin and octreotide. The search strategy covered PubMed, Scopus, and Cinahl databases, and the included studies involved adult patients with confirmed AVB undergoing endoscopic variceal band ligation (EVBL). Results: Seven RCTs meeting inclusion criteria were included in the meta-analysis. The assessed outcomes were: achieving haemostasis within 24 h, rebleeding rate, and mortality rate. The pooled analysis revealed no statistically significant differences between terlipressin and octreotide in achieving haemostasis (OR: 1.30, $p = 0.23$), rebleeding rates at 5 days (OR: 0.7, $p = 0.23$), and mortality at 42 days (OR: 0.9, $p > 0.5$). Conclusion: This meta-analysis suggests that terlipressin and octreotide exhibit similar efficacy in reducing bleeding, rebleeding rates, and mortality when used as adjuvants to EVBL in AVB. Clinicians are encouraged to consider individual patient characteristics and the broader clinical context when choosing between these agents. Future research should focus on addressing existing evidence gaps and enhancing understanding of variables influencing EVBL outcomes.

Keywords: variceal bleeding; band ligation; octreotide; terlipressin; haemostasis

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1. Introduction

Acute variceal bleeding (AVB) is a critical complication of portal hypertension, often arising from cirrhosis or other liver diseases [1,2]. Portal hypertension causes dilation of the collaterals between the portal venous system and systemic venous system [3]. In addition, it causes arterial vasodilation of the splanchnic circulation (dilation of the blood vessels supplying the digestive organs in the abdomen such as liver, pancreas, spleen, and intestines) [3]. One of the major locations of these collaterals is the distal third of the oesophagus and proximal part of the stomach. Therefore, portal hypertension leads to oesophageal varices, but proximal varices can occur as well in conditions affecting extra-portal venous circuits [4–6]. According to Frank's modification of the Laplace law, the tension on the walls of blood vessels is dependent upon the diameter of the blood vessel and the pressure gradient across the walls (that is, the difference between pressure inside the varices and the oesophageal pressure) [7]. Portal hypertension leads to an increase

in both the diameter of the blood vessels and in the pressure at which blood flows in the varices; therefore, the tension on the walls of the blood vessels increases. This results in dilation of the blood vessels at the lower end of the oesophagus and proximal part of the stomach, which in turn increases the tension further [7]. This vicious circle can eventually culminate in rupture of the varices leading to AVB [3,7].

AVB remains a significant cause of mortality worldwide necessitating prompt and effective management strategies [8]. In one study, it was noted that the thirty-day death rate following an acute variceal bleed was between eleven and twenty percent, while rebleeding rates exceeded ten percent according to another study. In 2014, a post-hoc examination of data from the 2007 UK national audit of acute upper gastrointestinal bleeding was published, and these data state that in 212 hospitals over an eight-week period, 526 incidences of acute variceal haemorrhage were found, and mortality at 30 days was 15% overall [9].

Endoscopic treatment is the mainstay of management of AVB [2]. It requires attention to technique and the appropriate choice of therapy for a given patient at a given point in time [2]. Subjects must be monitored continuously after initiation of therapy for control of bleeding [2].

Over the years, along with revolutions in endoscopic therapy, pharmacological interventions have evolved as well, to address the challenge of controlling AVB. Terlipressin and octreotide have emerged as prominent vasoactive agents, both being widely used in clinical practice as adjuvants to endoscopic variceal band legation (EVBL) [10–13]. Terlipressin, a synthetic analogue of vasopressin (V), acts on V1 receptors to induce vasoconstriction in splanchnic vessels, thus reducing portal pressure and blood flow to varices [14]. On the other hand, octreotide, a synthetic somatostatin analogue, exerts its therapeutic effect by inhibiting the release of various vasoactive substances and reducing splanchnic blood flow [15]. Both agents have other indications than AVB; terlipressin is indicated in hepatorenal syndrome due to its benefit in improving renal blood flow [16–18], and it may increase survival rate when given to patients prior to liver transplantation [19], while octreotide is indicated in endocrine diseases, in addition to hepatorenal syndrome [20–22]. Terlipressin administration may result in adverse effects such as mesenteric blood flow reduction and ischemia of the heart, splanchnic, and skin [23,24]. On the other hand, octreotide could be associated with gastrointestinal disturbances and bradycardia [25,26]. In terms of cost effectiveness, there were conflicting findings on which agent is more cost-effective; however, more studies were in favour of terlipressin [27–30]. Consequently, numerous studies have compared the efficacy and safety of terlipressin and octreotide in the management of AVB [31–37].

