Published in final edited form as:
Cochrane Database Syst Rev. ; (5): CD011980. doi:10.1002/14651858.CD011980.pub2.

Use of platelet transfusions prior to lumbar punctures or epidural anaesthesia for the prevention of complications in people with thrombocytopenia

Lise J Estcourt[1], **Callum Ingram**[2], **Carolyn Doree**[3], **Marialena Trivella**[4], and **Simon J Stanworth**[5]

[1]Haematology/Transfusion Medicine, NHS Blood and Transplant, Oxford, UK

[2]School of Cellular and Molecular Medicine, University of Bristol, Bristol, UK

[3]Systematic Review Initiative, NHS Blood and Transplant, Oxford, UK

[4]Centre for Statistics in Medicine, University of Oxford, Oxford, UK

[5]National Institute for Health Research (NIHR) Oxford Biomedical Research Centre, Oxford University Hospitals NHS Foundation Trust and the University of Oxford, Oxford, UK

Abstract

Background—People with a low platelet count (thrombocytopenia) often require lumbar punctures or an epidural anaesthetic. Lumbar punctures can be diagnostic (haematological malignancies, epidural haematoma, meningitis) or therapeutic (spinal anaesthetic, administration of chemotherapy). Epidural catheters are placed for administration of epidural anaesthetic. Current practice in many countries is to correct thrombocytopenia with platelet transfusions prior to lumbar punctures and epidural anaesthesia, in order to mitigate the risk of serious procedure-related bleeding. However, the platelet count threshold recommended prior to these procedures varies significantly from country to country. This indicates significant uncertainty among clinicians of the correct management of these patients. The risk of bleeding appears to be low but

Contact address: Lise J Estcourt, Haematology/Transfusion Medicine, NHS Blood and Transplant, Level 2, John Radcliffe Hospital, Headington, Oxford, OX3 9BQ, UK. lise.estcourt@nhsbt.nhs.uk. lise.estcourt@ndcls.ox.ac.uk.
Editorial group: Cochrane Haematological Malignancies Group.
Publication status and date: New, published in Issue 5, 2016.
Review content assessed as up-to-date: 3 March 2016.

Contributions of Authors
Lise Estcourt (LE): protocol and review development, searching, selection of studies, eligibility and quality assessment, data extraction and analysis and content expert.
Callum Ingram (CI): protocol and review development, searching, selection of studies, eligibility and quality assessment, data extraction and analysis.
Carolyn Doree (CD): protocol and review development, searching and selection of studies.
Marialena Trivella (MT): protocol and review development and methodological expert.
Simon Stanworth (SS): protocol and review development and content expert.

Declarations of Interest
Lise Estcourt (LE): partly funded by the National Institute of Health Research (NIHR) Cochrane Programme Grant - Safe and Appropriate Use of Blood Components.
Callum Ingram (CI): none known.
Carolyn Doree (CD): none known.
Marialena Trivella (MT): partly funded by the NIHR Cochrane Programme Grant - Safe and Appropriate Use of Blood Components.
Simon Stanworth (SS): none known.

Europe PMC Funders Author Manuscripts

if bleeding occurs it can be very serious (spinal haematoma). Therefore, people may be exposed to the risks of a platelet transfusion without any obvious clinical benefit.

Objectives—To assess the effects of different platelet transfusion thresholds prior to a lumbar puncture or epidural anaesthesia in people with thrombocytopenia (low platelet count).

Search methods—We searched for randomised controlled trials (RCTs) in CENTRAL (*The Cochrane Library* 2016, Issue 3), MEDLINE (from 1946), EMBASE (from 1974), the Transfusion Evidence Library (from 1950) and ongoing trial databases to 3 March 2016.

Selection criteria—We included RCTs involving transfusions of platelet concentrates, prepared either from individual units of whole blood or by apheresis, and given to prevent bleeding in people of any age with thrombocytopenia requiring insertion of a lumbar puncture needle or epidural catheter. We only included RCTs published in English.

Data collection and analysis—We used standard methodological procedures expected by Cochrane.

Main results—We identified no completed or ongoing RCTs in English. We did not exclude any completed or ongoing RCTs because they were published in another language.

Authors' conclusions—There is no evidence from RCTs to determine what is the correct platelet transfusion threshold prior to insertion of a lumbar puncture needle or epidural catheter. There are no ongoing registered RCTs assessing the effects of different platelet transfusion thresholds prior to the insertion of a lumbar puncture or epidural anaesthesia in people with thrombocytopenia. Any future RCT would need to be very large to detect a difference in the risk of bleeding. We would need to design a study with at least 47,030 participants to be able to detect an increase in the number of people who had major procedure-related bleeding from 1 in 1000 to 2 in 1000.

Background

Please see Published notes for an explanation of some technical terms.

Description of the condition

Thrombocytopenia—Thrombocytopenia is defined as a platelet count less than 150 x 10^9/L (BCSH 2003), and severe thrombocytopenia as a platelet count less than 50 x 10^9/L. Thrombocytopenia can occur due to: reduced platelet production in the bone marrow as a result of chemotherapy or a haematological malignancy (blood cancer) (Leguit 2010; Weinzierl 2013); increased platelet consumption, for example due to bleeding or disseminated intravascular coagulation (DIC) (Levi 2009); or increased platelet destruction, for example due to immune thrombocytopenia or neonatal alloimmune thrombocytopenia (Neunert 2013; Pacheco 2011; Provan 2010). Platelets are an essential component in the formation of a blood clot (BCSH 2003). A low platelet count can lead to a range of bleeding symptoms such as bruising, nosebleeds and, rarely, life-threatening or fatal bleeding.

A platelet count less than 150 x 10^9/L occurs commonly in pregnancy (7% to 12% of pregnancies), but severe thrombocytopenia (platelet count less than 50 x 10^9/L) is much more uncommon (0.05% to 1% of pregnancies) (Burrows 1990; Nisha 2012; Sainio 2000).

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

A platelet count less than 150 x 10^9/L is very common in people with chronic liver disease (up to 76%) (Afdhal 2008), people who are critically ill (up to 68%) (Hui 2011), and people with haematological malignancies (Leguit 2010; Weinzierl 2013).

Lumbar puncture

Diagnostic: A diagnostic lumbar puncture (LP) is an invasive procedure to obtain samples of cerebrospinal fluid (CSF) (Doherty 2014). CSF is the fluid that bathes and protects the brain and spinal cord. An LP is usually performed by inserting a needle into the lower back (underneath the spinal L4 bony process) (Williams 2008). The CSF obtained can then be used for the investigation of haematological malignancies (Vavricka 2003), subarachnoid haemorrhages, meningitis (Riordan 2002), or neurological disorders. LPs are per-formed by doctors or specially trained nurses.

Therapeutic: Therapeutic LPs administer drugs into the CSF. This can be for the administration of therapeutics such as intrathecal chemotherapy or antibiotics, or administration of local anaesthetic to the nerves of the lower spine when a spinal anaesthetic is administered (Doherty 2014). This usually involves inserting a fine needle into the lower back, administration of the therapeutic agent and then removal of the needle (Ng 2004).

Diagnostic or therapeutic LPs are relatively common hospital procedures in people with haematological disorders who are thrombocytopenic (up to 10% of all procedures) (Estcourt 2012).

Epidural anaesthesia

The most common indication for epidural anaesthesia is in pregnant women to aid in pain relief during labour (Venn 2015). However, epidural anaesthesia can also be used in postoperative pain management especially for people with lower limb ischaemia (Venn 2015), and people undergoing thoracic surgery (Mendola 2009), as alternatives to general anaesthesia. Epidural anaesthesia typically involves inserting a larger diameter needle than a spinal needle. The epidural needle passes through the same tissues as a spinal needle but stops short of penetrating the dura (tissue sac that contains CSF). An epidural catheter is often passed through the needle and left in position so that additional local anaesthetic medications can be administered (Ng 2004).

