Treatment of extravasation injuries in infants and young children: a scoping review and survey

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Scientific summary

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Background

Extravasation injuries are caused by unintended leakages of fluids or medicines from intravenous (i.v.) lines in which a fluid deviates from its planned pathway – the vein – into surrounding tissue. These injuries can cause pain, inflammation, tendon or nerve damage and predispose to local and invasive infection. Initial treatments aim to reduce pain and prevent or minimise local tissue necrosis and associated functional and cosmetic impairment. Injuries that result in tissue necrosis seem to be more prevalent in neonates and younger infants. This is likely to be due to their immature skin, fragile veins, lack of subcutaneous tissue, likelihood of needing longer periods of i.v. treatment and their limited ability to report pain.

Treatment strategies are normally driven by the type and extent of the injury and by the time interval between injury identification and subsequent intervention. Although treatment options are many and varied, there is no consensus on the best approach to management, with guidelines offering conflicting recommendations. This is likely a consequence of the limited research evidence available, particularly in newborns and infants.

Objectives

To begin the process of resolving the uncertainty surrounding which treatments are best for treating extravasation injuries in infants and young children. Results from a systematic scoping review will determine which treatments appear likely to be the most promising, and results from a NHS survey will inform on which treatment approaches are currently used across the NHS and will elicit opinions regarding which interventions are most worthy of future research.

Methods

Scoping review

A scoping review was undertaken based on the framework proposed in key methodology papers (Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2005;**8**:19–32; Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. *Implement Sci* 2010;**5**:69; Daudt HML, van Mossel C, Scott SJ. Enhancing the scoping study methodology: a large, inter-professional team's experience with Arksy and O'Malley's framework. *BMC Med Res Methodol* 2013;**13**:48). In February 2017, we searched 12 electronic databases without date restrictions, including MEDLINE, CINAHL (Cumulative Index to Nursing and Allied Health Literature) Plus and EMBASE (Excerpta Medica dataBASE) to identify published and unpublished studies in any language. We searched clinical trial registries for ongoing studies.

Eligible studies were of children (aged < 18 years) with an extravasation injury (of the skin, subcutaneous tissue or muscle tissue) associated with central or peripheral i.v. access. Any interventions or comparators were eligible. The outcomes of interest were wound healing time, scarring, infection, pain, contractures, functional impairment, disfigurement, requirement for surgery, mortality and anaphylactic reactions to extravasation treatments.

Two reviewers independently assessed titles and abstracts for eligibility. If deemed eligible, the full texts were then sought and assessed independently by the same two reviewers, with disagreements resolved through discussion or via a third reviewer. Piloted data extraction forms for comparative studies,

non-comparative studies and case reports were used to record details of study methods, population characteristics (such as age, type of infusate, and injury severity), interventions (type, number and frequency of treatments), comparators, outcome measures and results. Recommendations for future research that were relevant to the aims of this scoping review were extracted. Data were extracted by one researcher and checked by another. Study details and findings were presented in structured tables and described, synthesised and summarised narratively.

Survey

A systematic approach was used to develop the questionnaire content, informed mainly by initial findings from the scoping review and peer-to-peer consultation of clinicians. The questionnaire was piloted among colleagues at neonatal and paediatric units in York, Bradford and Leeds and was distributed to NHS staff at neonatal units, paediatric intensive care units (PICUs) and principal oncology/haematology units nationwide. Summary results were presented narratively with accompanying tables and figures.

Results

Scoping review

From the database searches, 3830 records were identified for title and abstract screening, from which 289 records were selected as being of interest. After screening full papers, we included 26 group studies (of which two were comparative), six guidelines, three reviews and 106 case report studies.

The two comparative studies (which were not randomised trials) had limitations with respect to the particular outcomes and results relevant to this review. Many types of extravasation injury treatments have been studied in non-comparative studies; most studies were small and retrospective. Seventeen of the 24 non-comparative studies had sample sizes of < 20, and only three were reported as having a prospective design. There was considerable heterogeneity across study populations in age, types of infusate, injury severity, location of injury and the time gaps between injury identification and subsequent treatment. The treatments studied were grouped into these broad categories: conservative management approaches, saline flush-out techniques with or without prior hyaluronidase, hyaluronidase without flush-out, artificial skin treatments, debridement and plastic surgery. Limitations inherent in non-comparative studies made it difficult to compare results across treatments. Some results were likely to have been subject to chance effects or biases. Few studies reported data on the grading of injury severities and the results sections of most studies were minimal. No studies reported pain as an outcome and few studies quantified outcomes, for example, by using measures of scarring such as scar scores. Only one study reported on whether or not interventions resulted in adverse effects. All three of the identified reviews were in agreement that, although immediate treatment is needed for the best outcomes, there is no consensus regarding which treatments constitute best practice (Clifton-Koeppel R. Wound care after peripheral intravenous extravasation: what is the evidence? *Newborn Infant Nurs Rev* 2006;**6**:202–11; Gopalakrishnan PN, Goel N, Banerjee S. Saline irrigation for the management of skin extravasation injury in neonates. *Cochrane Database Syst Rev* 2012;**2**:CD008404; Harrold K, Gould D, Drey N. The management of cytotoxic chemotherapy extravasation: a systematic review of the literature to evaluate the evidence underpinning contemporary practice. *Eur J Cancer Care* 2015;**24**:771–800). All mentioned saline flush-out with or without hyaluronidase as a frequently studied treatment, but no review could make conclusive statements on its effectiveness compared with other treatments because of the limited quality of evidence. Overall, the results from the reviews and guidelines, which included evidence from studies in adults, added little to the primary study evidence in babies and children.

