

Study Protocol for a Systematic Review and Meta-analysis of Goal Directed Intra-Operative Transfusion Protocols Guided by Viscoelastic Methods and Perioperative Outcomes in Children

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Abstract

Back ground: Transfusion can be necessary in certain critical situations however like any other medical treatment it can be associated to adverse side effects like transfusion related acute injury and transfusion associated circulatory overload. Transfusion has been found to be a factor of mortality and morbidity in critical ill and surgical adult and paediatric patients. It has been evidenced in adult patients that when point of care methods or viscoelastic haemostatic assays were used to guide transfusion in haemorrhagic surgery, outcome in terms of mortality and morbidity was reduced. In children studies have shown that when viscoelastic haemostatic assays were applied to guide blood product administration in haemorrhagic surgery, transfusion with red blood cells was diminished but it has not been demonstrated that outcome was improved. This study was undertaken to analyse the impact of viscoelastic haemostatic assays on outcome in the paediatric surgical population.

Methods: A systematic review and meta-analysis of randomised and non randomised starting in January 2019 until June 2019. Statistical analysis will be realised with RevMan 5.3 software.

Results are expected by June 2019.

Conclusion: This protocol was realised to describe the systematic review and meta-analysis which will be undertaken to clarify the impact on outcome of transfusion protocols using viscoelastic haemostatic assays in haemorrhagic surgery in children.

Keywords: Transfusion; Viscoelastic Haemostatic Assays; Children; Outcome

Introduction

Transfusion can be a necessary therapy in critically ill patients. However, like any other medical treatment it can be related to some side effects in critical patients such as TRALI (transfusion related acute lung injury), TACO (transfusion associated circulatory overload) [1,2]. Studies in paediatric surgical patients and critical paediatric patients have shown that transfusion was an independent factor of morbidity [3]. Are there any means to reduce transfusion or to improve transfusion protocols in order to reduce patient exposure to blood products and thus diminish morbidity? The European Society of Anaesthesiology has published previously guidelines concerning the use of viscoelastic methods to guide transfusion and reduce blood loss in haemorrhagic surgeries [4]. A recent Cochrane systematic

review and meta-analysis demonstrated that when viscoelastic methods are used to guide transfusion in haemorrhagic surgery in adults, mortality and morbidity were reduced [5].

In children, studies in craniosynostosis, cardiac surgery, hepatic transplantation have shown that when blood product administration was guided by these methods, packed red blood cells, platelets units and fresh frozen plasma transfusion was reduced [6-11].

Transfusion rates in paediatric haemorrhagic interventions varies according to the type of surgery: in craniosynostosis surgery it is between 17 - 45% [12], in scoliosis surgery it varies between 1.7% (idiopathic scoliosis), 36% (neuromuscular scoliosis) [13], in paediatric hepatic transplantation it is 31% [14] and in polytrauma patients 35% [15].

This study was undertaken to analyse if transfusion protocols guided with viscoelastic methods in haemorrhagic paediatric surgery reduce mortality, morbidity and length of hospital stay.

How the intervention might work?

When blood product administration is integrated in a protocol using viscoelastic methods, transfusion will be better targeted thus reducing the risk of administering other blood components which may not be necessary and minimising or diminishing transfusion related morbidity.

Why it is important to do this review?

In adults it is well established and evidenced that using these methods in haemorrhagic surgeries reduces morbidity and mortality. In children this has not yet been demonstrated.

Objectives of the Study

- To demonstrate whether intraoperative transfusion protocols using viscoelastic methods reduces perioperative morbi-mortality (primary outcome) (morbidity is defined as complications defined as organ failure or organ dysfunction and infections) in the paediatric surgical population.
- To demonstrate whether intraoperative transfusion protocols using viscoelastic methods reduces the intraoperative and postoperative amount and quality of blood products administered and the amount of blood loss intraoperatively and postoperatively (secondary outcomes).
- To demonstrate whether intraoperative transfusion protocols using viscoelastic methods reduces length of hospital stay (secondary outcome).

Description of the condition

Potential haemorrhagic surgical interventions in children aged 0 - 18 years where viscoelastic methods or standard care are used to guide transfusion (Inclusion criteria).

Exclusion criteria: patients over 18 years.

