TITLE: Chlorhexidine Gluconate (CHG) for Suturing in the Emergency Room and Perineal Washing During Vaginal Deliveries: A Review of Safety, Evidence-Based Guidelines and Recommendations

DATE: 04 June 2012

CONTEXT AND POLICY ISSUES

Open injuries have a potential for serious bacterial wound infections and may lead to long term disabilities, chronic wound or bone infection, and death. Therefore, it is important to manage injuries appropriately to reduce the likelihood of wound infections.

In addition to affecting open wounds, infection is a serious contributor to maternal and neonatal mortality and morbidity in developing and developed countries, with over 3 million neonatal deaths and 350,000 maternal deaths occurring annually worldwide. Maternal vaginal bacteria is a potential agent for neonatal infection and vaginal disinfection may be an important step to reducing infection rates.

Chlorhexidine belongs to a class of compounds known as bis-biguanides that can bind tightly to bacterial cell walls and disrupt osmotic equilibrium, resulting in eventual cell death. In addition to its antibacterial properties, chlorhexidine has low allergic and toxic potential and possesses an excellent resistance profile. Consequently, chlorhexidine is widely used in hospital settings as a topical skin antiseptic to reduce infection. Chlorhexidine is used in the forms of acetate, gluconate, or hydrochloride, primarily in an aqueous or saline solution for vaginal disinfection, either alone or in combination with other antiseptics.

The purpose of this review is to examine the safety and guidelines regarding the use of chlorhexidine gluconate (CHG) for suturing open wounds in the emergency room and for perineal washing during vaginal deliveries.

RESEARCH QUESTIONS

1. What is the safety of CHG for suturing in the emergency room and for perineal washing during vaginal deliveries?
2. What are the evidence-based guidelines and recommendations for the use of CHG prior to suturing in the emergency room?

3. What are the evidence-based guidelines and recommendations for the use of CHG as perineal wash during vaginal deliveries?

KEY MESSAGE

Evidence from two systematic reviews suggests that chlorhexidine for perineal and vaginal washing during labour does not appear to prevent maternal and neonatal infections; one guideline recommends that water be used for vaginal cleansing. No literature was identified regarding the safety or use of chlorhexidine prior to suturing in the emergency room. No literature was identified that specifically used chlorhexidine gluconate solution for these indications.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2012, Issue 4), University of York Centre for Reviews and Dissemination (CRD), Ebsco CINAHL, ECRI (Health Devices Gold) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No methodological filters were applied to limit retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2007 and May 4, 2012.

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and evaluated the full-text publications for the final article selection, according to selection criteria presented in Table 1.

Table 1: Selection Criteria

| Population | Patients of any age appearing at the trauma center or emergency room with an open wound or lacerations
|            | Patients of any age in the obstetrics population having a vaginal delivery |
| Intervention | Chlorhexidine |
| Comparator  | Other antiseptics, placebo, no treatment |
| Outcomes   | Safety, tissue damage and degradation, infection, guidelines and best practices |
| Study Designs | Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials (RCTs), observational studies, and evidence-based guidelines |
Exclusion Criteria

Studies were excluded if they did not meet the selection criteria, were duplicate publications or included in a selected systematic review, or were published prior to 2007.

Critical Appraisal of Individual Studies

The quality of included systematic reviews was assessed using the Assessment of Multiple Systematic Reviews (AMSTAR) tool. Guidelines were assessed for quality using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument. A numeric score was not calculated for each study. Instead, strengths and limitations of each systematic review and guideline were summarized and described.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 71 citations. Upon screening titles and abstracts, no potentially relevant articles were retrieved for full-text review. An additional 6 potentially relevant reports were identified through grey literature and hand searching. Of the 6 potentially relevant reports, 3 did not meet the inclusion criteria. Three publications were included in this review. The study selection process is outlined in a PRISMA flowchart (Appendix 1). Two systematic reviews and one evidence-based guideline regarding the use of chlorhexidine for perineal wash during vaginal deliveries were identified. No literature was identified regarding the safety or use of chlorhexidine prior to suturing in the emergency room.

Summary of Study Characteristics

Study design

Two systematic reviews\(^5\,10\) and one guideline\(^11\) were included in this review. Details on study characteristics, critical appraisal, and findings can be found in Appendices 2, 3 and 4, respectively.

