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Randomized study of vaginal chlorhexidine disinfection during labor to prevent vertical transmission of group B streptococci


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Abstract

Objective: To evaluate the effect of vaginal disinfection with chlorhexidine gel during labor on vertical transmission of group B streptococcus, as a method to prevent vertical transmission and subsequent neonatal early onset group B streptococcal disease.

Study Design: A prospective study with randomization of 1020 parturients to one of three groups as soon as labor started. In all parturients, anus, introitus and cervix were cultured semiquantitatively. Two groups were treated double-blindly with 10 ml of either a 0.3% chlorhexidine gel or a placebo gel, applicated around the portio and into the fornices. If labor still continued, a second application was given after 10 h. The third group received no treatment. Ear, pharynx and umbilicus of all newborns were also cultured semiquantitatively. Results: Nine hundred and eighty one women were evaluated. The overall incidence of group B streptococcal carriership was 19.4%. Vertical transmission was 52.4% in the chlorhexidine group, 71.4% in the placebo group and 66.7% in the control group ($P = 0.069$). When testing the transmission rates for the chlorhexidine versus the combined placebo plus control group (69.3%), the difference was 16.9% ($P = 0.026$). Conclusion: Vaginal disinfection with a chlorhexidine gel during labor modestly reduces group B streptococcal vertical transmission. Because the method is cheap, simple and safe, it should be considered for routine use. Our results indicate that it may reduce the incidence of early onset group B streptococcal sepsis by 2–32%.

Keywords: Streptococcus agalactiae; Primary prevention; Septicemia; Disinfection; Chlorhexidine

1. Introduction

Group B β-hemolytic streptococcus (GBS, Streptococcus agalactiae) is the leading cause of neonatal sepsis with eventual meningitis and accounts for 10–25% of postpartum maternal bacteremia [1,2]. Invasive neonatal GBS infections present themselves either as ‘early’ (usually within 24 h) or ‘late onset’ (7 days–3 months) disease. Early onset infections make up two thirds of cases and are usually acquired by vertical transmission from the mother's genital tract [1,2]. Asymptomatic maternal genital GBS colonization may be intermittent or temporary rather than permanent and occurs in 4–40% (usually about 20%) of pregnant women, depending on the population studied and culture technique used [1–3]. The rectum serves as a reservoir for colonization of the vagina, and genital tract isolation rates are reported highest from the lower vagina (introitus) and lowest from the cervix [1,2]. In infants born of GBS carriers, vertical transmission range from 40–70%, the higher percentage being associated with a high genital inoculum. Despite high prevalence rates for vertical
transmission, the incidence of early onset GBS infection is only 1–10/1000 live births. Albeit a small group, prevention is important because of the high mortality rate: 50–70% in older studies and 13–37% in more recent studies [1,2]. Furthermore, about half of the infants surviving GBS meningitis are left with permanent neurologic sequelae.

There is no consensus on the best approach to prevent early onset GBS infection [4]. It is important to recognize perinatal risk factors, including low birthweight, preterm delivery, prolonged rupture of membranes, intrapartum fever and heavy maternal GBS colonization [1,2,5]. Infants of mothers with low levels of serogroup-specific antibodies against GBS are at risk [1]. A program of active immunization aimed at pregnant women or, alternatively, at all women in the childbearing years would probably be most efficient in controlling perinatal GBS disease. However, an effective vaccine is not yet available [6]. Antibiotic treatment during pregnancy is not adequate [7], neither can single-dose penicillin prophylaxis in infants be recommended [8]. Intrapartum prevention with antibiotic therapy (ampicillin, penicillin G) has been shown to reduce GBS vertical transmission [9–16]. Vaginal chlorhexidine disinfection during labor has been proposed as a simple, cheap and safe [17] alternative without risk for development of bacterial resistance and only a very low risk for allergic complications [18–20]. It can be used not only in delivery wards but also in home deliveries and in the developing world. Chlorhexidine might also reduce the transmission of other potential pathogens. Moreover, as compared to antibiotic therapy, chlorhexidine disinfection would obviate the necessity of selection. The omission of rapid GBS antigen tests would be advantageous as, so far, they lack sufficient sensitivity [21].