Description of the intervention

Potential haemorrhagic surgical interventions such as scoliosis, craniosynostosis, liver transplantation, trauma and cardiac surgeries in children where blood product administration is guided by viscoelastic methods (TEG, Thromboelastography or ROTEM, Rotational thromboelastometry) and compared to the same interventions where transfusion is guided using standard protocols other than viscoelastic methods.

Types of studies included: Randomised and non randomised trials will be included.

Types of participants: Patients aged between 0 - 18 years.

Types of interventions: Potential haemorrhagic surgical interventions such as scoliosis, craniosynostosis, liver transplantation, trauma and cardiac surgeries in children where blood product administration is guided by viscoelastic methods (TEG, Thromboelastography or

ROTEM, Rotational thromboelastometry) and compared to the same interventions where transfusion is guided using standard protocols other than viscoelastic methods.

Outcomes

Primary outcome

Intraoperative and postoperative morbi-mortality.

Secondary outcomes

- Intraoperative and postoperative blood products administration.
- Intraoperative and postoperative blood loss.
- Length of hospital stay (LOS).

Outcome measures

Primary outcomes measures: complications defined as organ failure or organ dysfunction and infections.

Secondary outcomes measures

- Intraoperative and postoperative amount and quality of blood products administered.
- Intraoperative and postoperative amount of blood loss.
- Number of days spent in hospital until discharge.

Materials and Methods

This study was registered under the number CRD42018103163 in PROSPERO, the international registration data base for systematic reviews and meta-analyses.

Since this is a systematic review and meta-analysis ethical approval from the local ethic committee was not necessary.

Search methods for identification of studies

One or more reviewers will search electronically for titles and abstracts including keywords defined here above. Once these are searched abstracts with relevant content will be retained and complete articles searched and screened for further inclusion or exclusion.

Electronic searches

Electronic search will be done using MEDLINE, EMBASE, CENTRAL, GOOGLE SCHOLAR, CLINICALTRIALS.GOV, ABSTRACT CONFERENCE and DARE.

Searching other resources

Other sources will be searched like grey literature.

Data collection and analysis

Comparisons, outcomes and subgroups will be collected and analysed.

Data collection and analysis will be done using the RevMan 5.3 software

Selection of studies

Randomised trials and non-randomised trials will be included.

Data extraction and management

Data selection and extraction will be realised by one or more researchers. A flow chart will illustrate the selection process as recommended by the PRISMA statement.

Assessment of risk of bias in included studies: the risk of bias will be assessed using the tools proposed by the Cochrane Handbook for systematic reviews of interventions.

Measures of treatment effect

- Measures of treatment effect will be dichotomous for morbi-mortality and transfusion (how many patients died or how many patients presented complications or how many patients were transfused) and will be presented as relative risk or odds ratio with 95% CI. Forest plots will be used to provide visual summary of data included.
- Measures of treatment effect will be dichotomous for the quality of blood products administered (how many patients received packed red blood cells or fresh frozen plasma or concentrated units of platelets or fibrinogen or other type of coagulation factors (concentrated prothrombin complex).
- Measures of treatment effect will be continuous for the quantity of blood products administered, blood loss and LOS.

Unit of analysis issues will include

- Intraoperative and postoperative mortality and morbidity.
- Intraoperative and postoperative blood transfusion and blood loss.
- LOS.

Missing data will not be included.

Assessment of heterogeneity: Forest plot will be used and I^2 statistics will be used to assess for heterogeneity.

Assessment of reporting biases: Funnel plots will be used to assess for bias.

Data will be synthesised using the RevMan 5.3 software.

Sensitivity analysis: Sensitivity analysis will be done by restricting the analysis to a defined intervention (goal-directed intraoperative transfusion protocols guided by viscoelastic methods versus standard care) and or to a subgroup of patients if necessary.

Results

The study will begin 2nd January 2019 and results are expected on 30th June 2019.

Conclusion

This protocol was realised to describe the systematic review and meta-analysis which will be undertaken to clarify the impact on outcome of transfusion protocols using viscoelastic haemostatic assays in haemorrhagic surgery in children.

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Contributions of Authors

Authors will contribute either by searching or selecting the articles or by reviewing the work.

Declarations of Interest

There are no conflicting or competing interests.

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