Spinal haematoma

In the general population, the risk of a spinal haematoma is very low (1 in 200,000 epidural anaesthetic procedures during labour to 1 in 3600 epidural anaesthetic procedures in older women having knee surgery) (Li 2010; Moen 2004; Ruppen 2006; Vandermeulen 1994). Risk factors for major bleeding are multifactorial and include: increasing age (the procedure is more difficult in older people due to changes to the spine that occur with age), low platelet count, abnormal coagulation (including anticoagulant medication) and traumatic needle or catheter insertion (Erbay 2014; Li 2010; Moen 2004; Vandermeulen 1994). Performing an LP or administration of epidural anaesthesia is a relative contraindication in people with thrombocytopenia due to this perceived higher risk of complications (van Veen 2010).

Europe PMC Funders Author Manuscripts

However, overall, there are no current reliable estimates of the risks of adverse effects such as spinal haematomas in people with thrombocytopenia (van Veen 2010).

Description of the intervention

Current practice in many countries is to correct thrombocytopenia with platelet transfusions prior to an LP or epidural anaesthesia, in order to mitigate the risk of serious peri- or post-procedural bleeding. Up to 4% of all platelet components issued in the UK prior to a procedure are given to people with thrombocytopenia who need an LP (Qureshi 2007). The safe platelet count threshold recommended prior to an LP or epidural anaesthesia varies significantly from country to country.

For example, the platelet count threshold for LP in the US is 50 x 10^9/L (Kaufman 2015); in the UK it is 50 x 10^9/L in adults (BCSH 2003), but 20 to 40 x 10^9/L in children (BCSH 2004); and in Germany it is 20 x 10^9/L unless it is an urgent procedure (e.g. diagnosing bacterial meningitis) when an LP should be performed irrespective of the platelet count (GMA 2009).

The platelet count threshold for epidural anaesthesia also varies. In Italy and the UK, a platelet count of at least 50 x 10^9/L is recommended (BCSH 2003; Liumbruno 2011), while in France a platelet count of at least 80 x 10^9/L is recommended (Samama 2005).

As there is currently no consensus on the standard platelet count threshold prior to an LP or epidural anaesthesia, we compared the most commonly recommended platelet count threshold in national guidelines (50 x 10^9/L) against other recommended thresholds (10 x 10^9/L, 20 x 10^9/L, 30 x 10^9/L, 40 x 10^9/L, 80 x 10^9/L).

If guidelines recommend a platelet count threshold higher than is necessary to perform an LP or epidural anaesthesia safely then this will mean that people are exposed to the risks of a platelet transfusion unnecessarily. In 2014, 34% of all transfusion-related adverse events reported to the UK national reporting system (Serious Hazards of Transfusion (SHOT)) were due to platelet components. The most common adverse events due to platelet components were febrile and allergic reactions (Birchall 2015). Most of these reactions are not life-threatening but can be extremely distressing for the person. Rarer, but more serious sequelae, include: anaphylaxis (life-threatening allergic reaction), transfusion-transmitted infections (TTI) and transfusion-related acute lung injury (TRALI) (Blumberg 2010; Chapman 2015; Kaufman 2015; Slichter 2007; Vlaar 2013).

If guidelines recommend a platelet count threshold higher than is necessary to perform an LP safely, it may delay the start of life saving treatments, which can be time-critical in conditions such as bacterial meningitis or subarachnoid haemorrhage.

Epidural anaesthesia allows for a safer and more controlled, localised anaesthesia to be administered, reducing the complications associated with general anaesthesia and reducing patient time in hospital. If guidelines recommend a platelet count threshold higher than is necessary to administer an epidural anaesthetic, it may mean that a person is not offered an epidural anaesthetic and instead receives a general anaesthetic.

Europe PMC Funders Author Manuscripts

If guidelines recommend a platelet count threshold lower than is necessary to perform an LP or epidural anaesthesia safely, then this is putting people with thrombocytopenia at a higher risk of serious or life-threatening bleeding such as a spinal haematoma.

How the intervention might work

Platelet transfusions are given to people with low platelet counts to increase the platelet count and, therefore, reduce the risk of bleeding during invasive procedures.

However, the risk of bleeding during or after an LP may be low in people with a low platelet count. One systematic review of platelet transfusion indications showed that bleeding events were rare in people who had thrombocytopenia undergoing diagnostic LPs; however, the quality of the evidence was low (Kumar 2015). In the review, there were five case series in children who needed an LP, nearly all the children had acute lymphocytic leukaemia. In three of these studies, children were grouped by platelet count, 243 LPs were performed at a count less than 20 x 10^9/L and 817 at a platelet count between 21 x 10^9/L and 50 x 10^9/L and no bleeding complications occurred (van Veen 2010). Therefore, people may be exposed to the risks of a platelet transfusion without any obvious clinical benefit.

Why it is important to do this review

The platelet count threshold recommended prior to an LP or epidural anaesthesia varies significantly from country to country (BCSH 2003; BCSH 2004; GMA 2009; Kaufman 2015). This indicates significant uncertainty by clinicians of the correct management for safely performing an LP or administering an epidural anaesthetic.

Avoiding the need for unnecessary platelet transfusions in people with thrombocytopenia will have significant logistical and financial implications for national health services as well as decreasing people's exposure to the risks of transfusion. These factors are perhaps even more important in the development of platelet transfusion strategies in low-income countries, where access to blood components is much more limited than in high-income countries (Verma 2009).

Objectives

To assess the effects of different platelet transfusion thresholds prior to a lumbar puncture or epidural anaesthesia in people with thrombocytopenia (low platelet count).

Methods

Criteria for considering studies for this review

Types of studies—We included only randomised controlled trials (RCTs), irrespective of publication status.

Types of participants—We included people of any age with thrombocytopenia (as defined by the studies) requiring an LP or epidural anaesthesia. We excluded people who were experiencing clinically significant bleeding at the time of the procedure because such people are routinely given platelet transfusions to treat the bleeding.

Types of interventions—We planned to include RCTs comparing the following two types of procedure: LP needle insertion or epidural catheter insertion. We planned to compared platelet transfusion prior to the procedure when the platelet count was less than 50 x 10^9/L versus platelet transfusion prior to the procedure when:

- platelet count was less than 10 x 10^9/L;
- platelet count was less than 20 x 10^9/L;
- platelet count was less than 30 x 10^9/L;
- platelet count was less than 40 x 10^9/L;
- platelet count was less than 80 x 10^9/L.

We planned to report each analysis separately, as subgroups within the main comparisons, had we identified relevant studies.

Types of outcome measures

Primary outcomes

- Major procedure-related bleeding within 24 hours of the procedure.

  For example: spinal haematoma; intraventricular, intracerebral or subarachnoid haemorrhage; or major bleeding (not further defined) as reported by individual studies.
- All-cause mortality up to 30 days after the procedure.
- Serious adverse events:
  - Transfusion-related complications within 24 hours of the procedure (including transfusion-related acute lung injury (TRALI), transfusion-transmitted infection (TTI), transfusion-associated circulatory overload (TACO), transfusion-associated dyspnoea (TAD), acute transfusion reactions);
  - LP-related or epidural anaesthetic-related complications within seven days of the procedure (infection, headache, cerebral herniation, neurological symptoms such as radicular pain or numbness, back pain).

