A Summary of the Evidences Involved In Prevention of Neonatal Peripheral Venous Catheter Phlebitis

JOYNAUTH Jyotsnav¹, ZHOU Lian Juan¹, WU Shu Zhen¹

¹The Children's Hospital, Zhejiang University School of Medicine, Department of Neonatology, Zhejiang Province, Hangzhou, CHINA.
*Corresponding Author: Prof. Lizhong DU, The Children's Hospital, Zhejiang University School of Medicine, Department of Neonatology, No. 3333 Binsheng Road, Zhejiang Province, Hangzhou 310003, CHINA.

Abstract

Aim: Evaluating the best evidences for prevention of neonatal peripheral venous catheter (PVC) phlebitis.


Results: Two Guidelines, Eleven JBI, 14 Cochrane, 150 NCG papers were obtained. A total of 40 relevant literatures were retrieved from the Chinese Biomedical Literature CD-ROM Database in the Chinese Academic Full-Text Database. After de-duplication, 21 literatures of which 16 were in English and 5 in Chinese were obtained. Finally, the relevant guidelines’ title and abstract which amounted to 10 were screened. Lastly, 3 guidelines, 2 systematic evaluation and 5 original literatures were obtained. Conclusion: Neonatal departments should formulate relevant policies so that replacement of PVCs is carried out according to clinical indications. As latest evidence continues to be updated over time, the need to assess the hospital's characteristics and clinical environment is rising more than ever, in order to be able to target selected evidence for better treatment. Application of evidence-based neonatal care can reduce the incidence of peripheral phlebitis.

Key Words: Evidence-based Medicine, Phlebitis, Neonatal, Peripheral Venous Catheter

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I. Introduction

Premature or critically ill newborns often need to be fed with high nutritional content fluids intravenously. With the increasing use of PICC in newborns, most clinical studies have focused on the reduction of catheter-related phlebitis and complications by electrocardiographic localization of the tip of PICC, while less attention has been paid to peripheral venous catheters (PVC) [1]. Studies have shown that nearly 70% of adult patients admitted to wards need peripheral venous catheterization and intravenous drug therapy. [2] Its related complications include peripheral phlebitis, venous extravasation, catheter-related bacteremia (CRBSI) etc. The most common complication is phlebitis, with an incidence of 2.3%-60%. The incidence of CRBSI is low but could potentially lead to serious clinical consequences in about 0.1% of patients [3].

Newborns using PVC usually have a very low incidence of CRBSI [4]. However, the prevalence of infections may be relatively high, which remains undetected due to the short period of time the catheter is placed. Formation of biofilm and bacterial colonization of catheters are the main reasons causing catheter-related venous inflammation or bloodstream infection. Relevant neonatal studies have found that local complications are common, with 90% of the cannulas using PVC are associated with swelling and 3.2% of the cannulas usually develop into more serious complications [5]. Due of the fact that neonates have a relatively specific physiology compared to adults, adverse events caused by drug extravasation and phlebitis occur on a regular basis [6]. Evidence from the 2016 Intravenous Infusion Guideline on phlebitis is also specific to adults, with little emphasis on newborns [7]. The number of PVC used in neonatology is much larger than PICC. The use of peripheral catheters can increase the psychological and physiological pain of children, affect their resuscitation and treatment, thereby increasing the nursing tasks and prolong hospitalization time.

This study summarizes the best evidence for the prevention of neonatal PVC phlebitis, aiming to provide reference for the construction of clinical decision-making for the prevention and treatment of neonatal PVC phlebitis.

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II. Materials and Methods

2.1 Evidence Retrieval Strategy

Evidence-based Evidence Retrieval: PIPOST Construction.

Terms such as "neonate", "peripheral venous catheter" and "phlebitis" were used. Keywords in Chinese included: neonates, short peripheral catheters, catheters, peripheral phlebitis, prevention, treatment, intervention, evidence-based nursing, intravenous therapy, pathogens, bacteria, chemical, mechanical, vascular, suspicious, dysfunction. Terms in English included: Neonate* OR Newborn* OR Infant* OR Premature, “peripheral intravenous” OR “peripheral venous” OR “peripheral intra-vascular” Prevent* OR Protect* OR Intervene* OR Precaution OR Precautionary measures, Evidence-based, Infusion therapy, Pathogens OR Bacteria, Chemical, Mechanical, Blood vessel, Suspicious OR Dubious*, dysfunction.