In 1992, chlorhexidine disinfection during labor was reported to reduce excess neonatal morbidity associated with GBS [22]. However, the effect on vertical transmission was not investigated. Stimulated by the promising results of a small clinical pilot study [20], we investigated the effect of vaginal chlorhexidine gel disinfection on vertical transmission of GBS in a randomized trial.

2. Subjects and methods

2.1. Subjects and design

The trial was conducted from February 1991 through November 1992 in the two hospitals with obstetric services in the city of Nijmegen, The Netherlands. Eligible pregnant women received written information on the trial during pregnancy or at admission to the delivery ward. Exclusion criteria were: known GBS carriership (allowing responsible obstetricians to take different preventive measures), use of antibiotics during the 4 weeks before admission, planned caesarean section, antepartum fetal death, suspected congenital abnormalities and immature labor. The protocol was approved by the ethical committees of both institutions and written informed consent was obtained from all parturients enrolled in the trial.

The goal of the trial was to study the effect of chlorhexidine disinfection on the rate of GBS transmission to the neonate. Secondary goals were to study the vertical transmission rates of Escherichia coli, Staphylococcus aureus and Candida albicans, and to establish neonatal and maternal morbidity.

Two groups were treated in a double-blind manner with either a chlorhexidine or a placebo gel. To detect any possible effect of treatment with placebo gel, a third group received no treatment at all. A pre-study calculation of the required sample size was performed, assuming the prevalence of GBS among parturients to be 20%. With the probability of making a type I (α) and type II (β) error set at 0.05 and 0.20, respectively, and considering that a reduction in assumed normal GBS transmission rate of 50% to 25% or less would be of clinical importance, we estimated that data from about 340 deliveries per group would be required for the study. A total of 1020 participating women were randomly assigned, when labor had clearly started, to one of three groups according to a predefined block (10:10:10) allocation scheme.

2.2. Intervention

As in our pilot study, we used a viscous gel to apply the chlorhexidine because it adheres well to the mucosa and is a good lubricant [20]. The active gel consisted of chlorhexidine digluconate (3.0 g), hydroxypropylmethylcellulose 4000 centiPoise (20.0 g), 100 ml glycerol, natrium hydroxide to obtain a pH of 7.0, and water to a volume of 1000 ml. After mixing, the viscous aqueous solution was transferred into glass bottles and sterilized (20 min at 120°C). This product was transferred into disposable sterile syringes and stored at 4°C. The placebo gel had the same composition except for the chlorhexidine digluconate and it was handled identically. There were no visual differences between the syringes containing the different gels.

For the duration of the trial, all antiseptic solutions and lubricants for obstetric use were removed from the wards and, instead, sterilized placebo gel, perishable 24 h after opening, was available in 100 ml glass bottles. When a woman was in active labor, the attending obstetrician applied 10 ml gel (brought at room temperature) from the syringe attached to a 14 cm plastic catheter around the portio and into the fornices. This procedure was repeated after 10 h in case delivery had not yet occurred. For this purpose, all syringes were delivered in duplicate.
2.3. Data collection

All parturients were cultured before the application of any gel. Cotton tipped wooden swabs were used, moistened with Todd-Hewitt broth, with addition of 8% lecithin and 3% Tween 80 to inactivate any chlorhexidine remnants absorbed in the swab [23]. An unocentral swab was first taken, after which a second swab was used to sample the posterior half of the introitus. Using a sterile speculum, a third swab was rotated 360° in the cervical os to obtain a cervical specimen. Ear, pharynx and umbilicus of all neonates were cultured directly after birth.