Secondary outcomes

- Minor LP-related or epidural anaesthetic-related bleeding within 24 hours of the procedure (defined as prolonged bleeding at the insertion site that only required treatment with a pressure bandage) or minor bleeding (not further defined) as reported by individual studies.
- Duration of hospital stay (total number of days in hospital).
- Proportion of people receiving platelet transfusions.
- Quality of life, as defined by individual studies

Europe PMC Funders Author Manuscripts

Search methods for identification of studies

The Systematic Review Initiative's Information Specialist (CD) formulated the search strategies in collaboration with the Cochrane Haematological Malignancies Group.

Electronic searches—We limited our searches to five main electronic databases and two ongoing trial databases.

- Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 3 03 March 2016) (Appendix 1).
- MEDLINE (1946 to 03 March 2016) (Appendix 2).
- EMBASE (1974 to 03 March 2016) (Appendix 3).
- PubMed (e-publications only) (Appendix 4).
- Transfusion Evidence Library (www.transfusionevidencelibrary.com) (1950 to 03 March 2016) (Appendix 5).
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (03 March 2016) (Appendix 6).
- ClinicalTrials.gov (03 March 2016) (Appendix 7).

We combined searches in MEDLINE with the Cochrane RCT search filter, as detailed in the *Cochrane Handbook for Systematic Reviews of Interventions* (Lefebvre 2011). We combined searches in EMBASE with the relevant Scottish Intercollegiate Guidelines Network (SIGN) RCT studies filter (www.sign.ac.uk/methodology/filters.html). We planned to exclude studies published in languages other than English; however, our search identified no relevant non-English language RCTs. We did not limit searches by year of publication or publication type.

Searching other resources—We planned to handsearch reference lists of included studies in order to identify further relevant studies but there were no included studies. We planned to contact lead authors of included studies to identify any unpublished material, missing data or information regarding ongoing studies but we did not find any relevant RCTs.

Data collection and analysis

Selection of studies—We selected studies according to Chapter 7 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). The Systematic Review Initiative's Information Specialist (CD) initially screened all search hits for relevance against the eligibility criteria and discarded all those that were clearly irrelevant. Thereafter, two review authors (CI, LE) independently screened all the remaining references for relevance against the full eligibility criteria using Distiller SR software (DistillerSR). We retrieved full-text articles for all references for which a decision on eligibility could not be made from title and abstract alone. We planned to request additional information from study authors as necessary to assess the eligibility for inclusion of individual studies. The two review authors discussed the results of study selection and resolved any discrepancies between themselves

Europe PMC Funders Author Manuscripts

without the need for a third review author (SS). We reported the results of study selection using a PRISMA flow diagram (Moher 2009).

Data extraction and management—As recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a), two review authors (CI, LE) planned to independently extract data onto standardised forms using Distiller SR software (DistillerSR). However, the review included no completed RCTs.

We planned to extract the following information for each study.

- Source: study identity (ID), report ID, review author ID, date of extraction, ID of author checking extracted data, citation of paper, contact authors details.
- General study information: publication type, study objectives, funding source, conflict of interest declared, other relevant study publication reviewed.
- Study details and methods: location, country, setting, number of centres, total study duration, recruitment dates, length of follow-up, power calculation, primary analysis (and definition), stopping rules, method of sequence generation, allocation concealment, blinding (of clinicians, participants and outcome assessors) and any concerns regarding bias.
- Characteristics of interventions: number of study arms, description of experimental arm, description of control arm, type of platelet component (e.g. apheresis or pooled), dose of platelet component, type of LP needle used.
- Characteristics of participants: age, gender, primary diagnosis, type procedure (diagnostic LP, therapeutic LP, epidural anaesthesia), platelet count, coagulation abnormalities, anticoagulant medications, antiplatelet medications.
- Participant flow: total number screened for inclusion, total number recruited, total number excluded, total number allocated to each study arm, total number analysed (for review outcomes), number of allocated participants who received planned treatment, number of drop-outs with reasons (percentage in each arm), protocol violations, missing data.
- Outcomes: major procedure-related bleeding within 24 hours of the procedure, minor procedure-related (LP or epidural anaesthetic) bleeding within 24 hours of the procedure, transfusion-related complications within 24 hours of the procedure, procedure-related complications within seven days of the procedure, duration of hospital stay, proportion of participants receiving platelet transfusions within 24 hours of the procedure, all-cause mortality up to 30 days from the procedure, quality of life (as defined by the individual studies).

Assessment of risk of bias in included studies—We planned to perform an assessment of all RCTs using the Cochrane 'Risk of bias' tool according to Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b). We planned to use Cochrane's tool for assessing risk of bias, which includes the following domains.

- Selection bias: random sequence generation and allocation concealment.
- Performance bias: blinding of participants and personnel.
- Detection bias: blinding of outcome assessment.
- Attrition bias: incomplete outcome data.
- Reporting bias: selective reporting.
- Other bias.

However, the search identified no completed studies and therefore we performed no assessment of risk of bias.

Measures of treatment effect—We did not perform any of the planned analyses because the search identified no completed studies. We planned to record the following data for this review.

- Continuous outcomes: mean, standard deviation and total number of participants in both the treatment and control groups.
- Dichotomous outcomes: number of events and total number of participants in both the treatment and control groups. We planned the following analyses for this review and will perform them in future updates of this review.
- For continuous outcomes using the same scale: analyses using the mean difference (MD) with 95% confidence intervals (CIs).
- For continuous outcomes measured with different scales: analyses using the standardised mean difference (SMD).
- Extraction and reporting of hazard ratios (HRs) for mortality data or, if HRs were not available, every effort would be made to estimate the HR as accurately as possible using the available data and a purpose-built method based on the Parmar and Tierney approach (Parmar 1998; Tierney 2007).
- For dichotomous outcomes: reporting the pooled risk ratio (RR) with a 95% CI. Where the number of observed events was small (less than 5% of sample per group), and where trials had balanced treatment groups, we planned to report the Peto's odds ratio (OR) with 95% CI (Deeks 2011).

If data allowed, we planned to undertake quantitative assessments using Review Manager 5 (RevMan 2014).

Where appropriate, we planned to report the number needed to treat for an additional beneficial outcome (NNTB) and the number needed to treat for an additional harmful outcome (NNTH) with CIs.

If we could not report the available data in any of the formats described above, we planned to present a narrative report, and if appropriate we planned to present the data in tables.

Unit of analysis issues—We planned to treat any unit of analysis issues in accordance with the advice given in Chapter 16 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011c). However, the search identified no completed studies and there were therefore no unit of analysis issues.

Dealing with missing data—We did not need to contact any study authors directly to enable us to make a decision on whether a study should be excluded.

Assessment of heterogeneity—We did not perform any of the planned analyses because the search identified no completed studies.

We had planned to combine the data to perform a meta-analysis if the clinical and methodological characteristics of individual studies were sufficiently homogeneous. We planned to assess statistical heterogeneity of treatment effects between studies using a Chi^2 test with a significance level at P value less than 0.1. We planned to use the I^2 statistic to quantify the degree of potential heterogeneity, and classify it as moderate if I^2 was greater than 50%, or considerable if I^2 was greater than 80%. We perceived that we would identify at least moderate clinical and methodological heterogeneity within the studies selected for inclusion; in such cases, we planned to use the random-effects model. If statistical heterogeneity was considerable, we planned not to report the overall summary statistic. We planned to assess potential causes of heterogeneity by sensitivity and subgroup analyses (Deeks 2011).

Assessment of reporting biases—We did not perform a formal assessment of potential publication bias (small trial bias) by generating a funnel plot and statistically test using a linear regression test (Sterne 2011), because there were no completed trials within this review.