Patient population

All studies included pregnant women who were considered to be in labour. One systematic review only included pregnant women with gestational age greater than 28 weeks.\(^5\) The other systematic review included pregnant women with vaginal or rectal colonization with group B \(\beta\)-hemolytic streptococcus (GBS) confirmed by culture or a rapid screening test. The guideline provided recommendations on vaginal cleansing during labour to protect women, babies, and healthcare professionals.\(^11\)

Interventions and comparators

Both systematic reviews compared various formulations of chlorhexidine to placebo (water or placebo gel) or no treatment.\(^5\,10\) One systematic review included two studies that used 200 mL of 0.2% chlorhexidine solution for vaginal washing and one study that used 20 mL of 0.4% chlorhexidine solution.\(^5\) The other systematic review included five studies that used various...
formulations of chlorhexidine: 0.3% chlorhexidine digluconate gel; 0.2% chlorhexidine diacetate solution; 0.05% chlorhexidine acetate solution; 5 mL of 1% chlorhexidine digluconate cream; and 0.2% chlorhexidine diacetate solution.\textsuperscript{10} The guideline provided recommendations on the use of chlorhexidine vaginal douching for cleansing during labour.\textsuperscript{11}

Outcomes measured

The main study outcomes in one systematic review\textsuperscript{5} included infection and complications for the mother and neonate, but excluded group B streptococcal and HIV infections. Maternal outcomes included chorioamnionitis, fever, endometritis, and mortality, while neonatal outcomes included pneumonia, meningitis, sepsis, and mortality. In the other systematic review,\textsuperscript{10} the main study outcomes were early-onset neonatal infection with GBS, neonatal colonization with GBS within the first seven days of life, and mortality due to early-onset GBS infection.

Summary of Critical Appraisal

The methodological quality of evidence identified was high. Both systematic reviews\textsuperscript{5,10} were based on comprehensive literature searches and the scientific quality of included studies were assessed and described in detail. Unpublished studies were searched for and duplicate study selection and data extraction was performed in both systematic reviews. Publication bias was not assessed in either systematic review, but it was specifically stated in the reports that only systematic reviews that included 10 or more studies would be assessed for publication bias and neither systematic review included this many studies.

The evidence-based guideline\textsuperscript{11} had a clear objective, scope, and target population and was developed using clear methodology by appropriate professional groups with patient representation. Existing relevant guidelines were identified and a systematic search strategy using multiple databases was employed to identify published evidence. Unpublished literature was also searched, but without a systematic approach. Recommendations were derived directly from the evidence that supported them and levels of evidence supporting each recommendation were provided. Potential barriers and cost implications of applying the recommendations were not considered in the guideline.

Summary of Findings

What is the safety of CHG for suturing in the emergency room and for perineal washing during vaginal deliveries?

One systematic review examined the effectiveness of chlorhexidine vaginal douching during labour on maternal and neonatal outcomes.\textsuperscript{5} This review included three RCTs for a total of 3012 pregnant women. When the data from the RCTs were pooled, there was no statistically significant difference in the maternal incidence of chorioamnionitis or postpartum endometritis between chlorhexidine and placebo groups. With regards to neonatal outcomes, no significant difference in the incidence of pneumonia, meningitis, blood culture confirming sepsis, or mortality was found between chlorhexidine and placebo groups. The side effects of chlorhexidine were not reported in any of the three RCTs.

Another systematic review examined the effectiveness of vaginal disinfection with chlorhexidine during labour for preventing early-onset GBS infection in preterm and term neonates.\textsuperscript{10} This review included five RCTs for a total of 2190 term and preterm infants. Data from these RCTs
found no statistically significant reduction of neonatal early-onset GBS, pneumonia, or meningitis between in the chlorhexidine group versus placebo or no treatment. However, there was a statistically significant reduction in neonatal colonization with GBS in the chlorhexidine group. No notable neonatal adverse events were reported and no statistically significant difference in the incidence of maternal adverse events between chlorhexidine and placebo or no treatment groups were found. Maternal adverse events that were reported included stinging or local irritation.

Subgroup analysis comparing chlorhexidine vaginal washing with mechanical washing with saline or water showed a statistically significant reduction in neonatal GBS colonization in the chlorhexidine group. Subgroup analysis based on methods of chlorhexidine administration and preparation was also performed and showed that chlorhexidine digluconate gel or cream reduced the incidence of neonatal GBS colonization, though there was no significance in relative risk.

What are the evidence-based guidelines and recommendations for the use of CHG prior to suturing in the emergency room?

No evidence-based guidelines for the use of chlorhexidine prior to suturing in the emergency room was identified.

What are the evidence-based guidelines and recommendations for the use of CHG as perineal wash during vaginal deliveries?