All swabs were stored at 4°C and inoculated within 24 h in the same bacteriological laboratory. The following media were used to plate the swabs semiquantitatively: 5% defibrinated sheep blood agar (48 h at 36°C), Casman agar with 10 units/ml bacitracin and 5% defibrinated rabbit blood (anaerobically, 48 h at 36° C) and Sabouraud agar (72 h at 30° C). Sabouraud agar and Canman agar were used to detect yeasts and Haemophilus influenzae, respectively, the latter also being recognized as an important cause of neonatal infections [24]. After plating, the swabs were put in a selective enrichment broth consisting of Todd-Hewitt broth with 15 μg nalidixic acid per ml and 8 μg gentamicin per ml. After overnight incubation at 36°C, the swabs were plated on blood agar and incubated at 36°C for another 24 h. The growth density of microorganisms (1, 2, 3 or 4), expressed as growth in the corresponding streak area, on the directly plated agar plates was determined. Growth density 0 was scored if GBS were only isolated from the enrichment broth (or if only 1–2 colonies of other species were grown on blood agar). The identification of GBS was confirmed by a positive CAMP-reaction, absence of a zone of inhibition around a bacitracin disc (0.04 units) on Casman blood agar (18–24 h at 36°C), and a group B latex agglutination test (Streptex, Wellcome Diagnostics).

Standard forms were used to record the data of mothers and child. Prenatal data included information on age, ethnic origin, obstetric history, assessment of gestational age, use of drugs, alcohol and nicotine, any loss of blood, tocolysis, anemia and diabetes mellitus or gestational diabetes.

In addition to the usual parameters of labor and delivery, data also included time of rupture of membranes, admission to the delivery ward and application(s) of gel. Moreover, the following data were recorded: cervical dilatation at the moment of application of gel, number of vaginal examinations, use of internal monitoring, fetal blood sampling and infection parameters. Initial infant data were collected and whether the infant received intensive, special or regular care.

Women and infants were followed up during their hospital stay with special attention to infectious problems, results of additional cultures and antibiotic therapy. Neonatal septicemia, meningitis and pneumonia were diagnosed from positive cultures of blood, cerebrospinal fluid or tracheal aspirate, respectively. ‘Probable infection’ was based on clinical suspicion with negative cultures. Follow up was continued until 3 months and all women and their family doctors received a questionnaire for this purpose. In cases of twins, data on the first-born were processed only. Any spontaneously reported complaints were recorded.

2.4. Statistics

The Kruskal-Wallis test, Fisher’s exact test, logistic regression analysis and repeated measurement analysis of categorical data [25] were used for statistical analyses.

3. Results

Of the 1020 participating women, 522 were enrolled in one hospital and 498 in the other. Thirty-nine were not evaluated because cultures were incomplete or lost, or delivery took place before any gel could have been applied. Of the 981 analyzed mother-infant pairs, 327 were assigned to the chlorhexidine group, 328 to the placebo group and 326 to the control group. In total, 19 (1.9%) twin pregnancies and 41 (4.2%) premature deliveries were enrolled. Table 1 summarizes a number of characteristics of the three groups; no significant differences were found.

Table 1

<table>
<thead>
<tr>
<th>Characteristic*</th>
<th>Chlorhexidine</th>
<th>Placebo</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)* mean (SD)</td>
<td>30.1 (4.6)</td>
<td>30.1 (4.5)</td>
<td>30.3 (4.6)</td>
</tr>
<tr>
<td>Pregnancy, median (range)</td>
<td>2 (1–7)</td>
<td>2 (1–8)</td>
<td>2 (1–11)</td>
</tr>
<tr>
<td>Parity, median (range)</td>
<td>1 (0–5)</td>
<td>1 (1–6)</td>
<td>1 (1–9)</td>
</tr>
<tr>
<td>Gestational age (days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>278 (11)</td>
<td>279 (11)</td>
<td>278 (11)</td>
</tr>
<tr>
<td>P5; P95</td>
<td>260; 295</td>
<td>260; 295</td>
<td>259; 295</td>
</tr>
<tr>
<td>Ethnic origin (% non-Caucasian)</td>
<td>6.7</td>
<td>7.9</td>
<td>7.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Growth density (%):</th>
<th>Chlorhexidine</th>
<th>Placebo</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: anorectum/introitus/cervix</td>
<td>3.1/3.4/3.1</td>
<td>6.1/4.0/2.7</td>
<td>4.6/2.8/4.9</td>
</tr>
<tr>
<td>1–2: anorectum/introitus/cervix</td>
<td>3.4/5.8/4.9</td>
<td>6.4/6.7/5.2</td>
<td>3.1/3.7/3.4</td>
</tr>
<tr>
<td>3–4*: anorectum/introitus/cervix</td>
<td>10.4/5.2/3.7</td>
<td>7.0/4.9/2.7</td>
<td>7.7/6.1/3.7</td>
</tr>
<tr>
<td>Number of GBS carriers (%)</td>
<td>63 (19.3)</td>
<td>70 (21.3)</td>
<td>57 (17.5)</td>
</tr>
<tr>
<td>Heavily colonized (% of GBS carriers)</td>
<td>40 (63.5)</td>
<td>33 (47.1)</td>
<td>35 (61.4)</td>
</tr>
</tbody>
</table>

