Selected Summary

Transfusion strategy in patients with traumatic brain injury

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SUMMARY

The effect of a liberal transfusion strategy when compared with a restrictive one on outcomes in critically ill patients with traumatic brain injury (TBI) is still unclear. In this study, adults with moderate

and severe TBI (Glasgow Coma Scale [GCS] score 3–12) with concomitant anaemia (haemoglobin [Hb] <10 g/dl) were randomized to receive packed red cells via a liberal strategy (transfusions at Hb \leq 10 g/dl) or a restrictive one (transfusions at Hb \leq 7 g/dl). A total of 742 patients were included, with 371 assigned to each cohort. The median Hb level in the intensive care unit (ICU) was 10.8 g/dl in the liberal strategy group and 8.8 g/dl in the other group.

Cohorts were compared on the basis of occurrence of an unfavourable outcome assessed by Extended Glasgow Outcome Scale Score (GOS-E), designated as the primary outcome. It was dichotomized as a GOS-E score \leq 4. Secondary outcomes were mortality, functional independence, quality of life and depression at 6 months follow up. Analysis of the primary outcome included 722 patients. An unfavorable GOS-E was seen in 249 of 364 patients (68.4%) in the liberal group and in 263 of 358 (73.5%) in the restrictive one (adjusted absolute difference, restrictive strategy v. liberal strategy, 5.4 percentage points; 95% confidence interval: -2.9 to 13.7). The liberal approach was associated with higher scores on some but not all of the scales measuring functional independence and quality of life. No association was established between the transfusion strategy and mortality or depression. In both groups around 8.4% of patients had venous thromboembolic events while acute respiratory distress syndrome (ARDS) was seen in 3.3% of the liberal and 0.8% of the restrictive group. Therefore, in this study, a liberal transfusion strategy did not lower the probability of a poor neurological outcome at 6 months in critically ill patients with TBI and anaemia.

COMMENTS

The cut-off haemoglobin values indicating the need of blood transfusion in TBI has been a matter of debate. The TRICC (Transfusion Requirements in Critical Care) trial¹ compared restrictive and liberal transfusion strategies in ICU patients. It was not limited to TBI patients. No overall difference in 30-day mortality was seen when the transfusion Hb threshold was kept at either 7 or 10 g/dl (18.7% v. 23.3%). However, upon subgroup analysis, those patients who were less acutely ill had favourable mortality rates with restrictive threshold. Similarly, when considering patients with clinically important cardiac disease although the mortality rates with restrictive strategy were lower (20.5% v. 22.9%), significance was not achieved.

McIntyre *et al.*² compared clinical outcomes in patients with moderate or severe TBI who were transfused for a Hb <7 g/dl (restrictive threshold; goal of 7–9) at presentation or 10 g/dl (liberal threshold; goal of 10–12) at presentation. They found a significantly higher rate of thromboembolic events in the liberal threshold group but no significant difference in other outcomes. There was no significant difference in 30-day mortality in the liberal arm compared with the restrictive one. The rates of multi-organ dysfunction syndrome and length of ICU stay were comparable in both groups.

However, Gobatto *et al.*,³ favoured a liberal transfusion strategy. A higher rate of favorable outcomes and lower rates of mortality and post-traumatic vasospasm as measured by middle cerebral artery doppler, were seen with a transfusion threshold of 9 g/dl (liberal) compared to 7 g/dl (restrictive) in their study.

Another single-center retrospective analysis⁴ compared outcomes at initial transfusion thresholds between 7 and 10 g/dl, for TBI patients with abnormal head CT scan. They found that both the initial presenting Hb and the lowest Hb during the ICU stay were significant predictors of an unfavourable outcome. More severe levels of anaemia predicted a poorer GCS score and also a greater injury severity score. However, blood transfusion at Hb thresholds of 9 or 10 g/dl were associated with poorer outcomes when compared with lower cut-offs. Hence a transfusion threshold of 8 g/dl was recommended in their study.

Another multi-centre study of >1100 patients⁵ compared the Hb transfusion thresholds in patients with TBI with GCS <8, and showed that patients who were transfused at a Hb threshold <10 g/dl had worse 28-day survival and ARDS-free survival rates compared to patients who were transfused with Hb of 7–10 g/dl or <7 g/dl. When the Hb was kept >10 g/dl the probability of organ dysfunction events increased by 0.45 with each unit of blood transfused.

Hence, in reference to all the above studies it can be concluded that the larger multicentric randomized controlled trials (RCTs) have shown equivocal mortality rates and clinical outcomes when comparing restrictive versus liberal transfusion strategy. However, subgroup analysis in most RCTs and the retrospective study,⁴ have shown the potential benefit of restrictive strategy especially with regards to lower incidence of thromboembolic complications, cardiovascular overload and transfusion-related acute lung injury in the restrictive versus liberal groups. On the contrary, the upside of liberal transfusion as observed by Gobatto et al.,3 stems from better oxygen carrying capacity of blood and reduced rates of post-traumatic vasospasm in the liberal transfusion groups. Interestingly the beneficial effect of liberal transfusion was observed with a lower transfusion threshold of 9 g/dl compared to 10 g/dl used in other studies. There is growing evidence suggesting that an intermediate threshold between 7 and 9 g/dl, may be worth investigating. In conclusion, a marginally lower transfusion threshold Hb of 7-9 g/dl may be kept in patients with moderate to severe TBI patients in critical care settings, although this decision needs to vary on a case-tocase basis especially with concomitant comorbid conditions such as coronary artery disease and polytrauma. However, more studies are needed to further analyze and formulate a definitive hypothesis and guidelines on this topic.

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