資料 2

様式1

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理事長
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院長	顧問	顧問	顧問	副院長	副院長	副院長	事務長	受領者
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小山記念病院倫理審査申請書

2024　年　5　月　24　日

小山記念病院倫理員会委員長　殿

申請者　　深水　勇伍　　印

小山記念病院倫理委員会規定による審査を申請します。

1.課題名

正常分娩時の抗菌薬投与中止に関する実態調査

2.代表者名　　所属

深水　勇伍　　薬剤部（主任補佐）

3.共同担当者名※共同の場合のみ　　所属

酒井　謙	産婦人科（産科部長）
大畠　孝則	感染制御部（部長）
堂園　渓	産婦人科
花香　淳一	薬剤部（部長）
石井　美咲	薬剤部（主任）
坂本　理恵	薬剤部

4.概要(具体的に記載すること)

〔1〕目　的

2023年5月まで、当院ではクリニカルパスにてルーチンに抗菌薬が処方されていた。しかし、WHOでは、合併症のない褥婦に対する予防的抗菌薬投与は推奨されておらず、2023年5月8日以降、産婦人科医師と感染制御部で相談の上、抗菌薬処方は削除とした。クリニカルパスを変更してから約1年が経過し、パス中止後に感染症患者が増えていないかを後向きに調査した。

[2]対象及び方法

別紙参照のこと

[3]審査を希望する理由

後向きの観察研究であるが、当院の取り組みとして、感染症専門学会にて発表するため。また、学会で専門的意見を受けた上で論文化につなげたいと考えており、事前に病院としての評価を受けたいため。

正常分娩時の抗菌薬投与中止に関する実態調査

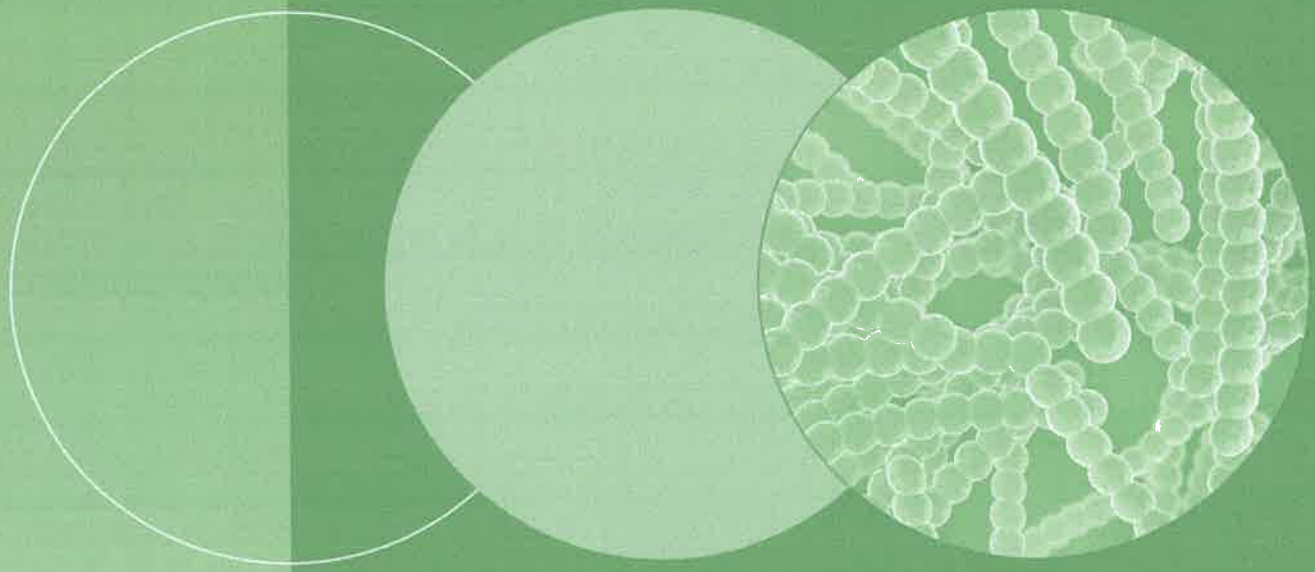
【背景】正常分娩時において、ガイドライン上ルーチンに抗菌薬投与の規定はない。当院では、分娩目的に入院された患者に対し、クリニカルパスにて経験的に第三世代経口セフェム系抗菌薬であるセフカペンピボキシル(CFPN-PI)が処方されていた。一方、WHOでは合併症のない経膣分娩をした褥婦への抗菌薬投与は推奨されないとなっており、産婦人科医師と相談の上、クリニカルパスによる抗菌薬処方を中止することとした。