*aNo significant differences between the three groups; means and medians tested with the Kruskal-Wallis test; percentages tested with two tailed Fisher’s exact test; growth densities tested for each culture site. bHeavily colonization.
Intrapartum GBS carrier state was established in 190 (19.4%) of 981 women, 108 (56.8%) of the carriers being heavily colonized (growth density 3 or 4). Anorectal, introital, and cervical colonization was found in 169 (88.9%), 139 (73.2%) and 112 (58.9%) of carriers, respectively; the differences being statistically significant ($P < 0.001$ [25]). Genitals plus anorectum were colonized in 67.9%, only the genitals in 11.1% and just the anorectum in 21.1% of the carriers.

Pregnancy characteristics of intrapartum GBS carriers were compared to that of non-carriers (Table 2). No differences in obstetric histories were found, nor in the use of tocolytic therapy during pregnancy or in gestational age at delivery. More insulin-dependent diabetes mellitus was found in the GBS carrier group (two-tailed Fisher's exact test, $P = 0.05$), while non-carriers suffered from anemia more often (two-tailed Fisher's exact test, $P = 0.04$).

Group assignment of GBS carriers did not significantly influence the clinical characteristics of deliveries and infants at birth (Table 3). In 98.4% of the chlorhexidine-group-assigned GBS carriers, the gel was applied more than 30 min before birth. A second gel application was given to 5.8% of the total chlorhexidine group and 4.9% of the placebo group. Gel was administered after the membranes had ruptured in 70.0% of GBS carriers.
The median interval between admission and the first application of gel was 4 cm. No significant differences in infection parameters were detected between the three groups of GBS carriers, regarding the incidence of temperature ≥38°C, endometritis, wound infection (following perineal rupture, episiotomy, or caesarean section), antibiotic therapy and various other infectious complications. Similarly, there were no significant differences between the control groups of GBS carriers and non-carriers (n = 269). No cases of endometritis or wound infection were registered among GBS carriers. Among the non-carriers (n = 791), four suffered from endometritis and two from infected wounds, caused by other pathogens than GBS.

There was no mortality among the infants born of GBS carriers. One male infant (3635 g at 295 gestational days), born of a heavily colonized GBS carrier from the chlorhexidine group, suffered from early onset GBS sepsis and was discharged after successful treatment with ampicillin and gentamicin. The membranes had ruptured 3 h before the application of gel and some signs of infection were present during labor. Another boy, whose mother was heavily colonized with E. coli but not with GBS and was treated with placebo gel, suffered from pneumonia (E. coli and S. aureus) and was also successfully treated with ampicillin and gentamicin without further sequelae.

Two children born of non-carriers died: a small-for-gestational-age term boy at age 3 months died from cot death and a girl died within the first week due to transposition of the great vessels.

There were no significant differences regarding the infection parameters detected between the three groups of GBS colonized parturients. Group assignment had no influence on the condition of infants born of GBS carriers, although significantly more infants from both the chlorhexidine and control group were admitted to the special care unit, as compared to the neonates from the placebo group (two-tailed Fisher's exact test, P = 0.012).

The vertical transmission rate of S. agalactiae was lower in the chlorhexidine group, but the difference did not reach significance (two-tailed Fisher's exact test, P = 0.069; Table 4). When testing the transmission rate for the chlorhexidine group (52.4%) versus that for the combined placebo plus control group (69.3%), the difference of 16.9% (95% confidence interval CI 2.2–31.6%) was significant (two-tailed Fisher's exact test, P = 0.017). These transmission rates resulted in 10.1%, 15.2% and 17.1% neonatal GBS colonization in the chlorhexidine, placebo and control group, respectively. Logistic regression analysis for the maternal carriers, with correction for the treatment group (no interaction), reveals the introitus as the colonization site yielding the highest GBS vertical transmission rate (odds ratio 10.2; 95% CI 4.3–24.5%).