Search Results: A total of 40 relevant literatures were retrieved from the Chinese Biomedical Literature CD-ROM Database in the Chinese Academic Full-Text Database. After de-duplication, 21 literatures of which 16 were in English and 5 in Chinese were obtained. Finally, the relevant guidelines’ title and abstract which amounted to 10 were screened. Lastly, 3 guidelines, 2 systematic evaluation and 5 original literature were obtained.

2.1.1 Inclusion and exclusion criteria of evidence

Evidence types: clinical practice guidelines, best clinical practice and systematic evaluation. Research scope was set to "hospitalization". Time limit: 2012-present. Study population: Neonates born within 28 days after umbilical cord ligation, including full-term and premature infants. Exclusion criteria: Abstract of clinical practice guides with incomplete information, incomplete recommended practices and summaries of published evidence of systematic evaluation. The language of publication searched was limited to English and Chinese.

2.2 Evidence Evaluation Criteria

2.2.1 Quality Evaluation Criteria of Guidelines

Appraisal of guidelines for research and evaluation (AGREE 11), from the year 2012 was used [11]. Each item was evaluated by a scoring system of 1-7 points (1 = disagreement, 7 = agreement). The score of each field was equal to the sum of the scores of all items in the field and was standardized as the percentage of the highest possible score in the respective field. The calculation method used was standardized percentage of scores in each field = the actual score / the lowest possible score * 100%.

2.2.2 Quality Evaluation Criteria for Systematic Evaluation

AMSTAR (Assessment of Multiple Systematic Reviews) tool was used to carry out a methodical evaluation [12]. A total of 11 items were evaluated and classified according to their qualities which were: high, general, poor, unclear and lastly, inappropriate.

2.2.3 Quality evaluation criteria for original research

The quality evaluation criteria of randomized controlled trials (RCTs) were evaluated by the Australian JBI Evidence-based Health Care Center Randomized Controlled Trials Evaluation Criteria (2016). The quality evaluation criteria of cohort studies were evaluated by the JBI Evidence-based Health Care Center (2016) in Australia [13]. Expert consensus quality evaluation criteria such as the Australian JBI Evidence-based Health Care Center Expert Consensus Evaluation Criteria (2016) were used to evaluate such studies [13]. This study included three guidelines [9, 14, 15], one randomized controlled trial [16], two cohort studies [17, 18], two expert consensus [19, 20] and two systematic reviews [21, 22].

2.2.4 Evidence Quality Evaluation Process

Several researchers independently graded and evaluated the literatures according to the quality evaluation criteria set. Whenever agreements could not be reached, a third researcher (expert in evidence-based methodology) intervened and consensus was reached whereby inclusion or exclusion was decided. When the evidence from different sources conflicted, priority was given to evidence-based evidence, high-quality evidence, evidence publication time and domestic guidelines from an ascending to descending basis.
III. Results

3.1 The general characteristics of the literature included in this paper are shown in Table 1. Three guidelines [9, 14-15], one randomized controlled trial [16], two cohort studies [17-18], two expert consensus [19, 20] and two systematic reviews [21-22] were included.

3.2 Quality evaluation results included in the study

3.2.1 Quality Evaluation Results of Guidelines

This study included three guidelines, all of which were independently evaluated by four evaluators. The standardized percentage of each field and the average score of two comprehensive evaluations are shown in Table 2.

3.2.2 Quality Evaluation Results of Systematic Evaluation

This study included two systematic evaluation [21-22], from the Cochrane Library database, comprising of a total of 11 items, including Sinha A and other [21] studies. 8 of which were "yes", 2 of them were "No" and 1 unclear. Item 5 was as follows: "Is there a list of studies on inclusion and exclusion criteria included?". Item 11: "Does it indicate a conflict of interest?", both of which were "no", added with item 4: "Has the publication status been considered in the inclusion criteria, such as grey literature?" for which results were "unclear". The research design was relatively complete and the overall quality was high to such an extent that it was included in Zheng G H and other [22] studies.

3.2.3 Quality Evaluation Results of Randomized Controlled Trials

One randomized controlled trial evaluated in this study was from the BMJ database [16]. In Kieran E A, et al. [16], all items were evaluated except Item 8: "Is the follow-up complete, if incomplete, were measures taken to deal with irregular visits?", Item 12, "Is the data analysis method appropriate?". The evaluation result was "unclear", other items were "yes", Research design which were relatively complete and of high quality were allowed to be included.