Data synthesis—We planned to perform analyses according to the recommendations of Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions,* using aggregated data for analysis (Deeks 2011). We did not perform any of the planned analyses because the search identified no completed studies.

'Summary of findings' table—We planned to use the GRADE approach to create a 'Summary of findings' table, as suggested in Chapters 11 and 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2011a; Schünemann 2011b). We planned to use the GRADE approach to rate the quality of the evidence as 'high', 'moderate', 'low' or 'very low' using the five GRADE considerations.

- Risk of bias: serious or very serious.

- Inconsistency: serious or very serious.
- Indirectness: serious or very serious.
- Imprecision: serious or very serious.
- Publication bias: likely or very likely.

We planned to report separate 'Summary of findings' tables for LPs and epidural anaesthesia. We planned to report the subgroup for each comparison that contained the largest number of studies. The outcomes we planned to include are listed below.

- Major procedure-related bleeding within 24 hours of the procedure.
- All-cause mortality up to 30 days after the procedure.
- Transfusion-related complications within 24 hours of the procedure.
- Procedure-related (LP or epidural anaesthetic) complications within seven days of the procedure.
- Quality of life (as defined by the individual studies).

However, we identified no completed studies and therefore we could not produce a 'Summary of findings' table or assess the quality of the evidence.

Subgroup analysis and investigation of heterogeneity—We planned to perform subgroup analyses for each of the following outcomes in order to assess the effect on heterogeneity.

- Type of procedure (diagnostic LP, therapeutic LP, epidural anaesthesia).
- Type of participant (intensive care, liver disease, obstetric, leukaemia, other).
- Age of participant (neonate, child (aged one to 15 years), adult (aged 16 years or older)).
- Whether participants had associated clotting abnormalities, including DIC, or concomitant use of anticoagulant or antiplatelet agents.

If appropriate, we also planned to investigate heterogeneity between studies as follows.

- Type of platelet component.
- Dose of platelet component.

However, we identified no completed studies and therefore could not perform subgroup analyses.

Sensitivity analysis—We planned to assess the robustness of our findings by performing the following sensitivity analyses where appropriate.

- Including only studies with a 'low risk of bias' (e.g. RCTs with methods assessed as low risk for random sequence generation and concealment of treatment allocation).

- Including only studies with less than a 20% drop-out rate.
- Including only studies that were published in full.

However, we identified no completed studies and therefore we could perform no sensitivity analyses.

Results

Description of studies

See Characteristics of excluded studies.

Results of the search—The search (conducted on 3 March 2016) identified 1060 potentially relevant records (see the PRISMA Flow Diagram, Figure 1). There were 596 records after we removed duplicates. Two review authors (LE and CI) excluded 592 records on the basis of the abstract. We retrieved four full-text articles for assessment by the same two review authors, who excluded all four studies.

Included studies: We identified no completed or ongoing studies.

Excluded studies: We excluded all four full-text papers. See Characteristics of excluded studies for further details.

- Two studies compared the wrong intervention (NCT01972529; NCT01976104).
- One paper was a review (Mitchell 2012).
- One study was not randomised (NCT00042367).

Risk of bias in included studies—We did not perform a 'Risk of bias' assessment because there were no completed studies.

Effects of interventions—We could not assess the effects of interventions because there were no completed studies.

Discussion

Summary of main results

There were no completed or ongoing RCTs that were relevant to this review.

Overall completeness and applicability of evidence

This review identified no completed RCTs and therefore there is no evidence that can be assessed.

Any future RCT would need to be very large to detect a difference in the risk of bleeding. For example, if we assumed that major bleeding occurred in 1 out of 1000 people who had an LP when their platelet count was raised to 50 x 10^9/L or above, and that the risk of major bleeding doubled to 2 out of 1000 when their platelet count was only raised to 20 x 10^9/L or

above, we would need to design a study with at least 47,030 participants to be able to detect this difference with 80% power and 5% significance (calculated using a power calculator at Sealed Envelope).

Therefore, it is unlikely that any future RCTs will be performed with a primary outcome of major bleeding because the event is rare and if major bleeding does occur it can cause significant neurological impairment.

We cannot answer this review question using evidence from RCTs. We had not planned to include non-randomised studies as part of this review because potential biases are likely to be greater for non-randomised studies compared with RCTs (especially selection bias and reporting bias) (Reeves 2011). However, as there was no evidence from RCTs, we will include evidence from non-randomised studies in any future updates of this review in accordance with Chapter 13 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Reeves 2011).

Quality of the evidence

This review identified no completed RCTs and therefore there is no evidence that can be assessed.

Potential biases in the review process

To our knowledge, our review process is free from bias. We conducted a comprehensive search, searching data sources (including multiple databases and clinical trial registries) to ensure that we would capture all relevant trials. We carefully assessed the relevance of each paper identified and performed all screening in duplicate. We had planned to exclude any non-English language publications but the search identified no relevant publications.

We pre-specified all outcomes and subgroups prior to analysis.

Agreements and disagreements with other studies or reviews

We know of two systematic reviews that were relevant to this review (Kumar 2015; van Veen 2010).

The review by Kumar 2015 assessed the evidence for the use of platelet transfusions prior to LPs but did not assess the evidence prior to epidural anaesthesia. Like this review, Kumar 2015 found no RCTs that were relevant to this review's question. The Kumar 2015 review also assessed the evidence from non-randomised studies. They identified seven observational retrospective single centre studies (1536 participants; 6440 LPs) with varying platelet count thresholds. The studies did not report outcomes separately for those participants who received prophylactic platelet transfusions and those who did not. In addition, the studies did not describe the eligibility criteria or the criteria for transfusion. However, the studies, although poor quality, seemed to indicate a lack of severe bleeding associated with the insertion of an LP needle. There were no serious bleeding complications in five case series of 1450 children with thrombocytopenia. There were two cases of spinal haematoma (86 participants) in two case series of adults with thrombocytopenia. The van Veen 2010 review

identified the same seven non-randomised studies because Kumar 2015 used the search performed by van Veen 2010 that was first published online in September 2009.

The van Veen 2010 review also assessed the evidence for the use of platelet transfusions prior to epidural anaesthetics; there were no RCTs, six observational studies only included participants receiving an epidural anaesthetic and no spinal haematomas occurred. Only one of the included studies included participants who were not pregnant.

Both of these reviews concluded that there is a scarcity of evidence supporting prophylactic platelet transfusions prior to the insertion of a spinal needle for an LP or for the delivery of anaesthetic (Kumar 2015; van Veen 2010).

The most recently published platelet transfusion guidelines from the American Association of Blood Banks used this non-randomised evidence (Kaufman 2015; Kumar 2015). Another recently published guideline based its recommendations on expert opinion (NICE 2015).

Authors' Conclusions

Implications for practice

This review provided no evidence to guide practice.

Implications for research

It is unlikely that any future randomised controlled trials will be performed with a primary outcome of major bleeding because the event is rare. To detect a doubling in the number of participants with major bleeding from 0.1% to 0.2% would require a study with more than 47,000 participants. A summary of the best available evidence from non-randomised studies is required, the last systematic search of the non-randomised literature was performed before 2010.

Acknowledgements

We thank the editorial base of the Cochrane Haematological Ma-lignancies Review Group.

We thank the National Institute of Health Research (NIHR). This review is part of a series of reviews that have been funded by the NIHR Cochrane Programme Grant - Safe and Appropriate Use of Blood Components. This research is also supported by the NIHR Oxford Biomedical Research Centre Programme. The views and opinions expressed in this review are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health.

We thank Sally Hopewell who was an author on the protocol.