A combination of endoscopic treatment with pharmacological treatment is better than either alone for active bleeding, and was associated with significant improvement in bleeding-related outcomes and survival advantage compared to EVBL alone [2]. While both terlipressin and octreotide have demonstrated efficacy in managing AVB and reducing rebleeding events and mortality when they are used as adjuvant to EVBL, there remains a lack of consensus on which agent provides superior outcomes. Existing studies have reported conflicting results regarding their comparative effectiveness, optimal dosing strategies, and safety profiles [38]. Few systematic reviews and meta-analyses have investigated the effect of several vasoactive drugs in EVB, such as terlipressin, octreotide, and other agents, but none of these studies included head to head comparison between octreotide and terlipressin in terms of achieving haemostasis, and reducing rebleeding and mortality [39–42]. One meta-analysis that was conducted in 2015, pooled the effect of several randomized control trials, including only two head-to-head studies comparing both agents, and concluded that there is no difference between the two agents in terms of efficacy [38].

Given the clinical relevance of this issue, a comprehensive and updated analysis comparing the efficacy of terlipressin versus octreotide in AVB is warranted. The present study aimed to address this gap by conducting a systematic review and meta-analysis of all available RCTs in the literature, to provide a more robust understanding of the relative

benefits of terlipressin and octreotide in the management of AVB in conjunction with EVBL. It is the only study that has included all RCTs, and only involved head-to-head comparison between terlipressin and octreotide. This research has the potential to inform clinical decision making and guide therapeutic choices for clinicians managing patients with variceal bleeding.

2. Materials and Methods

2.1. Study Registration

This study was registered in PROSPERO [43] (The International Prospective Register of Systematic Reviews) records under the code CRD42023457669.

2.2. Case Definition and Intervention

Acute variceal bleeding was confirmed among included studies when there is either bleeding from oesophageal or gastric varices visible at the time of endoscopy, or the presence of a blood clot over oesophageal or gastric varices, with no other endoscopically observed source of bleeding.

Endoscopic variceal band ligation (EVBL) is now primarily recommended for the endoscopic control of oesophageal variceal bleeding (EVB) in combination with vasoactive drugs [44–46]. In all of the included studies in this review, octreotide and terlipressin were compared with each other when they were used as adjuvants to EVB.

The terlipressin dose used in the included studies was 1–2 mg intravenously every 6 h for 3 days, while the octreotide dose was a 50 μg intravenous bolus followed by 50 μg/h as a continuous intravenous infusion.

2.3. Search Strategy

The PRISMA (Preferred Reporting Items for Systematic Review and Meta-analysis) criteria were followed for this systematic review and meta-analysis, which took into account an evidence-based collection of items for reporting systematic reviews and meta-analyses [47].

Three databases have been searched systemically. Those databases are PubMed, Scopus, and Cinahl. All articles that matched the search keywords were included for screening and review. The search strategy in this study followed the PIO (population, intervention, and outcome) model and the keywords used were P ((gastrointestinal OR oesophageal OR esophageal OR varices OR variceal) AND bleeding) AND I (terlipressin OR somatostatin OR octreotide OR vasopressor OR vasoconstrictor OR vasoactive) AND C (haemostasis OR hemostasis OR efficacy OR effective OR "bleeding control"). Table 1 presents the full search strategy.

Table 1. Search strategy.

Database	Search Within	Number of Results	Key Words
PubMed	All fields (Filter: Randomized Clinical Trials, English)	364	**P** ((gastrointestinal OR oesophageal OR esophageal OR varices OR variceal) AND (haemorrhage OR hemorrhage OR bleeding)) AND **I** (terlipressin OR somatostatin OR octreotide OR vasopressor OR vasoconstrictor OR vasoactive) AND **O** (haemostasis OR hemostasis OR efficacy OR effective OR "bleeding control")
Scopus	(Filter: TITLE-ABS-KEY, Medicine, Article, Journal, Final, English only)	811	
Cinahl	(Filter: Academic journals, All adults, English only)	94	

2.4. Study Selection

Two independent investigators (A. A. Sadeq and N. Abou Khater) screened the generated titles and abstracts with an aim to include articles that meet the inclusion criteria. Any disagreements or differences in articles' selection between the two investigators were resolved by discussions and consensus. For an article to be selected for further review and retrieval, it had to indicate a comparison of the efficacy in achieving haemostasis between

octreotide and terlipressin when used as an adjuvant to EVBL in AVB. We decided to include in our review all randomized control trials (RCTs) with head-to-head comparison between octreotide and terlipressin. Furthermore, those RCTs had to have been conducted on adult patients with EVB and have undergone EVBL and administered either octreotide or terlipressin in conjunction. We did not specify any period as we wanted to include all studies that met our inclusion criteria. Non-randomized control trials, observative studies, and studies conducted on different patient populations have been excluded. It should be noted that exclusion criteria did not omit results with high risk of bias. Inclusion and exclusion criteria assessment were carried out by two reviewers (A. A. Sadeq and N. Abou Khater).

2.5. Outcomes

The final articles selected for this review were discussed in detail by two reviewers (A. A. Sadeq and N. Abou Khater) and agreed upon independently and then by consensus. The study outcomes that we were looking for were: the rate of achieving haemostasis within 24 h after EVBL combined with either octreotide or terlipressin; mortality rate; and rebleeding rate after achieving haemostasis.