3.2.4 Quality evaluation results of Cohort Studies

Two cohort studies were evaluated in this study and two [17-18] were from the original literatures of LinPubmed and BMJ databases. Among them, Danski M T et al. [17] item 4, "whether the confounding factors are taken into account?" and item 5, "whether the measures are taken to control the confounding factors?" had an evaluation result of "no", while all the other results were "yes". Therefore the research design was relatively complete, of high quality and was allowed to be included. Similarly for Lma J et al. [18] The evaluation results of the study were all "yes" except for items 9 and 10 which were "no". The design of the study was relatively complete and the overall quality was high, so it was allowed to be included.

3.2.5 Quality Evaluation Results of Expert Consensus

Two expert consensus [19-20], one [19] from BMJ database and the other [20] came from the official website of People's Human Health, which proceeded for evaluation. The evaluation results of the two expert consensus items were all "yes" and their research design was complete and the overall quality was high, so they were allowed to be included.

3.3 Evidence Description and Summary

This study used JBI Evidence-based Health Care Center Evidence Classification and Evidence Recommendation Level System (2014) in Australia to evaluate and classify the included evidence. According to the different types of research designs, the evidence grade was categorized into 5 levels, namely Level 1-5.

3.4 Summary of the Best Evidence

After FAME evaluation of evidence, items number 3/4/5 were not included because they were inappropriate, not recommended or did not match the age characteristics. Evidence in Article 1 does not describe the PH value but only the osmotic pressure range. Wang Jianrong [14] Gorski LA and others [15] believe that besides osmotic pressure, drugs given via peripheral veins need to in an optimal PH range of 5-9 to reduce phlebitis, especially in neonates where peripheral blood vessels are thin and slight stimulation can cause phlebitis. The evidence finally demonstrates that chemical phlebitis may be caused by one of the following reasons: content of glucose in liquid drugs higher than 10%, or osmotic pressure > 900 mOsm/L and lastly PH value < 5 or > 9. Certain medicines (depending on the dosage and length of infusion), such as potassium chloride, amiodarone, antibiotics and particulate matter in liquid medicines; excessive diameter of catheter; undried disinfectant, enter the vein during catheter placement. The use of midline catheters or central venous catheters via peripheral puncture for the drugs and reasons listed above causes phlebitis, which in turn, depends on the
length of infusion and the expected duration of treatment. When disinfectant is used, the skin becomes dry thoroughly (Grade IV evidence).

Evidence from article number 14 has 1 expert consensus, 2 systematic reviews and 2 cohort studies published after 2016 [20-22] all of which strictly follow the protocols of evaluation. It also includes the latest available evidence: ethanol solution containing more than 0.5% chlorhexidine can be used in newborns but poses a risk of skin burns in allergic children and attention should be paid when used in preterm infants less than 26 weeks whereby 0.2% chlorhexidine solution was deemed as more appropriate, but the disinfecting potency needs to be further studied. The above-mentioned information is an update from the 2016 guideline for intravenous infusion. The evidence level of the conclusions is IV. The evidences gathered, timely drug intervention, post-removal monitoring, dressing replacement, hand hygiene, disinfectant selection, fixation and other eight aspects were summarized and 14 best evidences were established, as shown in Table 4.

**Table 1: Evidence Sources and their Respective Information(s).**

<table>
<thead>
<tr>
<th>Source of Evidence</th>
<th>Type of Evidence</th>
<th>Contents of Evidence</th>
<th>Date of Publication</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMJ[9]</td>
<td>Randomized controlled study</td>
<td>2% chlorhexidine–70% isopropyl alcohol versus 10% povidone–iodine for insertion site cleaning before central line insertion in preterm infants: a randomized trial</td>
<td>2017</td>
</tr>
<tr>
<td>BMJ[19]</td>
<td>Cohort Research</td>
<td>0.2% chlorhexidine acetate as skin disinfectant prevents skin lesions in extremely preterm infants: a preliminary report</td>
<td>2017</td>
</tr>
<tr>
<td>BMJ***</td>
<td>Expert Consensus</td>
<td>Catheter sepsis and antisepsis: matters off life, death, obscurity and resistance</td>
<td>2018</td>
</tr>
<tr>
<td>Cochrane Library***</td>
<td>Systematic Evaluation</td>
<td>Chlorhexidine skin or cord care for prevention of mortality and infections in neonates</td>
<td>2015</td>
</tr>
</tbody>
</table>

**Table 2: Articles and their Respective Recommendations**

<table>
<thead>
<tr>
<th>Articles</th>
<th>Percentage standardization in various fields (%)</th>
<th>≥60%</th>
<th>≥30%</th>
<th>Degree to which it is recommended[a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016INS[9]</td>
<td>91.67 81.25 84.52 86.46 65.28 87.5</td>
<td>6</td>
<td>6</td>
<td>A</td>
</tr>
<tr>
<td>Pubmed[15]</td>
<td>86.11 87.5 80.36 79.17 59.72 72.92</td>
<td>5</td>
<td>6</td>
<td>B</td>
</tr>
<tr>
<td>Wang Jian Rong[14]</td>
<td>83.33 56.25 58.33 77.08 45.83 72.92</td>
<td>3</td>
<td>6</td>
<td>B</td>
</tr>
</tbody>
</table>