No significant differences in transmission rates of E. coli, S. aureus and C. albicans were found between the three groups (two-tailed Fisher's exact test; Table 4). Overall, transmission rates of microorganisms declined in the following order: S. agalactiae (63.5%), S. aureus (53.5%), E. coli (35.6%) and C. albicans (32.7%). The degree of neonatal colonization with the various microorganisms, reflected by the sumscore of the growth densities for all three culture-sites, did not differ significantly among the three groups (Kruskal-Wallis test; Table 4). Haemophilus species (not associated with morbidity) were cultured from two women in the chlorhexidine group: H. influenzae type B only from one cervix and Haemophilus parainfluenzae from the introitus of both women. Only the ear of one symptom-free neonate, born of a non-colonized woman from the control group, was colonized with H. influenzae (non type B). Microbial growth, which can be considered as a quality control of sample and culture techniques, was present in 95.1% of all maternal cultures (n = 2943) and in 90.5% of neonatal cultures from the placebo plus control groups (n = 1962).

Follow-up data until three months postpartum were obtained from all 981 mother-infant pairs. No significant differences between the three groups of GBS colonized mothers were detected, regarding the incidence of temperature ≥38°C, endometritis, wound infection (following perineal rupture, episiotomy, or caesarean section), antibiotic therapy and various other infectious complications. Similarly, there were no significant differences between the control groups of GBS carriers and non-carriers (n = 269). No cases of endometritis or wound infection were registered among GBS carriers. Among the non-carriers (n = 791), four suffered from endometritis and two from infected wounds, caused by other pathogens than GBS.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Chlorhex-Placebo</th>
<th>Control</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus agalactiae</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transmission (%)</td>
<td>52.4</td>
<td>66.7</td>
<td>0.069</td>
</tr>
<tr>
<td>Sumscoreb: median</td>
<td>1</td>
<td>2</td>
<td>&lt;0.10</td>
</tr>
<tr>
<td>P5; P95</td>
<td>0; 13</td>
<td>0; 15</td>
<td>0; 14</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transmission (%)</td>
<td>36.3</td>
<td>32.0</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>Sumscoreb: median</td>
<td>0</td>
<td>0</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>P5; P95</td>
<td>0; 6</td>
<td>0; 7</td>
<td>0; 6</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transmission (%)</td>
<td>42.9</td>
<td>56.7</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>Sumscoreb: median</td>
<td>0</td>
<td>3</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>P5; P95</td>
<td>0; 6</td>
<td>0; 12</td>
<td>0; 13</td>
</tr>
<tr>
<td><em>Candida albicans</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transmission (%)</td>
<td>27.9</td>
<td>39.1</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>Sumscoreb: median</td>
<td>0</td>
<td>0</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>P5; P95</td>
<td>0; 4</td>
<td>0; 4</td>
<td>0; 5</td>
</tr>
</tbody>
</table>

*Percentages tested with two tailed Fisher's exact test; medians tested with the Kruskal-Wallis test.
Cases with positive neonatal culture(s) while negative maternal culture(s) for concerning pathogen are excluded.
Total score (growth density + 1) of ear, pharynx, and umbilicus (range 0–15).
incidence of 'probable infection', antibiotic therapy and duration of hospital stay for various neonatal reasons between the three groups of infants born of GBS carriers. The same was true for the infants born of mothers from the control groups of carriers and non-carriers.

No adverse effects of chlorhexidine or placebo gel were reported or observed.

4. Discussion

Colonization rates for the anorectum, introitus and cervix support the concept that the lower gastrointestinal tract is the principal reservoir for GBS. The introitus seems the most suitable site for screening, in view of the high GBS vertical transmission rate and relatively high GBS isolation rate at this location.

Maternal diabetes was identified as a risk factor for GBS colonization, as earlier reported by Baker [26].