2.6. Data Extraction Process

The primary investigators established a standard data extraction form using Microsoft Word® (version 2403). The following data were collected for the included studies: author name; year of article publishing; country where the RCT was conducted; study objectives; sample size; study design; study outcomes; and findings. Data extraction was performed independently by two reviewers (A. A. Sadeq and N. Abou Khater) and then discussed and agreed upon by consensus.

2.7. Risk of Bias/Quality Assessment

All included articles were assessed for risk of bias using Version 2 of the Cochrane risk-of-bias tool (RoB2) for randomized control trials [48]. Based on the responses to the signalling questions, an algorithm generated a proposed judgment regarding the risk of bias resulting from each area as 'Low risk of bias', 'High risk of bias', or 'Some concerns'. The overall risk of bias generally corresponds to the worst risk of bias in any of the domains. The risk of bias assessment was performed by two investigators (A. A. Sadeq and F. A. Issa) independently, and any differences were resolved by discussion.

2.8. Statistical Analysis

We used SPSS software version 28.0.1.1 (15) to perform the analyses with a random-effects model to pool and evaluate data from eligible studies which reported the same outcomes. Pooled estimates were represented as a forest plot with a 95 percent confidence interval (CI) range for the odds ratio. The percentage of overall variation that can be attributable to between-study heterogeneity is determined by the I_2 statistic, which was used to examine heterogeneity. An I2 value of <50% represents no statistical heterogeneity among studies. Finally, we created funnel plots to examine the potential for small study effects, one of which is publication bias.

3. Results

3.1. Search Results

Figure 1 is a flow diagram of the process of study selection. A total of 1251 studies were identified in the three data bases: PubMed, Scopus, and Cinahl. Eighty-six duplicated articles were removed and 1165 were eligible for title screening. After screening retrieved abstracts, forty-one studies were fully retrieved. After excluding those which did not meet inclusion criteria, seven articles met study inclusion criteria and outcomes, and were included in this review.