[a]: A implies strongly recommended, B implies less recommended.
Mechanical phlebitis may be caused by the stimulation of vessel wall, which may be caused by excessive catheter size relative to vessel lumen, catheter activity, trauma caused by insertion or by the hardness of the catheter. Therefore the smallest catheter should be chosen as far as possible for intravenous infusion, such as 20 or 20 Ga, and a fixator should be used to stabilize the catheter; catheterization at the limb flexion site should be avoided and joints should be stabilized as needed.

Chemical phlebitis: Evaluate infusion therapy and the need for different vascular access devices, different drugs or lower infusion velocity to determine whether catheter removal is necessary. Provide the corresponding interventions mentioned above

Bacterial phlebitis: Catheter should be fixed; hot compress can be carried out, limb elevation and monitoring for 24-48 hours should be performed and if the duration of symptoms and signs exceeds 48 hours, removal of catheter should be considered.

Bacterial phlebitis: If in doubt, the catheter should be removed. When removing vascular access devices, evaluation should be carried out by specialist nurses to decide whether alternative vascular access devices should be used or not.

Post-infusion phlebitis: If infection is bacterial, the signs of systemic infection should be monitored: if it is non-bacterial, hot compress should be given, the affected limbs should be elevated, sedative drugs should be provided as required and other drug interventions should be considered, such as the use of anti-inflammatory drugs or corticosteroids, when the need arises.

When removing a peripheral venous needle, a midline catheter or a central venous catheter through peripheral puncture, the puncture site should be monitored for 48 hours in order to detect the phlebitis after infusion in time; or when discharged, the patient and/or the caregiver should be informed of the symptoms and signs of phlebitis in writing and a contact detail in case of phlebitis.

For neonates and children, peripheral venous indwelling needles should be evaluated hourly; for patients receiving blister infusion, the frequency should be increased. [17]

The puncture site should be cared handled immediately whenever dampness, loosening or visible stains are found under the dressing or when moisture, exudation or blood is found under the dressing, including skin disinfection and dressing replacement. Peripheral venous indwelling needle should be replaced at every least 5-7 days[4].

Hygienic procedures should be strictly enforced before and after touching the puncture site, before, after inserting, resetting and touching the catheter. Soap and water, or hand liquid wiped with ethanol can be used[5,6].

In addition to osmotic pressure, drugs with PH ranging from 5 to 9 should be used in peripheral veins to reduce phlebitis.

Ethanol solution containing more than 0.5% chlorhexidine can be used in newborns but poses a risk of skin burns in allergic children and attention should be paid when used in preterm infants less than 26 weeks whereby 0.2% chlorhexidine solution is deemed as appropriate, but the disinfecting potency needs to be further studied.

Table 3: Summary of evidence(s).

<table>
<thead>
<tr>
<th>Items</th>
<th>Contents of Evidence</th>
<th>Evidence Grade[a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Chemical phlebitis may be caused by the following reasons: glucose content in liquid medicines is greater than 10% or osmotic pressure &gt;900 mOsm/L; certain medicines (depending on infusion dose and time length), such as potassium chloride, amiodarone and some antibiotics; particulate matter in liquid medicines; blood vessels with insufficient blood volume, for example, large diameter catheter; disinfectant solution not completely dry and enters the vein during the catheter placement. The use of midline catheters or central venous catheters via peripheral puncture for the drugs listed or identified above that cause phlebitis depends on the length of infusion and the expected duration of treatment. Therefore after using the disinfectant, let the skin should be allowed to dry completely.</td>
<td>IV</td>
<td></td>
</tr>
</tbody>
</table>
FTER using the disinfectant, let the skin dry and the need for different vascular access devices should be carried out by nurses, including skin disinfection and dressing replacement.

10% ethanol solution containing more than 0.5% chlorhexidine can be used in newborns but poses a risk of skin burns in allergic children and attention should be paid when used in preterm infants less than 26 weeks whereby 0.2% chlorhexidine solution is deemed as appropriate, but the disinfecting potency needs to be further studied.

