Use of prothrombin complex concentrates in liver transplantation: a systematic review and meta-analysis

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Background: Liver transplantation (LT) is often associated with high transfusion requirements. Fresh frozen plasma (FP) is commonly used despite inconsistent efficacy and safety data. Prothrombin complex concentrate (PCC) is increasingly utilized as an alternative, but its role in LT remains uncertain. This systematic review and meta-analysis evaluates the efficacy and safety of PCC in LT.

Methods: The review was registered with PROSPERO (CRD42024561866). A comprehensive search of MEDLINE, Embase, Cochrane. Studies involving adults undergoing LT that reported PCC use in relation to clinical outcomes were included. Random-effects models were used to estimate pooled effects.

Results: Eight studies were included, all retrospective. Among studies reporting PCC exposure specifically, 392 out of 1901 patients (21%) received PCC. Patients receiving PCC had worse preoperative coagulopathy, higher Model for End-Stage Liver Disease scores, and more comorbidities. Transfusion volumes of red blood cells (RBC), plasma, and platelets were comparable between PCC-exposed and non-exposed patients. However, the use of viscoelastic testing (VET)-based algorithms incorporating PCC, compared to usual care, was associated with reduced odds of RBC transfusion (odds ratio [OR] 0.53, 95% CI 0.32–0.86) and FP transfusion (OR 0.35, 95% CI 0.13–0.92), but not platelet transfusion. Safety outcomes were largely influenced by one large study in which PCC was used as high-dose rescue therapy and was associated with increased thrombotic events.

Conclusions: No randomized trials directly compare PCC and FP in LT. Based on available observational data, the efficacy and safety of PCC appear comparable to FP. PCC, particularly when integrated into VET-guided transfusion algorithms, may reduce RBC and FP transfusions. Higher-quality randomized trials are needed to definitively assess the efficacy and safety of PCC for managing coagulopathic bleeding in liver transplantation.

Major Limitations Identified:

1. Dominant Influence of a Single, Confounded Study: The overall meta-analysis results, especially regarding safety, are disproportionately driven by the large retrospective study by Dehne et al. The validity of this study's conclusion—that factor concentrate (PCC/fibrinogen) use increases thrombosis and mortality—is highly questionable due to severe baseline imbalances and unmeasured confounding:

2. Significant Patient Risk Disparity: The factor concentrate group had a higher BMI, significantly higher MELD scores, and a much greater proportion of patients transplanted under "high urgency" status. These patients likely had multi-organ failure, which itself carries a high inherent mortality risk.

3. Lack of Critical Data: The study fails to report Donor Risk Index (DRI). Given that German centers in the studied era (2004-2017) frequently accepted organs with high DRI (>1.5) in more than 63% of the cases and DRI > 2 in 23% of the cases (Schlitt, Z Gastroenerol 2011), this is a major unaccounted confounder for graft outcomes and thrombosis.

4. Contradictory Transfusion Practice: The factor concentrate group received nearly double the amount of FFP (mean 24 units vs. 13 units). Since FFP itself is a known risk factor for volume overload and thromboembolic complications, it is impossible to disentangle the effects of PCC from the substantial FFP exposure. The rationale for concurrent high-volume FFP use in a cohort also receiving targeted factor concentrates is not explained.

5. Conclusion: The meta-analysis's findings are compromised by heterogeneous and often suboptimal PCC application, and are heavily skewed by a single study with critical confounding variables. The reported association between PCC and adverse outcomes is more likely explained by the greater baseline illness severity, high-risk donor organs, and excessive concomitant FFP transfusion in the PCC group, rather than by PCC itself. This underscores the urgent need for prospective, protocol-driven studies where PCC is used judiciously within VET-based algorithms and not as an unguided rescue therapy.