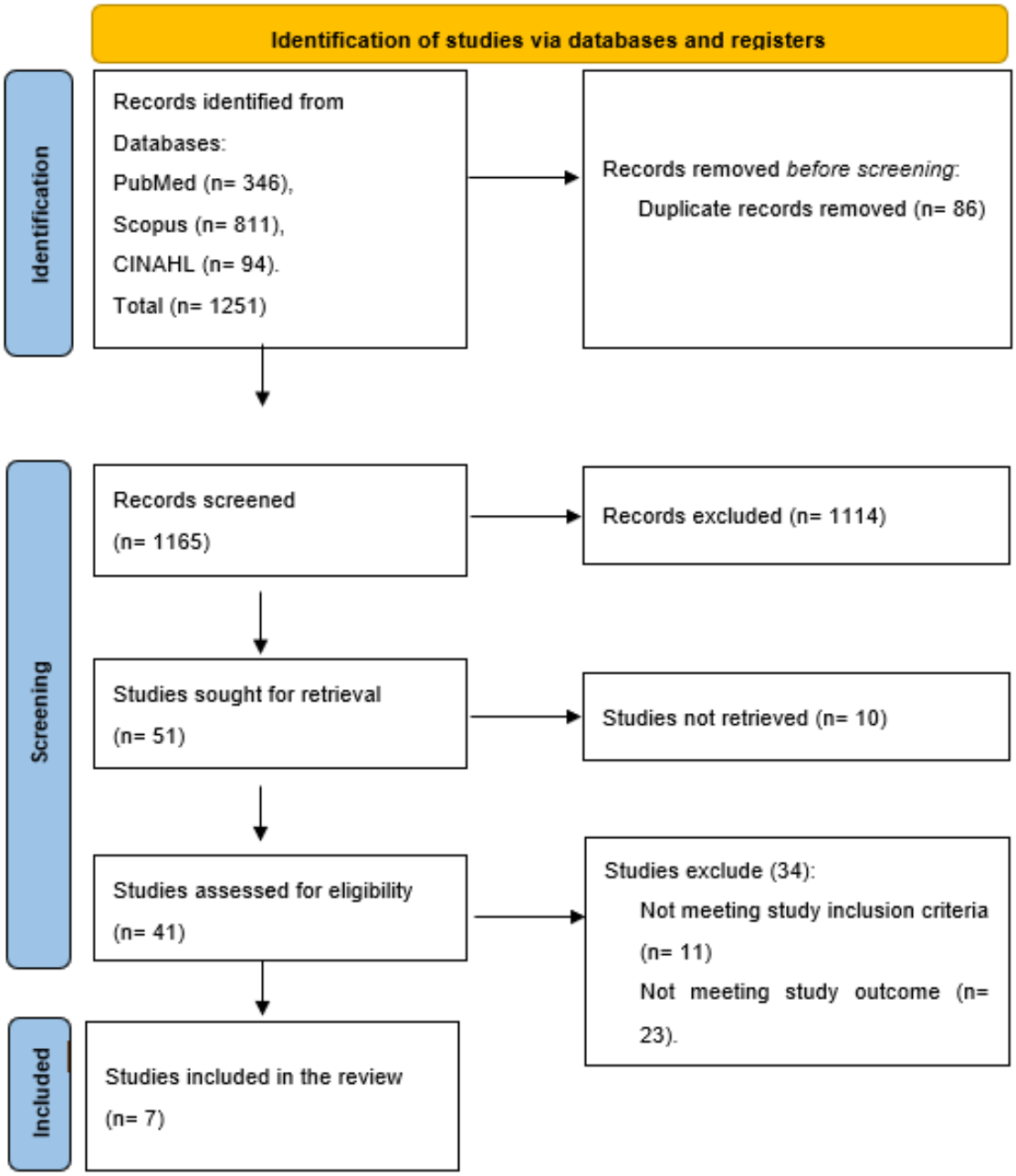

Figure 1. PRISMA flow diagram of the process of study selection.

Table 2 represents a summary of the seven included studies in this review [31–36]. The overall number of patients are 660 and 661 in the terlipressin arm and in the octreotide arm, respectively. All of the included studies are randomized control trials, with six being open label [31–33,35–37] and one study being double blinded [34].

Table 2. Summary of included articles.

Author, Year, Country	Objective	Study Design	Sample Size	Outcomes	Findings
Asad et al. 2014 [31] Pakistan.	To compare the efficacy and safety of terlipressin versus octreotide as an adjuvant therapy to EVBL in patients with EVB.	Randomized control trial. Open label study.	terlipressin: 40 octreotide: 40	Rate of achieving haemostasis within 24 h. Five-day and 30-day rebleeding. Five-day and 30-day mortality.	**Rate of achieving haemostasis** **terlipressin:** 97.5% (39/40 patients) **octreotide**: 87.5% (35/40 patients) $p > 0.5$ **Rebleeding rates at 5 days:** **terlipressin** 5% (2/40 patients) **octreotide:** 7.5% (12/43 cases) $p > 0.5$ **Rebleeding rates at 30 days:** **terlipressin** 10% (4/40 patients) **octreotide:** 10% (4/40 patients) $p > 0.5$ **Mortality rate at 5 days** **terlipressin:** 5% (2/40 patients) **octreotide:** 7.5% (3/40 patients) $p > 0.5$ **Mortality rate at 30 days** **terlipressin:** 10% (4/40 patients). **octreotide:** 12.5% (5/40 patients). $p > 0/05$.
Cho et al. 2006 [32] Korea	To compare the efficacy and safety of terlipressin versus octreotide as an adjuvant therapy to EVBL in patients with EVB.	Randomized control trial. Open label study.	terlipressin: 43 octreotide: 45	Rate of achieving haemostasis within 24 h. Five-day and 42-day rebleeding. Forty two-day mortality.	**Rate of achieving haemostasis** **terlipressin:** 98% (42/43) **octreotide:** 96% (43/45) $p > 0.05$ **Rebleeding rate at 5 days** **terlipressin:** 12% (5/43) **octreotide:** 9% (4/45 cases) $p > 0.05$ **Rebleeding rate at 42 days** **terlipressin:** 28% (6/43) **octreotide:** 24% (11/45 cases), $p > 0.05$ **Mortality rate at 42 days** **terlipressin**: 14% (6/43) **octreotide: 18**% (8/45) $p > 0.05$
Seo et al. 2014 [33] Korea	To evaluate the control of bleeding, prevention of rebleeding, and survival during 5 days of treatment when comparing terlipressin versus octreotide as adjuvant therapy to EVBL in patient with EVB.	Randomized control trial. Open label study.	terlipressin: 261 octreotide: 260	Rate of achieving haemostasis within 24 h. Five-day rebleeding. Five-day and 42-day mortality.	**Rate of achieving haemostasis.** **terlipressin:** 90% (234/261) **octreotide:** 87% (227/260) $p > 0.05$ **Rebleeding rate at 5 days** **terlipressin:** 3% (8/261) **octreotide:** 4% (10/260) $p > 0.05$ **Mortality rate at 42 days** **terlipressin:** 13% (34/261) **octreotide:** 12% (30/260) $p > 0.05$