Survey

Sixty-three questionnaires were received from 56 different hospitals: 71% were from neonatal units, 21% were from principal oncology/haematology units and 8% were from PICUs. Most responders were consultant neonatologists (48%), nursing staff (16%) or consultant paediatricians (13%). Of 57 responding units, 82% said they had a written protocol or guideline for treating extravasation injuries, although a

staging system for grading injury severity was included in only around one-third of protocols or guidelines. Almost all responders indicated that peripheral lines were the access site most associated with extravasation injuries. In neonatal units, parenteral nutrition was the cause of the largest proportion of extravasation injuries. In principal oncology/haematology units, the largest proportion of injuries was due to vesicant chemotherapies.

The most frequently used intervention approaches were elevation of the affected area and analgesics. In most units warm or cold compresses were either rarely or never used. In neonatal units, there was notable variation regarding the use of occlusive dressings, ranging from always being used (8% of responses) to never being used (31% of responses). Variation in the use of saline flush-out, either with or without hyaluronidase, was also evident; these interventions seem to be either usually used or sometimes used in around half of neonatal units, and never used in around one-third of units. Results for principal oncology/haematology units and PICUs were broadly similar to the neonatal unit results.

When asked about a future research study, 65% of the 57 responders thought that a randomised controlled trial (RCT) might be viable, 21% did not think a RCT was viable and 14% did not know. However, the results varied by setting: the proportion thinking a RCT was viable was 83% of the 40 neonatal unit responses, 33% of the 12 principal oncology/haematology unit responses and 0% of PICU responses. Almost all of the responders who thought that a RCT was viable mentioned one or more of the following types of treatment when asked which treatments they would most like to see studied: saline irrigation/wash-out, hyaluronidase and conservative management. Of those who thought that a RCT was not viable, various reasons were provided including: the presence of too many variables which could affect outcomes, timeliness of treatment when using randomisation, low numbers of patients and unwillingness to deviate from current practice.

Conclusions

Studies exist that, together, cover a wide range of treatments for extravasation injuries. However, in considering the study methods and designs used, small sample sizes and the variation across population and intervention characteristics, the quality of evidence overall is very low. Consequently, there is uncertainty about which treatments are most promising, particularly with respect to treating earlier-stage injuries. Notwithstanding the evidence limitations, the results of studies of flush-out techniques suggest that these treatments may be worthy of further research. This finding was echoed in the NHS survey results, with flush-out techniques, hyaluronidase and conservative management approaches frequently suggested as being treatments where further study would be most worthwhile.

In planning a future comparative study of extravasation injury treatments, population heterogeneity and low rates and sporadic incidence of injuries are key issues. In the light of this, the most viable population for any randomised trial may be preterm neonates receiving i.v. parenteral nutrition at a peripheral site (but this is rare and not recommended). A paucity of standardised relevant outcome measures used in previous studies in neonates is a concern. Outcome measures used in a future study would need to be clinically practicable yet also demonstrate adequate reliability and validity. Some of the practicalities involved in undertaking a conventional RCT are the recruitment of adequate numbers of participants, avoiding treatment delays and selection bias. Although a prospective, observational database study would maximise the number of patients recruited, and eliminate concerns about treatment delays, its results would inherently be subject to uncertainty due to the likelihood of selection bias.

An alternative to a conventional RCT design is the randomised registry trial, which incorporates many of the best aspects of both conventional RCTs and observational database studies. However, a key relevant database {the UK National Neonatal Research Database [www.imperial.ac.uk/neonatal-data-analysis-unit/neonatal-data (accessed 27 July 2018)]} does not currently record data on extravasation injuries. Further issues to be considered in any randomised registry trial of neonates include the lack of a protocol or

guideline for treating extravasation injuries in 25% of units, and the absence of the use of a staging system for grading injury severity in over half of the units that do have access to a protocol or guideline.

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