This study summarized the best evidence for prevention and treatment of neonatal peripheral venous catheter phlebitis. The authors suggest that professional nurses in venous therapy should evaluate the risk factors of phlebitis individually and dynamically according to best evidence and carry out effective management of phlebitis in high-risk groups according to relevant guidelines, so as to ensure the safety of peripheral veins in neonates.

### IV. Conclusion

This study summarized the best evidence for prevention and treatment of neonatal PVC phlebitis and provided enough evidence for medical institutions to establish systems, procedures and practical standards for the evaluation and intervention in neonatal peripheral venous phlebitis. The authors suggest that professional nurses in venous therapy should evaluate the risk factors of phlebitis individually and dynamically according to the best evidence and carry out effective management of phlebitis in high-risk groups according to relevant guidelines, so as to ensure the safety of peripheral veins in neonates.

### Declaration of conflicting interests

The authors declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

### Ethical approval

This study was approved by the Ethics committee The Children's Hospital, Zhejiang University School of Medicine.

### Table 4: Summary of the best evidences found in this study.

| Item | Contents of Evidence | Evidence Grade [

| 1 | Chemical phlebitis may be caused by the following reasons: glucose content in liquid medicines is greater than 10% or osmotic pressure >900 mOsm/L; certain medicines (depending on infusion dose and time length), such as potassium chloride, amiodarone and some antibiotics; particulate matter in liquid medicines; blood vessels with insufficient blood volume, for example, large diameter catheter; disinfectant solution not completely dry and enters the vein during the catheter placement. The use of midline catheters or central venous catheters via peripheral puncture for the drugs listed or identified above that cause phlebitis depends on the length of infusion and the expected duration of treatment. Therefore after using the disinfectant, let the skin be allowed to dry completely. | IV |

| 2 | Mechanical phlebitis may be caused by the stimulation of vessel wall, which may be caused by excessive catheter size relative to vessel lumen, catheter activity, trauma caused by insertion or by the hardness of the catheter. Therefore the smallest catheter should be chosen as far as possible for intravenous infusion, such as 20 or 20 Ga; and a fixator should be used to stabilize the catheter; catheterization at the limb flexion site should be avoided and joints should be stabilized as needed. | IV |

| 3 | Chemical phlebitis: Evaluate infusion therapy and the need for different vascular access devices, different drugs or lower infusion velocity to determine whether catheter removal is necessary. Provide the corresponding interventions mentioned above. | IV |

| 4 | Mechanical phlebitis: Catheter should be fixed; hot compress should be given, the affected limbs should elevate and monitoring for 24-48 hours should be performed and if the duration of symptoms and signs exceeds 48 hours, removal of catheter should be considered. | V |

| 5 | Bacterial phlebitis: If in doubt, the catheter should be removed. When removing vascular access devices, evaluation should be carried out by specialist nurses to decide whether alternative vascular access devices should be used or not. | IV |

| 6 | Post-infusion phlebitis: If infection is bacterial, the signs of systemic infection should be monitored; if it is non-bacterial, hot compress should be given, the affected limbs should be elevated, sedative drugs should be provided as required and other drug interventions should be considered, such as the use of anti-inflammatory drugs or corticosteroids, when the need arises. | V |

| 7 | When removing a peripheral venous needle, a midline catheter or a central venous catheter through peripheral puncture, the puncture site should be monitored for 48 hours in order to detect the phlebitis after infusion in time; or when discharged, the patient and/or the caregiver should be informed of the symptoms and signs of phlebitis in writing and a contact detail in case of phlebitis. | V |

| 8 | For neonates and children, peripheral venous indwelling needles should be evaluated hourly; for patients receiving blister infusion, the frequency should be increased. [7] | IV |

| 9 | The puncture site should be cared handled immediately whenever dampness, loosening or visible stains are found under the dressing or when moisture, exudation or blood is found under the dressing, including skin disinfection and dressing replacement. Peripheral venous indwelling needle should be replaced at every least 5-7 days [8]. | V |

| 10 | Hygienic procedures should be strictly enforced before and after touching the puncture site, before, after inserting, resetting and touching the catheter. Soap and water, or hand liquid wiped with ethanol can be used [9,10]. | V |

| 11 | In addition to osmotic pressure, drugs with PH ranging from 5 to 9 should be used in peripheral veins to reduce phlebitis. | V |

| 12 | Ethanol solution containing more than 0.5% chlorhexidine can be used in newborns but poses a risk of skin burns in allergic children and attention should be paid when used in preterm infants less than 26 weeks whereby 0.2% chlorhexidine solution is deemed as appropriate, but the disinfecting potency needs to be further studied. | IV |

**[b]** Grade V represents the most superior Grading; Grade I represents the most inferior Grading.
**References**