Table 2. *Cont.*

Author, Year, Country	Objective	Study Design	Sample Size	Outcomes	Findings
Abid et al. 2009 [34] Pakistan	To compare the efficacy and safety of terlipressin versus octreotide as an adjuvant therapy to EVBL in patients with EVB.	Randomized control trial. Double blinded study.	terlipressin: 163 octreotide: 161	Rate of achieving haemostasis within 24 h. Mortality within hospital stay.	**Rate of achieving haemostasis** **terlipressin:** 96.9% (158/163) **octreotide:** 99.4% (160/161) $p > 0.05$ **Mortality (at any time)** **terlipressin:** 8% (9/163) **octreotide:** 9% (7/161) $p > 0.05$
Asif et al. 2020 [35] Pakistan	To compare rebleeding rates of terlipressin versus octreotide as an adjuvant therapy to EVBL in patients with EVB.	Randomized control trial. Open label study.	terlipressin: 50 octreotide: 50	Three-day rebleeding	**Rebleeding at 3 days** **terlipressin**: 8% (4/50) **octreotide**: 28% (14/50) $p < 0.05$
Adarsh et al. 2009 [36] Pakistan	To compare the efficacy and safety of terlipressin versus octreotide as an adjuvant therapy to EVBL in patients with EVB.	Randomized control trial. Open label study.	terlipressin: 69 octreotide: 68	Rate of achieving haemostasis within 24 h. Forty two-day rebleeding. Forty two -day mortality.	**Rate of achieving haemostasis** **terlipressin:** 81% (56/69) **octreotide:** 75% (51/68) $p > 0.05$ **Rebleeding at 42 days** **terlipressin:** 16% (11/69) **octreotide:** 27% (18/68) $p > 0.05$ **Mortality at 42 days** **Terlpressin:** 10% (7/69). **octreotide:** 18% (12/68) $p > 0.05$
Kim et al., 2005 [37] Korea	To compare the efficacy and safety of terlipressin versus octreotide as an adjuvant therapy to EVBL in patients with EVB.	Randomized control trial. Open label study.	terlipressin: 36 octreotide: 37	Rate of achieving haemostasis within 24 h. Forty two-day rebleeding. Forty two-day mortality.	**Rate of achieving haemostasis** **terlipressin:** 92% (33/36) **octreotide:** 85% (35/37) $p > 0.05$ **Rebleeding at 42 days** **terlipressin:** 5.5% (2/36) **octreotide:** 8.1% (3/37) $p > 0.05$ **Mortality at 42 days** **Terlpressin:** 2.8% (1/36). **octreotide:** 5.4% (2/37) $p = 0.572$

3.2. Quality Assessment

Figure 2 presents the quality assessment of included studies using Version 2 of the Cochrane risk-of-bias tool (RoB2) for randomized control trials. Our quality assessment revealed three studies were at 'low-risk of bias' [32–34], two studies had 'some concerns' [31,37], and two studies scored 'high-risk of bias' [35,36].

3.3. Outcomes

3.3.1. Achieving Haemostasis within 24 h

Six out of seven articles shared the same outcome of achieving haemostasis within 24 h after administering octreotide or terlipressin as an adjuvant to EVBL [31–34,36,37], and the difference in the outcome between the two medications in each individual study was statistically insignificant. The pooled odds ratio for achieving haemostasis from all those six articles resulted in an insignificant difference between octreotide and terlipressin (OR: 1.30; 95% confidence interval 0.85, 2.00; $p = 0.23$), as shown in Figure 3.

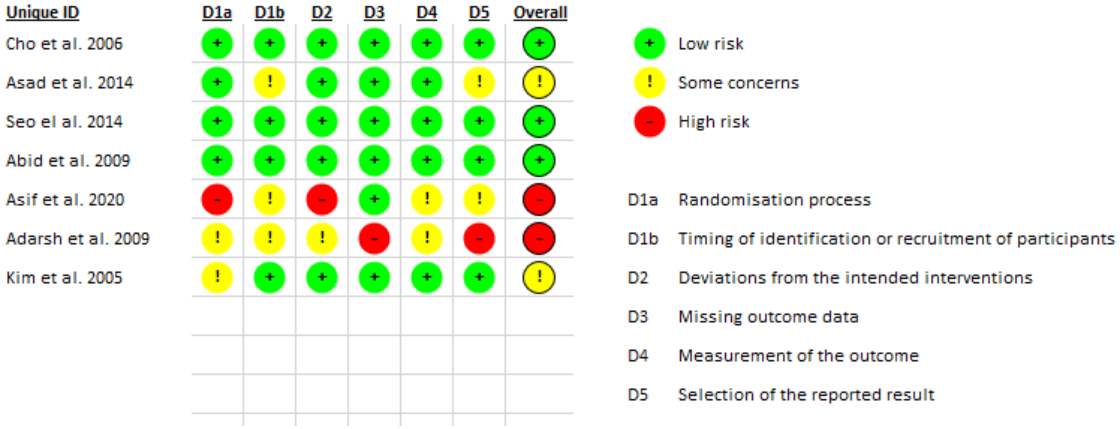

Figure 2. RoB2 quality assessment of the included articles. Citations for the references: Cho et al. 2006 [32]; Asad et al. 2004 [31]; Seo et al. 2004 [33]; Abid et al. 2009 [34]; Asif et al. 2020 [35]; Adarsh et al. 2009 [36]; Kim el tal. 2005 [37].