Sources of Support

Internal sources

- NHS Blood and Transplant, Research and Development, UK.

To fund the work of the Systematic Review Initiative (SRI)

External sources

- Cochrane Haematological Malignancies Group, Department for Internal Medicine, Germany. For editorial support

Europe PMC Funders Author Manuscripts

- National Institute for Health Research (NIHR) Cochrane Programme Grant, UK. To provide funding for systematic review authors and methodological support from the Centre for Statistics in Medicine, Oxford

Characteristics of Studies

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Mitchell 2012	Review
NCT00042367	Non-randomised study
NCT01972529	Wrong intervention
NCT01976104	Wrong intervention

Data and Analyses

This review has no analyses.

Appendix 1. CENTRAL search strategy

#1 MeSH descriptor: [Blood Platelets] explode all trees

#2 (platelet* or thrombocyte*):ti

#3 MeSH descriptor: [Platelet Transfusion] explode all trees

#4 MeSH descriptor: [Plateletpheresis] explode all trees

#5 ((platelet* or thrombocyte*) near/5 (prophyla* or transfus* or infus* or administ* or requir* or need* or product or products or component* or concentrate* or apheres* or pooled or single donor* or random donor*))

#6 thrombocyt?pheres* or plateletpheres*

#7 ((platelet* or thrombocyte*) near/5 (protocol* or trigger* or threshold* or schedul* or dose* or dosing or usage or utilisation or utilization))

#8 #1 or #2 or #3 or #4 or #5 or #6 or #7

#9 MeSH descriptor: [Spinal Puncture] this term only

#10 MeSH descriptor: [Anesthesia, Epidural] explode all trees

#11 MeSH descriptor: [Anesthesia, Spinal] this term only

#12 MeSH descriptor: [Injections, Spinal] explode all trees

#13 MeSH descriptor: [Myelography] this term only

#14 MeSH descriptor: [Nerve Block] explode all trees

Europe PMC Funders Author Manuscripts

#15 ((spine or spinal or intraspinal or dura* or intradural or epidural or lumbar* or intralumbar* or theca* or intrathecal or subarachnoid* or peridural* or caudal*) near/6 (punctur* or inject* or infus* or anesth* or anaesth* or needle* or tap* or block* or drug* or administ*))

#16 ((intrathecal or theca*) near/6 (treatment* or chemotherapy or antibiotic* or therapy or inject*))

#17 myelogra*

#18 #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17

#19 #8 and #18

Appendix 2. MEDLINE (OvidSP) search strategy

1. Spinal Puncture/

2. Anesthesia, Epidural/

3. Anesthesia Spinal/

4. exp Injections, Spinal/

5. Myelography/

6. exp Nerve Block/

7. ((spine or spinal or intraspinal or dura* or intradural or epidural or lumbar* or intralumbar* or theca* or intrathecal or subarachnoid* or peridural* or caudal*) adj6 (punctur* or inject* or infus* or anesth* or anaesth* or needle* or tap* or block* or drug* or administ*)).tw,kf.

8. ((intrathecal OR theca*) adj6 (treatment* OR chemotherapy OR antibiotic* OR therapy OR inject*)).tw,kf.

9. myelogra*.tw,kf.

10. or/1-9

11. Platelet Transfusion/

12. Plateletpheresis/

13. Blood Platelets/

14. ((platelet* or thrombocyte*) adj5 (prophyla* or transfus* or infus* or administ* or requir* or need* or product* or component* or concentrate* or apheres* or pooled or single donor or random donor)).tw,kf.

15. (thrombocytopheres* or plateletpheres*).tw,kf.

16. ((platelet* or thrombocyte*) adj5 (protocol* or trigger* or threshold* or schedul* or dose* or dosing or usage or utili?ation)).tw,kf.

17. (platelet* or thrombocyte*).ti.

18. or/11-17

19. 10 and 18

20. randomized controlled trial.pt.

21. controlled clinical trial.pt.

22. randomi*.tw,kf.

23. placebo.ab.

24. exp clinical trials as topic/

25. randomly.ab.

26. trial.tw.

27. groups.ab.

28. or/20-27

29. 19 and 28

Appendix 3. EMBASE (OvidSP) search strategy

1. Lumbar Puncture/

2. Puncture/

3. exp Intraspinal Drug Administration/

4. exp Epidural Anesthesia/

5. Spinal Anesthesia/

6. Myelography/

7. exp Nerve Block/

8. ((spine or spinal or intraspinal or dura* or intradural or epidural or lumbar* or intralumbar* or theca* or intrathecal or subarachnoid* or peridural* or caudal*) adj6 (punctur* or inject* or infus* or anesth* or anaesth* or needle* or tap* or block* or drug* or administ*)).tw.

9. ((intrathecal OR theca*) adj6 (treatment* OR chemotherapy OR antibiotic* OR therapy)).tw.

10. myelogra*.tw.

11. or/1-10

12. Thrombocyte Transfusion/

13. Thrombocytopheresis/

14. Thrombocyte/

15. ((platelet* or thrombocyte*) adj5 (prophyla* or transfus* or infus* or administ* or requir* or need* or product* or component* or concentrate* or apheres* or pooled or single donor or random donor)).tw.

16. (thrombocyt?pheres* or plateletpheres*).tw.

17. ((platelet* or thrombocyte*) adj5 (protocol* or trigger* or threshold* or schedul* or dose* or dosing or usage or utili?ation)).tw.

18. (platelet* or thrombocyte*).ti.

19. or/12-18

20. 11 and 19

21. Randomized Controlled Trial/

22. Randomization/

23. Single Blind Procedure/

24. Double Blind Procedure/

25. Crossover Procedure/

26. Placebo/

27. exp Clinical Trial/

28. Prospective Study/

29. (randomi* or double-blind* or single-blind* or RCT*).tw.

30. (random* adj2 (allocat* or assign* or divid* or receiv*)).tw.

31. (crossover* or cross over* or cross-over* or placebo*).tw.

32. ((treble or triple) adj blind*).tw.

33. or/21-32

34. Case Study/

35. case report*.tw.

36. (note or editorial).pt.

37. or/34-36

38. 33 not 37

39. 20 and 38

40. limit 39 to embase

Appendix 4. PubMed search strategy (epublications only)

#1 ((spine OR spinal OR intraspinal OR dura OR dural OR intradural OR epidural OR lumbar* OR intralumbar* OR theca* OR intrathecal OR subarachnoid* OR peridural* OR caudal*) AND (punctur* OR inject* OR infus* OR anesth* OR anaesth* OR needle* OR tap* OR block* OR drug* OR administ*))

#2 ((intrathecal OR theca*) AND (treatment* OR chemotherapy OR antibiotic* OR therapy OR inject*))

#3 myelogra*

#4 #1 OR #2 OR #3

#5 ((platelet* OR thrombocyte*) AND (prophyla* OR transfus* OR infus* OR administ* OR requir* OR need* OR product* OR component* OR concentrate* OR apheres* OR pooled OR single donor* OR random donor*))

#6 (thrombocytopheres* OR plateletpheres*)

#7 ((platelet* OR thrombocyte*) AND (protocol* OR trigger* OR threshold* OR schedul* OR dose* OR dosing OR usage OR utilisation OR utilization))

#8 platelet*[TI] OR thrombocyte*[TI]

#9 #5 OR #6 OR #7 OR #8

#10 #4 AND #9

#11 (random* OR blind* OR control group OR placebo OR controlled trial OR controlled study OR groups OR trials OR systematic review OR meta-analysis OR metaanalysis OR literature search OR medline OR cochrane OR embase) AND (publisher[sb] OR inprocess[sb] OR pubmednotmedline[sb])