One guideline provided recommendation on the use of chlorhexidine as perineal wash during vaginal deliveries. This guideline, developed by the National Collaborating Centre for Women’s and Children’s Health (NCC-WCH), states (p. 88): “Tap water may be used if cleansing is required prior to vaginal examination.” This recommendation was based on what was considered high quality evidence from one systematic review that was included in this report and one well-conducted controlled study that compared centrimide/chlorhexidine to tap water for perineal cleaning during labour. In both the systematic review and study, there was no evidence to suggest that the use of chlorhexidine was more effective than water for perineal cleaning during labour.

Limitations

In both systematic reviews, a limited number of studies were identified that reported on the maternal and neonatal outcomes of interest and individual study sample sizes were relatively small, limiting the power to detect small effect size. In addition, the studies identified in both systematic reviews used a variety of chlorhexidine volumes and formulations, making it difficult to determine what is the appropriate concentration and volume of vaginal chlorhexidine irrigation solution and to generalize results to other chlorhexidine formulations. Studies using chlorhexidine gluconate solution were not identified in either systematic review.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

The use of chlorhexidine for perineal and vaginal wash during labour does not appear to prevent maternal and neonatal infections when compared to water or no treatment. Although chlorhexidine was associated with a reduction in neonatal GBS colonization, this did not translate to a reduction in neonatal sepsis, pneumonia, meningitis, or mortality. However,
limited data suggested that chlorhexidine is safe for both the mother and neonate when used for vaginal cleansing during labour. There is a need for a well-designed, randomized controlled trial with adequate sample size and relevant outcomes.

One guideline recommended that tap water be used instead of chlorhexidine if vaginal cleansing is required. Therefore, it appears that chlorhexidine is not required for perineal wash during vaginal deliveries.

No evidence was identified regarding the safety and use of chlorhexidine prior to suturing in the emergency room.

PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca
REFERENCES


APPENDIX 1: Selection of Included Studies

71 citations identified from electronic literature search and screened

71 citations excluded

0 potentially relevant articles retrieved for scrutiny (full text, if available)

6 potentially relevant reports retrieved from other sources (grey literature, hand search)

6 potentially relevant reports

3 reports excluded:
- already included in at least one of the selected systematic reviews (1)
- other (review articles, editorials) (2)

3 reports included in review
APPENDIX 2: Characteristics of Included Systematic Reviews

<table>
<thead>
<tr>
<th>First Author, Publication Year, Country</th>
<th>Patient Characteristics</th>
<th>Intervention</th>
<th>Comparator(s)</th>
<th>Clinical Outcomes Measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbiganon* 2011 Thailand</td>
<td>3 RCTs including 3012 pregnant women with gestational age greater than 28 weeks considered to be in labour</td>
<td>Chlorhexidine vaginal douching during labour (n=1514) - 2 RCTs used 200 mL of 0.2% chlorhexidine, 1 RCT used 20 mL of 0.4% chlorhexidine</td>
<td>Sterile water placebo (n=1498)</td>
<td>Infection and complications for the mother and neonate</td>
</tr>
<tr>
<td>Stade* 2008 Canada</td>
<td>5 RCTs including 2190 women with vaginal or rectal colonization with GBS (confirmed by culture or rapid screening test) during labour</td>
<td>Chlorhexidine vaginal wash or gel application during onset of labour - Chlorhexidine formulations used: 0.3% chlorhexidine digluconate gel; 0.2% diacetate chlorhexidine solution; 0.05% chlorhexidine acetate solution; 5 mL of 1% chlorhexidine digluconate cream; 0.2% diacetate chlorhexidine solution</td>
<td>Placebo (water or placebo gel) No intervention</td>
<td>Early-onset neonatal infection with GBS</td>
</tr>
</tbody>
</table>

GBS=group B β-hemolytic streptococcus; RCT=randomized controlled trial
APPENDIX 3: Summary of Critical Appraisal of Included Studies

<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systematic Reviews</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumbiganon⁷ 2011</td>
<td>• Comprehensive literature search based on pre-defined criteria</td>
<td>• Risk of publication bias not assessed</td>
</tr>
<tr>
<td></td>
<td>• Summary of study characteristics and list of included and excluded studies provided</td>
<td>• Included studies used differing volumes of chlorhexidine solution</td>
</tr>
<tr>
<td></td>
<td>• Scientific quality and risk of bias of included studies assessed and documented</td>
<td></td>
</tr>
<tr>
<td>Stade⁴ 2008</td>
<td>• Comprehensive literature search based on pre-defined criteria</td>
<td>• Risk of publication bias not assessed</td>
</tr>
<tr>
<td></td>
<td>• Summary of study characteristics and list of included and excluded studies provided</td>
<td>• Included studies used a variety of chlorhexidine formulations</td>
</tr>
<tr>
<td></td>
<td>• Scientific quality and risk of bias of included studies assessed and documented</td>
<td></td>
</tr>
<tr>
<td><strong>Guidelines</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>National Collaborating Centre for Women’s and Children’s Health¹¹ 2007</td>
<td>• Clearly defined objectives, scope and target populations</td>
<td>• Potential barriers and cost implications of applying the recommendations not considered in detail</td>
</tr>
<tr>
<td></td>
<td>• Guideline development group included individuals from relevant professional groups and patient representation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Guideline development methodology clearly described</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Recommendations are directly linked to evidence</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Guideline was externally reviewed prior to publication</td>
<td></td>
</tr>
</tbody>
</table>
### APPENDIX 4: Summary of Findings of Included Systematic Reviews