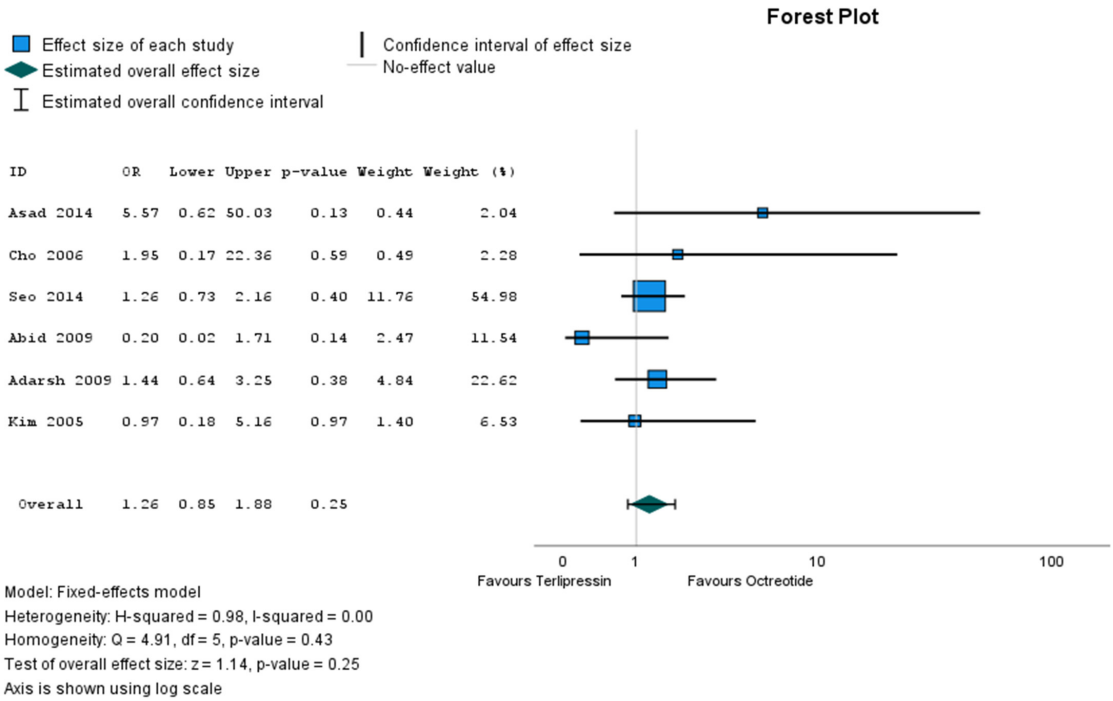

Figure 3. Pooled rate of achieving haemostasis within 24 h post EVBL. Citations for the references: Cho et al. 2006 [32]; Asad et al. 2004 [31]; Seo et al. 2004 [33]; Abid et al. 2009 [34]; Adarsh et al. 2009 [36]; Kim el tal. 2005 [37].

3.3.2. Rebleeding after Achieving Haemostasis

The rate of rebleeding after achieving haemostasis with octreotide or terlipressin in conjunction with EVBL was measured in all included articles but at different timings, as three articles measured rebleeding at 5 days [31–33], and three articles at 42 days [32,36,37], and all individually showed insignificant difference between both agents. On the other hand, one article reported rebleeding at 3 days and concluded that octreotide resulted in significantly higher rebleeding rates compared to terlipressin ($p < 0.05$) [35]. The pooled odds ratio for rebleeding at 5 days showed an insignificant difference (OR: 0.57; 95% confidence interval 0.17, 1.96; $p = 0.38$), as shown in Figure 4.