#12 #10 AND #11

Appendix 5. Transfusion Evidence Library search strategy

Search box: (lumbar OR spinal OR puncture OR injection OR needle OR epidural OR intradural OR dural OR intrathecal OR subarachnoid OR peridural OR caudal OR block OR anaesthetic OR anesthetic OR anesthesia OR anaesthesia OR drug OR tap OR administration OR procedure)

Filter: Platelets

Appendix 6. WHO ICTRP search strategy

(Title: lumbar OR spinal OR puncture OR injection OR epidural OR intradural OR dural OR peridural OR caudal OR intrathecal OR subarachnoid OR administration OR procedure)

AND

(Intervention: platelet OR platelets)

Appendix 7. Clinical.trials.gov search strategy

Search terms: (lumbar puncture OR spinal injection OR epidural OR intradural OR dural OR peridural OR caudal OR intrathecal OR subarachnoid OR nerve block) AND (platelets OR platelet transfusion)

AND

Study d esign: Intervention Studies

Differences between Protocol and Review

We have clarified two of the outcomes so that the outcomes include both LP-related and epidural anaesthetic-related complications are reported in future versions of this review and not just LP-related complications.

There are several differences between the protocol (Estcourt 2015), and this review due to lack of data.

The search found no completed studies and therefore we could not:

- report on any of the primary or secondary outcomes of the review;
- perform a ’Risk of bias’ assessment;
- assess the quality of the evidence or produce a ’Summary of findings’ table;
- assess publication bias;
- perform any analyses or subgroup analyses.

Europe PMC Funders Author Manuscripts

We had not planned to include non-randomised studies as part of this review; however, we will include evidence from non-randomised studies in any future updates of this review in accordance with Chapter 13 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Reeves 2011).

Notes

This review was a rapid review (definition of a rapid review as previously agreed with the Haematological Malignancies Group), we only included English language publications. The searches identified no relevant non-English language reports.

Disseminated intravascular coagulation (DIC)

DIC is a rare, life-threatening condition that prevents blood from clotting normally. The blood clots reduce blood flow and can block blood from reaching the body's organs. This increased clotting can use up the platelets and clotting factors in the blood and mean that fewer platelets and clotting factors are available. This can then lead to excessive bleeding.

Haematological malignancies

Blood cancers and related diseases that primarily affect the bone marrow or blood cells. The bone marrow is the soft inner part of bones where blood is made.

The three main types of blood cells are:

- red blood cells, which carry oxygen from the lungs to every part of the body;
- white blood cells, which help the body fight infection;
- platelets, which help control bleeding.

Neonatal alloimmune thrombocytopenia (NAIT)

NAIT is characterised by the destruction of platelets in the foetus or newborn by antibodies produced by the mother. The foetus has proteins on the surface of the platelet that it has inherited from its father but are not present in the mother. The mother sees these proteins as 'foreign' and may respond by producing antibodies against these intruders. Antibodies, are an important part of the body's immune system. The antibodies produced by the mother may cross the placenta, enter the baby's bloodstream and destroy the unborn baby's platelets.

References to studies excluded from this review

Mitchell 2012 {published data only} . Mitchell MD, Umscheid CA, Schweikert W. Guidelines for platelet or plasma transfusion in lumbar puncture patients (Structured abstract). Centre for Evidence-Based Practice. 2012

NCT00042367 {published data only} . NCT00042367. Study of systemic and spinal chemotherapy followed by radiation for infants with brain tumors (BB'98). [(accessed 6 July 2015)] clinicaltrials.gov/ct2/show/NCT00042367.

Europe PMC Funders Author Manuscripts

NCT01972529 {published data only} . NCT01972529. Treatment of thrombocytopenia in patients with chronic liver disease undergoing an elective procedure. [(accessed 6 July 2015)] clinicaltrials.gov/ct2/show/NCT01972529.

NCT01976104 {published data only} . NCT01976104. Treatment of thrombocytopenia in patients with chronic liver disease undergoing an elective procedure. [(accessed 6 July 2015)] clinicaltrials.gov/ct2/show/NCT01976104.

Additional references

Afdhal 2008 . Afdhal N, McHutchison J, Brown R, Jacobson I, Manns M, Poordad F, et al. Thrombocytopenia associated with chronic liver disease. Journal of Hepatology. 2008; 48(6): 1000–7. [PubMed: 18433919]

BCSH 2003 . BCSH. British Committee for Standards in Haematology: guidelines for the use of platelet transfusions. British Journal of Haematology. 2003; 122(1):10–23. [PubMed: 12823341]

BCSH 2004 . Gibson BE, Todd A, Roberts I, Pamphilon D, Rodeck C, Bolton-Maggs P, et al. Transfusion guidelines for neonates and older children. British Journal of Haematology. 2004; 124(4):433–53. [PubMed: 14984493]

Birchall 2015 . Birchall, J.; Tinegate, H.; Regan, F. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. Chapter 14 Acute transfusion reactions (ATR). The 2014 Annual SHOT Report. Bolton-Maggs, PHB.; Poles, D., et al., editors. Manchester, UK: SHOT; 2015. p. 106-12.

Blumberg 2010 . Blumberg N, Heal JM, Phillips GL. Platelet transfusions: trigger, dose, benefits and risks. F1000 Medicine Reports. 2010; 2:1–5. [PubMed: 20948877]

Burrows 1990 . Burrows RF, Kelton JG. Thrombocytopenia at delivery: a prospective survey of 6715 deliveries. American Journal of Obstetrics and Gynecology. 1990; 162:731–4. [PubMed: 2316579]

Chapman 2015 . Chapman, C. [(accessed 26 November 2015)] Transfusion-related lung injury (TRALI). 2015. www.shotuk.org/wp-content/uploads/SHOT-2014-Annual-Report v11-Web-Edition.pdf

Deeks 2011 . Deeks, JJ.; Higgins, JPT.; Altman, DG. Chapter 9: Analysing data and undertaking meta-analyses. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. Higgins, JPT.; Green, S., editors. The Cochrane Collaboration; 2011c. Available from www.cochrane-handbook.org

DistillerSR [Computer program] . Evidence Partners. DistillerSR: Data Management Software. Ottawa, ON: Evidence Partners; 2015.

Doherty 2014 . Doherty CM, Forbes RB. Diagnostic lumbar puncture. Ulster Medical Journal. 2014; 83(2):93–102. [PubMed: 25075138]

Erbay 2014 . Erbay, RH.; Senoglu, N.; Atalay, H. Topics in Spinal Anaesthesia. Rijeka, Croatia: In-Tech; 2014. Spinal or epidural haematoma.

Estcourt 2012 . Estcourt LJ, Birchall J, Lowe D, Grant-Casey J, Rowley M, Murphy MF. Platelet transfusions in haematology patients: are we using them appropriately? Vox Sanguinis. 2012; 103(4):284–93. [PubMed: 22775395]

GMA 2009 . The Board of the German Medical Association on the recommendation of the Scientific Advisory Board. Platelet transfusions. Transfusion Medicine and Hemotherapy. 2009; 36:372–82. [PubMed: 21245968]

Higgins 2011a . Higgins, JPT.; Deeks, JJ. Chapter 7: Selecting studies and collecting data. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. Higgins, JPT.; Green, S., editors. The Cochrane Collaboration; 2011a. Available from www.cochrane-handbook.org

Higgins 2011b . Higgins, JPT.; Altman, DG.; Sterne, JAC. Chapter 8: Assessing risk of bias in included studies. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. Higgins, JPT.; Green, S., editors. The Cochrane Collaboration; 2011b. Available from www.cochrane-handbook.org

Higgins 2011c . Higgins, JPT.; Deeks, JJ.; Altman, DG. Chapter 16: Special topics in Statistics. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. Higgins, JPT.; Green, S., editors. The Cochrane Collaboration; 2011c.