In contrast to our pilot study [20], a modest reduction in vertical transmission rate of *S. agalactiae* by chlorhexidine gel was found in the present, first randomized, study. In the non-randomized pilot study, however, the vagina was cleaned with saline before the application of the 0.3% chlorhexidine gel and only the cervix and anus of parturients were cultured. Moreover, 0.01% benzalkoniumchloride was added to the gel as a preservative; any extra disinfecting effect, although unlikely in view of the high chlorhexidine concentration, not being excluded.

In 1992, the Swedish Chlorhexidine Study Group concluded that intravaginal chlorhexidine flushing during labor reduced morbidity among full-term newborn infants compared to placebo treatment with saline [22]. Parturients were cultured from the posterior fornix for GBS only. The infants were not cultured to assess the vertical transmission rate of GBS. The excess morbidity among the infants born of GBS carriers was only statistically significant when respiratory disorder and (probable) infection were taken together, while infection alone did not reach significance. Culture-proven septicemia/meningitis occurred in one infant of both groups of GBS carriers. Parturients delivering prematurely were not included, nor was a second control group receiving no treatment at all to assess the impact of flushing the vagina with saline.

It is known that chlorhexidine kills 99% of vaginal bacteria within 5 min [18]. In 98.4% of parturients, chlorhexidine gel was applied more than 30 min before birth, while the median interval was 4.3 h. Although no experimental data for chlorhexidine are available yet, the use of a gel as a vehiculum may have advantages over an aequous solution such as a longer duration of action, as is the case for povidone-iodine gel [27]. Activity of chlorhexidine is reduced in the presence of serum, blood, pus and other organic matter [17]. This problem can be overcome by using a sufficiently high concentration [18]. The chlorhexidine concentration used in our study was 600 times or more the minimal bactericidal concentration for GBS [28] and at least as high as in other clinical studies [19,20,22].

Preferably, chlorhexidine is applied before rupture of the membranes, as the risk for ascending colonization and infection of the genital tract increases substantially after membrane rupture. The prevalence of positive genital cultures for GBS is significantly lower immediately after rupture of the membranes [29]. This may be due to a 'wash out' effect and/or inherent bacteriostatic properties of amniotic fluid [30]. The duration of this effect is not known. Reduction of vaginal pathogens by chlorhexidine and thereupon amniorrhexis would seem most beneficial. In the present study, the chlorhexidine gel was given in only 30% of GBS carriers before the membranes ruptured. In these cases, transmission occurred in 44%; transmission occurred in 56% when gel was applied after the membranes ruptured. For the placebo group, these percentages were 77% and 69%, respectively.

The effect of chlorhexidine might be increased by earlier application, preferably before membrane rupture, and possibly by increasing the concentration and/or quantity. Randomizing patients during pregnancy instead of during labor could probably have gained time in this trial. Earlier application in routine use is possible because there is no need for the time-consuming process of enrolling, randomizing and culturing of a trial.

We conclude that vaginal disinfection with 0.3% chlorhexidine gel during labor modestly reduces vertical transmission of GBS. This raises the question of whether this reduction is of sufficient clinical importance to implement chlorhexidine disinfection in clinical practice. We theorize that the qualitative and quantitative reduction in vertical transmission in the Netherlands (195 000 deliveries/year) may subsequently lead to a reduction by 4–62 cases of an estimated annual 195 cases of early onset GBS sepsis. The costs of implementation can roughly be calculated analogous to the costs of a comparable product as catheter lubricant. This is manufactured at an industrial scale and purchased at prices of about Dfl. 2.50 per ready to use unit. The price of such products is mainly dependent on the costs of manufacturing and the applicator tip, whereas the ingredients contribute less than 5% to the final costs. The use of 250 000 packages/year would cost Dfl. 0.63 million. The financial benefit would result from fewer admissions to neonatal intensive care units (average Dfl. 30 000/neonate) and less handicapped children (up to Dfl. 2 million/lifetime). Assuming that early onset GBS sepsis will leave 1 out of 8 neonates severely handicapped, the total benefit would range between Dfl. 1.12–17.36 million/year. Because the method is cost-effective, simple and safe, it should be considered for
routine use, not as a panacea but as a contribution to the prevention of GBS infections in newborns.

Acknowledgments

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