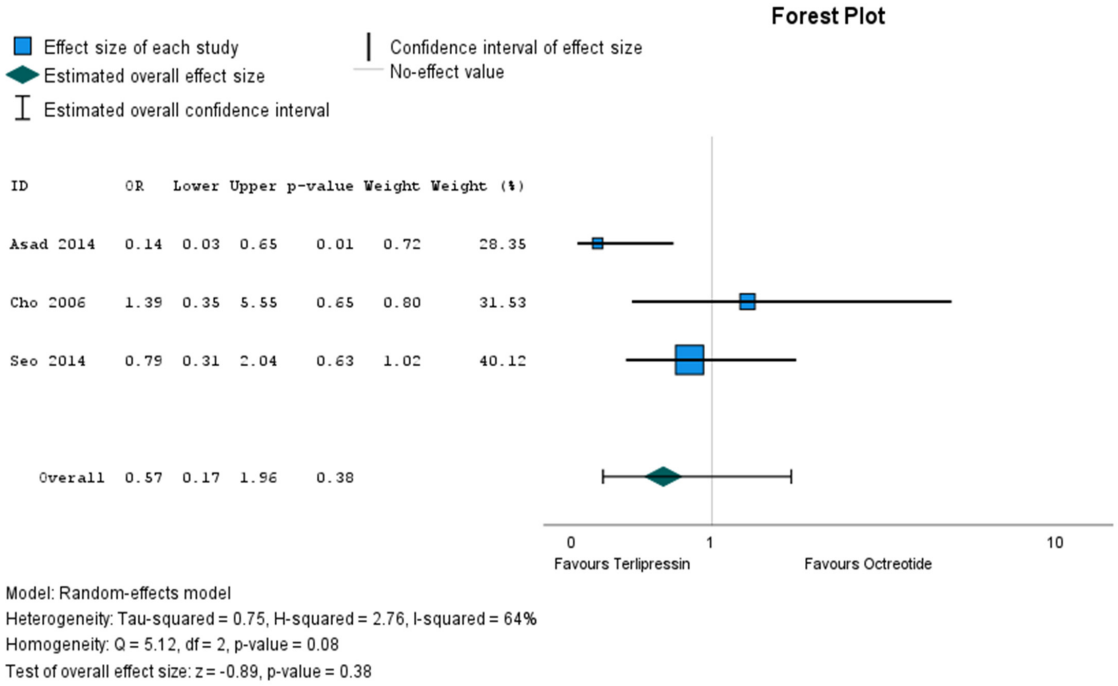

Figure 4. Pooled rebleeding rate at 5 days post EVBL. Citations for the references: Cho et al. 2006 [32]; Asad et al. 2004 [31]; Seo et al. 2004 [33].

3.3.3. Mortality

Mortality difference was another outcome that was also measured by six articles at different timings after administration of octreotide or terlipressin [31–34,36,37]: Four articles at 42 days [32,33,36,37], one article at 5 days and at 30 days [31], and one article did not measure mortality at a specific day [35]. The difference in mortality between octreotide and terlipressin in those articles individually was always statistically insignificant, and by pooling the odds ratio of mortality at 42 days, the difference was statistically insignificant, too (OR: 0.9; 95% confidence interval 0.54, 1.49, $p > 0.5$), as shown in Figure 5.

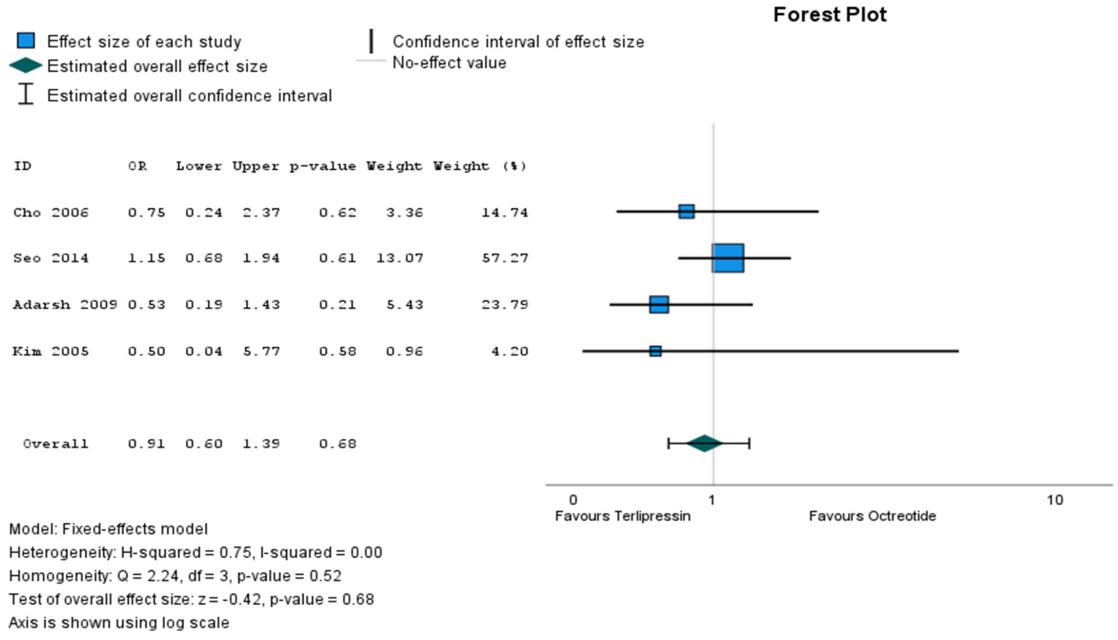

Figure 5. Pooled mortality rate at 42 days post EVBL. Citations for the references: Cho et al. 2006 [32]; Seo et al. 2004 [33]; Adarsh et al. 2009 [36]; Kim el tal. 2005 [37].

3.4. Funnel Plots

To evaluate for publication bias risk, a bias assessment in the form of funnel plots has been conducted for each of the three outcomes, as shown in Figure S1.