Hui 2011 . Hui P, Cook DJ, Lim W, Fraser GA, Arnold DM. The frequency and clinical significance of thrombocytopenia complicating critical illness: a systematic review. Chest. 2011; 139(2):271–8. [PubMed: 21071526]

Kaufman 2015 . Kaufman RM, Djulbegovic B, Gernsheimer T, Kleinman S, Tinmouth AT, Capocelli KE, et al. Platelet transfusion: a clinical practice guideline from the AABB. Annals of Internal Medicine. 2015; 162(3):205–13. [PubMed: 25383671]

Kumar 2015 . Kumar A, Mhaskar R, Grossman BJ, Kaufman RM, Tobian AA, Kleinman S, et al. Platelet transfusion: a systematic review of the clinical evidence. Transfusion. 2015; 55(3):1116–27. [PubMed: 25387589]

Lefebvre 2011 . Lefebvre, C.; Manheimer, E.; Glanville, J. Chapter 6: Searching for studies. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. Higgins, JPT.; Green, S., editors. The Cochrane Collaboration; 2011. Available from www.cochrane-handbook.org

Leguit 2010 . Leguit RJ, van den Tweel JG. The pathology of bone marrow failure. Histopathology. 2010; 57(5):655–70. [PubMed: 20727024]

Levi 2009 . Levi M, Toh CH, Thachil J, Watson HG. Guidelines for the diagnosis and management of disseminated intravascular coagulation. British Journal of Haematology. 2009; 145(1):24–33. [PubMed: 19222477]

Li 2010 . Li S-L, Wang D-X, Ma D. Epidural hematoma after neuraxial blockade: a retrospective report from China. Anesthesia & Analgesia. 2010; 111(5):1322–4. [PubMed: 20705781]

Liumbruno 2011 . Liumbruno GM, Bennardello F, Lattanzio A, Piccoli P, Rossetti G. Recommendations for the transfusion management of patients in the peri-operative period. I. The pre-operative period. Blood Transfusion. 2011; 9(1):19–40. [PubMed: 21235852]

Mendola 2009 . Mendola C, Ferrante D, Oldani E, Cammarota G, Cecci G, Vaschetto R, et al. Thoracic epidural analgesia in post-thoracotomy patients: comparison of three different concentrations of levobupivacaine and sufentanil. British Journal of Anaesthesia. 2009; 102(3): 418–23. [PubMed: 19189982]

Moen 2004 . Moen V, Dahlgren N, Irestedt L. Severe neurological complications after central neuraxial blockades in Sweden 1990-1999. Anesthesiology. 2004; 101(4):950–59. [PubMed: 15448529]

Moher 2009 . Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-Analyses: the PRISMA Statement. Annals of Internal Medicine. 2009; 151(4): 264–9. [PubMed: 19622511]

Neunert 2013 . Neunert CE. Current management of immune thrombocytopenia. Hematology. 2013; 2013:276–82. [PubMed: 24319191]

Ng 2004 . Ng KW, Parsons J, Cyna AM, Middleton P. Spinal versus epidural anaesthesia for caesarean section. Cochrane Database of Systematic Reviews. 2004; (2)doi: 10.1002/l4651858.CD003765.pub2

NICE 2015 . National Institute for Health and Care Excellence (NICE). [(aAccessed 10 March 2016)] Blood transfusion NG24. 2015. www.nice.org.uk/guidance/ng24

Nisha 2012 . Nisha S, Amita D, Uma S, Tripathi AK, Pushplata S. Prevalence and characterization of thrombocytopenia in pregnancy in Indian women. Indian Journal of Hematology and Blood Transfusion. 2012; 28(2):77–81. [PubMed: 23730013]

Pacheco 2011 . Pacheco LD, Berkowitz RL, Moise KJ, Bussel JB, McFarland JG, Saade GR. Fetal and neonatal alloimmune thrombocytopenia: a management algorithm based on risk stratification. Obstetrics and Gynecology. 2011; 118(5):1157–63. [PubMed: 22015886]

Parmar 1998 . Parmar M, Torri V, Stewart L. Extracting summary statistics to perform meta-analyses of the published literature for survival endpoints. Statistics in Medicine. 1998; 17(24):2815–34. [PubMed: 9921604]

Provan 2010 . Provan D, Stasi R, Newland AC, Blanchette VS, Bolton-Maggs P, Bussel JB, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010; 115(2):168–86. [PubMed: 19846889]

Qureshi 2007 . Qureshi H, Lowe D, Dobson P, Grant-Casey J, Parris E, Dalton D, et al. National comparative audit of the use of platelet transfusions in the UK. Transfusion Clinique et Biologique. 2007; 14(6):509–13. [PubMed: 18359658]

Reeves 2011 . Reeves, BC.; Deeks, JJ.; Higgins, JPT.; Wells, GA. on behalf of the Cochrane Non-Randomised Studies Methods Group. Chapter 13: Including non-randomized studies. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. Higgins, JPT.; Green, S., editors. The Cochrane Collaboration; 2011a. Available from www.cochrane-handbook.org

RevMan 2014 [Computer program] . The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan) Version 5.3. The Nordic Cochrane Centre, The Cochrane Collaboration; Copenhagen: 2014.

Riordan 2002 . Riordan FA, Cant AJ. When to do a lumbar puncture. Archives of Disease in Childhood. 2002; 87(3):235–37. [PubMed: 12193440]

Ruppen 2006 . Ruppen W, Derry S, McQuay H, Moore RA. Incidence of epidural hematoma, infection, and neurologic injury in obstetric patients with epidural analgesia/anesthesia. Anesthesiology. 2006; 105(2):394–99. [PubMed: 16871074]

Sainio 2000 . Sainio S, Kekomäki R, Riikonen S, Teramo K. Maternal thrombocytopenia at term: a population-based study. Acta Obstetricia et Gynecologica Scandinavica. 2000; 79:744–9. [PubMed: 10993097]

Samama 2005 . Samama CM, Djoudi R, Lecompte T, Nathan-Denizot N, Schved JF. Perioperative platelet transfusion: recommendations of the Agence Francaise de Securite Sanitaire des Produits de Sante (AFSSaPS) 2003. Canadian Journal of Anaesthesia. 2005; 52(1):30–7. [PubMed: 15625253]

Schünemann 2011a . Schünemann, HJ.; Oxman, AD.; Higgins, JPT.; Vist, GE.; Glasziou, P.; Guyatt, GH. Chapter 11: Presenting results and 'Summary of findings' tables. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. Higgins, JPT.; Green, S., editors. The Cochrane Collaboration; 2011a. Available from www.cochrane-handbook.org

Schünemann 2011b . Schünemann, HJ.; Oxman, AD.; Vist, GE.; Higgins, JPT.; Deeks, JJ.; Glasziou, P., et al. Cochrane Applicability and Recommendations Methods Group. Chapter 12: Interpreting results and drawing conclusions. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. Higgins, JPT.; Green, S., editors. The Cochrane Collaboration; 2011b. Available from www.cochrane-handbook.org

Slichter 2007 . Slichter SJ. Evidence-based platelet transfusion guidelines. Hematology. 2007; 1520:172–78. [PubMed: 18024626]

Sterne 2011 . Sterne, JAC.; Egger, M.; Moher, D. Chapter 10: Addressing reporting biases. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. Higgins, JPT.; Green, S., editors. The Cochrane Collaboration; 2011c. Available from www.cochrane-handbook.org