<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Main Study Findings</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lumbiganon</strong>&lt;sup&gt;3&lt;/sup&gt; 2011</td>
<td>Pooled data from three trials (n=3012) found no statistically significant difference in the maternal incidence of chorioamnionitis between the chlorhexidine and placebo groups (RR 1.10, 95% CI 0.86-1.42). Data from these three trials suggested a small reduction in the risk of postpartum endometritis in the chlorhexidine group, but the difference was not statistically significant (RR 0.83, 95% CI 0.61-1.13). One trial (n=910) found no significant difference in the incidence of neonatal pneumonia between the two groups (RR 0.33, 95% CI 0.01-8.09). One trial (n=1021) found no significant difference in neonatal meningitis between the two groups (RR 0.034, 95% CI 0.01-8.29). Two trials (n=2077) found no significant difference in blood culture confirming sepsis (RR 0.75, 95% CI 0.17-3.35) and perinatal mortality (RR 1.00, 95% CI 0.17-5.79). Side effects of chlorhexidine were not reported in the three trials.</td>
<td>“There was no evidence of an effect of vaginal chlorhexidine during labour in preventing maternal and neonatal infections.” p. 8</td>
</tr>
<tr>
<td><strong>Stade</strong>&lt;sup&gt;10&lt;/sup&gt; 2008</td>
<td>Chlorhexidine versus placebo or no treatment Pooled data from two studies (n=987) found no statistically significant reduction of neonatal early-onset GBS (RR 2.32, 95% CI 0.34-15.63) or neonatal early-onset GBS pneumonia (RR 0.35, 95% CI 0.01-8.60) in the chlorhexidine group versus placebo or no treatment. Three studies (n=1066) found no statistically significant reduction in neonatal GBS meningitis (RR 0.35, 95% CI 0.01-8.60). Pooled data from three studies (n=328) found a statistically significant (P=0.006) reduction in neonatal colonization with GBS (RR 0.72, 95% CI 0.56-0.91) in the chlorhexidine group versus placebo or no treatment. Two studies found no neonatal death due to early-onset GBS infection. Four studies (n=2131) found no notable neonatal</td>
<td>“There were no statistically significant reductions in early-onset GBS sepsis, early-onset GBS pneumonia, early-onset GBS meningitis, or mortality due to early-onset GBS infection. There was no statistically significant between-study heterogeneity for these outcomes. Adverse effects to the mother were minor: stinging or local irritation. There was statistically significant between-study heterogeneity for this outcome. This heterogeneity might be explained by differences in preparation; differences in dose or frequency of dose, or both; differences in reported outcomes. No adverse effects to the infant were noted.” p. 7</td>
</tr>
</tbody>
</table>
Chlorhexidine Gluconate for Suturing in the Emergency Room and Perineal Wash for Vaginal Deliveries

<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Main Study Findings</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>adverse events.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Four studies found no statistically significant difference in the incidence of maternal adverse events (RR 1.88, 95% CI 0.90-3.96) between the chlorhexidine and placebo/no treatment groups. Adverse events that were reported including stinging or local irritation.</td>
<td></td>
</tr>
<tr>
<td>Chlorhexidine wash versus mechanical washing with placebo</td>
<td>One study (n=79) showed a statistically significant reduction in neonatal GBS colonization (RR 0.32, 95% CI 0.12-0.90) in the chlorhexidine group compared to mechanical washing with placebo.</td>
<td></td>
</tr>
<tr>
<td>Chlorhexidine digluconate gel or cream versus placebo or no treatment</td>
<td>Two studies (n=249) showed a statistically significant reduction in neonatal GBS colonization, but no significance in RR (0.79, 95% CI 0.62-1.00).</td>
<td></td>
</tr>
</tbody>
</table>

CI=confidence interval; GBS=group B β-hemolytic streptococcus; RR=relative risk