4. Discussion

Our systematic review and meta-analysis set out to assess the comparative effectiveness of terlipressin and octreotide as adjuvants to endoscopic variceal band ligation in terms of controlling bleeding, rebleeding rates, and overall mortality on patients with acute variceal bleeding. In view of the small number of articles comparing both agents, and in lights of the insignificant results concluded in those studies, this systematic review and meta-analysis was performed to obtain stronger evidence after pooling data from all head-to-head randomised control trials comparing octreotide to terlipressin.

Seven articles were included, and all of them are RCTs that share similar outcomes. The quality assessment of those articles revealed that three out of seven studies are at low risk of bias, while two have some risk, and two articles have some concerns regarding their bias risk. The overarching finding of our study indicate that the differences in the three critical outcomes (achieving haemostasis, rebleeding, and mortality) between terlipressin and octreotide are statistically insignificant.

Terlipressin and octreotide did not significantly differ in their capacity to control bleeding in EVB patients undergoing EVBL, according to our meta-analysis. This is consistent with the increasing amount of data indicating that both medications are equally effective in achieving haemostasis [31–34,36,37,49,50]; however, this is in contrast to one meta-analysis, conducted in 2018, which concluded that terlipressin had a significantly inferior control of bleeding compared with octreotide [51]. Therefore, our results highlight how practitioners should choose between terlipressin and octreotide depending on patient tolerance and institutional preferences. One should also bear in mind that the main factors impacting immediate control of variceal bleeding are the technique, efficacy, and complications of EVBL itself.

There was no discernible difference in our analysis of rebleeding rates after EVBL with terlipressin or octreotide supplementation. Although different viewpoints about rebleeding outcomes have been reported in the literature [31–33,35–37,52], our thorough analysis confirms that neither terlipressin nor octreotide clearly offers an advantage over the other when it comes to preventing recurrent bleeding. Our finding was in line with another meta-analysis conducted in 2015 where the combined odds ratio (OR) of 0.87 [95% confidence interval (CI) 0.51, 1.50] indicated that there was no difference in the rebleeding rate between patients [38].

Similarly, terlipressin and octreotide did not differ significantly in terms of mortality when examined in our investigation, and that was the case in multiple studies [31–34,36,37]. This highlights the relative safety of both treatments in promoting patient survival after EVBL. No systematic review and/or meta-analysis has investigated mortality as an outcome when comparing both agents. It is imperative to recognize that mortality is subject to multifactorial influences, such as the severity of underlying liver disease and comorbidities, which may persist beyond the initial post-procedural period.

The clinical implications of our findings are significant. Since both agents are widely available nowadays along with endoscopic intervention, clinical implications and preferential outcomes are always an area to question in clinical practice. Our study looked at the main potential preferential differences in terms of efficacy of both agents and found no significant difference in outcomes, which indicates that factors other than their ability to reduce bleeding, rebleeding rates, and mortality should be taken into account when choosing between terlipressin and octreotide. When making a decision, considerations such as patient-specific characteristics, cost-effectiveness, and adverse event patterns should be carefully considered.

Though we endeavoured to perform a thorough meta-analysis, there are a few limitations that should be taken into account. Possible explanations for the reported lack of

significance include heterogeneity among the included studies. Each study had its unique specifications in inclusion and exclusion criteria, as some studies maintained strict criteria for inclusion while others were far looser; however, we ensured that the selected studies fitted, within acceptable range of inclusion criteria, our research question and did not deviate from guideline-oriented clinical practice. In addition, the insignificant result could be due to the fact that all included studies have reported insignificant conclusions for most of the outcomes. Furthermore, there were differences in the quality of evidence between the studies, which could have affected how strong our results were. Finally, the number of included trials may have been relatively low, but we included all the trials that met our inclusion criteria, and we left the date open.

5. Conclusions

In conclusion, our meta-analysis suggests that when used as EVBL adjuvants, terlipressin and octreotide show similar efficacy in reducing bleeding, rebleeding rates, and mortality. When choosing between these agents, clinicians are advised to take the individual patient's characteristics into account, as well as cost-effectiveness, adverse event patterns, and the larger clinical context. Subsequent investigations ought to concentrate on filling in the current gaps in the evidence and improving our comprehension of the complex variables affecting EVBL outcomes.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/gastroent15020028/s1, Figure S1: Funnel plots measuring publication bias for outcomes.

Author Contributions: Conceptualization, all authors.; methodology, A.A.S. and N.A.K.; software, A.A.S.; validation, A.A.S. and A.A.-R.; formal analysis, A.A.S. and F.A.I.; resources, A.A.S., N.A.K. and A.A.-R.; writing—original draft preparation, A.A.S. and N.A.K.; writing—review and editing, all authors; supervision, A.A.-R.; project administration, all authors. All authors have read and agreed to the published version of the manuscript.

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