Tierney 2007 . Tierney JF, Stewart LA, Ghersi D, Burdett S, Sydes MR. Practical methods for incorporating summary time-to-event data into meta-analysis. Trials. 2007; 8(16)doi: 10.1186/1745-6215-8-16

van Veen 2010 . van Veen JJ, Nokes TJ, Makris M. The risk of spinal haematoma following neuraxial anaesthesia or lumbar puncture in thrombocytopenic individuals. British Journal of Haematology. 2010; 148(1):15–25. [PubMed: 19775301]

Vandermeulen 1994 . Vandermeulen EP, Van Aken H, Vermylen J. Anticoagulants and spinal-epidural anesthesia. Anesthesia &Analgesia. 1994; 79:1165–77. [PubMed: 7978443]

Vavricka 2003 . Vavricka SR, Walter RB, Irani S, Halter J, Schanz U. Safety of lumbar puncture for adults with acute leukaemia and restrictive prophylactic platelet transfusion. Annals of Hematology. 2003; 82(9):570–73. [PubMed: 12904898]

Venn 2015 . Venn, PJH. [(accessed 26 November 2015)] Key points on the provision of anaesthesia services. 2015. www.rcoa.ac.uk/gpas2015

Verma 2009 . Verma A, Agarwal P. Platelet utilization in the developing world: strategies to optimize platelet transfusion practices. Transfusion and Apheresis Science. 2009; 41(2):145–9. [PubMed: 19716339]

Vlaar 2013 . Vlaar AP, Juffermans NP. Transfusion-related acute lung injury: a clinical review. Lancet. 2013; 382(9896):984–94. [PubMed: 23642914]

Weinzierl 2013 . Weinzierl EP, Arber DA. The differential diagnosis and bone marrow evaluation of new-onset pancytopenia. American Journal of Clinical Pathology. 2013; 139(1):9–29. [PubMed: 23270895]

Williams 2008 . Williams J, Lye DC, Umapathi T. Diagnostic lumbar puncture: minimising complications. Internal Medicine Journal. 2008; 38(7):587–91. [PubMed: 18422562]

References to other published versions of this review

Estcourt 2015 . Estcourt LJ, Ingram C, Hopewell S, Trivella M, Doree C, Stanworth SJ. Use of platelet transfusions prior to lumbar punctures or epidural anaesthesia for the prevention of complications in people with thrombocytopenia. Cochrane Database of Systematic Reviews. 2015; (12)doi: 10.1002/14651858.CD011980* *Indicates the major publication for the study*

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

Plain language summary

Comparison of different platelet transfusion thresholds prior to a lumbar puncture or epidural anaesthetic in people with a low platelet count

Review question

We evaluated the evidence about whether people with a low platelet count require a platelet transfusion prior to insertion of a lumbar puncture needle or epidural catheter, and if so what is the platelet count level at which a platelet transfusion is required.

Background

Platelets are found in the blood and are an essential part of forming a blood clot. A low platelet count increases the risk of bleeding. People with a low platelet count often require a lumbar puncture or epidural anaesthetic for administration of treatment or to aid in diagnosis.

A lumbar puncture is usually performed by inserting a needle between the bones (vertebrae) of the spine in the lower back into the fluid surrounding the spinal cord (the bundle of nerves that runs down the spine and connects the brain with the body). Lumbar punctures are performed either to obtain a sample of this fluid or to administer treatment into the fluid (chemotherapy or an anaesthetic). The lumbar puncture needle is removed immediately after any fluid samples have been taken or treatment has been administered.

An epidural involves inserting a larger diameter needle than a lumbar puncture needle. The epidural needle passes through the same tissues as the lumbar puncture needle but stops short of penetrating the sac of fluid surrounding the spinal cord. Instead any treatment is injected into the space just outside the sac of fluid (called the epidural space). A small tube (an epidural catheter) is often passed through the epidural needle and left in position so that additional local anaesthetic medicines can be given.

Current practice in many countries is to increase the platelet count above a pre-specified level with platelet transfusions (platelets are given into a vein) to prevent serious bleeding due to the lumbar puncture or epidural anaesthetic. Although the risk of bleeding appears to be low, if bleeding does occur, it can be very serious. Due to a lack of evidence the platelet count level recommended prior to lumbar puncture or epidural anaesthetic varies significantly from country to country. This means that doctors are uncertain about which is the correct platelet count level, or if a platelet transfusion is required. Therefore, people may be exposed to the risks of a platelet transfusion without any obvious clinical benefit.

Study characteristics

We searched scientific databases for clinical trials of people of any age with low platelet counts requiring a lumbar puncture or epidural anaesthesia. The evidence is current to 3 March 2016. In this review, we found no relevant RCTs.

Key results

There are no results because we found no relevant RCTs. We would need to design a study with at least 47,030 participants to be able to detect an increase in the number of

people who had bleeding after lumbar puncture or epidural anaesthetic from 1 in 1000 to 2 in 1000.

Quality of the evidence

There is no evidence from randomised controlled trials to answer our review questions.

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

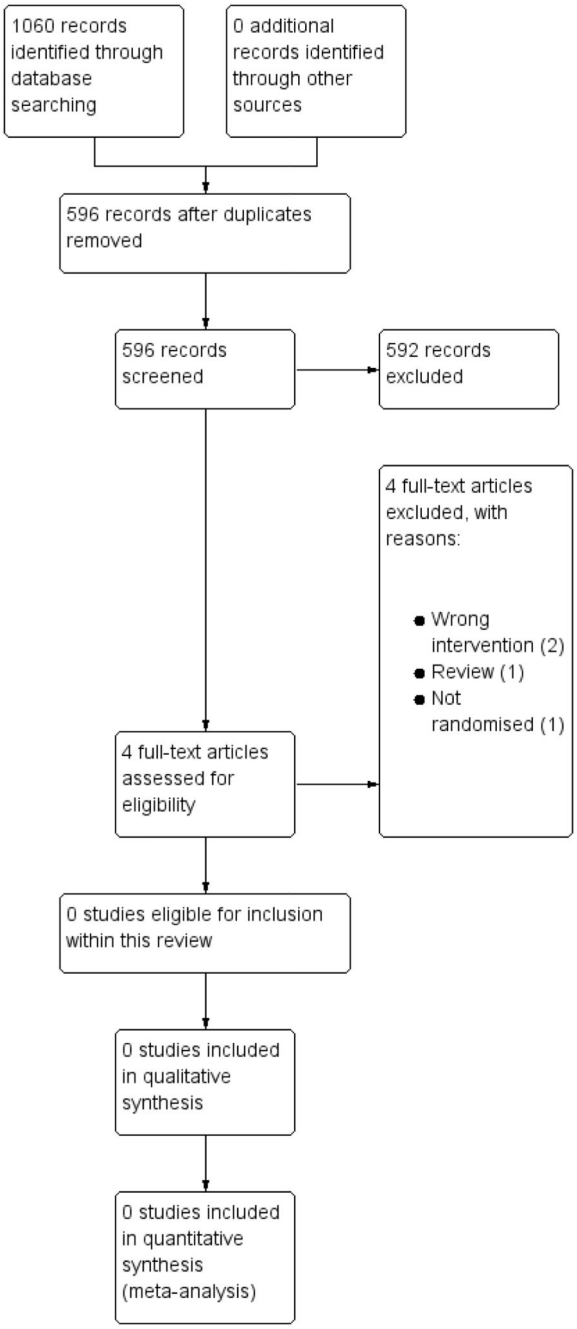

Figure 1. Study flow diagram.