【方法】2023年5月8日から12月までの期間に、経膣分娩を経験した150名の褥婦のうち、器械及び吸引分娩ならびにGBS陽性及び前期破水、会陰裂傷III度以上で抗菌薬を投与した者を除く、正常分娩された93名を対象に電子診療録から後向きに情報収集した。事象発生は、産後の骨盤蜂巣炎を含む子宮内膜炎の発症及び抗菌薬処方とした。

【結果】CFPN-PIをクリニカルパスから除外後、正常分娩した褥婦において産後の骨盤蜂巣炎を含む子宮内膜炎の発症を認めなかった。また、産後健診でも同様に、感染症の発症は認められなかった。

【考察】正常分娩した褥婦において、予防的な抗菌薬投与がなくても感染症の発症が増加しないことが示唆された。妊産婦において、母子ともに安全を保つことが重要である一方、薬剤耐性の観点から両者の今後の抗菌薬選択が限定されてしまうリスクも考慮し、必要に応じた抗菌薬処方を検討した方がよいと考えられた。

WHO recommendations for prevention and treatment of maternal peripartum infections



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RECOMMENDATION 15

Routine antibiotic prophylaxis is not recommended for women with uncomplicated vaginal birth. *(Strong recommendation based on very low-quality evidence)*

REMARKS

- The GDG was concerned about the potential public health implication of the high rate of routine use of antibiotics following vaginal birth without any specific risk factors in some settings. The group puts its emphasis on the negative impact of such policy on the global efforts to contain antimicrobial resistance and, therefore, made a strong recommendation against routine antibiotic prophylaxis.
- "Uncomplicated vaginal birth" in this context connotes vaginal birth in the absence of any specific risk factor for or clinical signs of maternal peripartum infection.
- Careful monitoring of all women after birth is essential to promptly identify any sign of endometritis and institute appropriate antibiotic treatment (see *Recommendation 20*).
- Recommendations on antibiotic use for common intrapartum conditions or interventions that often raise concerns about increased risk of infection are available in this guideline.

Review question:

Among pregnant women with uncomplicated vaginal birth (P), does antibiotic prophylaxis after birth (I), compared with no prophylaxis or placebo (C) prevent infectious morbidities and improve outcomes (O)?

Summary of evidence

- Evidence on the impact of antibiotic prophylaxis in women with uncomplicated ("normal") vaginal birth was extracted from a systematic review which identified two eligible randomized controlled trials involving 1653 women *(38)*. The two trials compared antibiotic prophylaxis with no prophylaxis. The trials were conducted in France and Japan.
- One of the trials described women with "uncomplicated vaginal birth" as those who had vaginal delivery, no fever (> 38 °C) during labour or the hour following delivery, an interval of < 24 hours between rupture of membranes and labour onset, no evidence of extragenital infection (e.g. urinary tract infection) and no known allergy to Amox-CA or betalactam. The study excluded women with evidence of amniotic fluid infection at the time of admission. The second trial excluded women with a history of hypersensitivity to the tested antibiotics (cefteram or cephem), fourth-degree perineal lacerations, birth after PROM at term, underlying medical conditions such as gestational hypertension and diabetes mellitus and at the discretion of the physician.
- One trial used a single dose of Amox-CA 1 g intravenously, while the other trial used oral 300 mg cefteram pivotal for three or five days.
- In terms of outcomes, one of the trials used clinical and/or laboratory criteria for diagnosing endometritis: pyrexia > 38 °C confirmed on two separate occasions and accompanied by pain on mobilizing the uterus and/or fetid lochia, and/or leucocytosis of more than 10 000/mm^3. The other trial used only clinical criteria that included the occurrence of "fever more than 37 °C for more than two days, or infected lochia, or low abdominal pain detected and diagnosed by the doctor in charge, after 24 hours from birth".

Antibiotic prophylaxis versus no prophylaxis/ placebo (EB Table 13)

- Women receiving antibiotic prophylaxis after uncomplicated vaginal birth experienced significantly reduced incidence of endometritis (RR 0.26, 95% CI 0.09 to 0.73; 2 trials, 1653 women). However, no statistically significant difference was observed in the risks of puerperal fever (RR 0.26, 95% CI 0.02 to 3.97, 2 trials, 1653 women), wound infection (RR 0.80, 95% CI 0.07 to 8.68; 1 trial, 362 women), urinary tract infection (RR 0.51, 95% CI 0.18 to 1.45; 1 trial, 1291 women) and duration of hospital stay (MD -0.15 days, 95% CI -0.31 to 0.01; 1 trial, 1291 women).
- All other outcomes reported in the review were not prespecified as critical outcomes for this recommendation question.

Considerations related to the strength of evidence

Quality of evidence

The quality of evidence was graded as very low for four out of the five critical outcomes reported. Overall the quality of evidence was graded as very low.

Balance of benefits and harms

There is very low-quality evidence of clinical benefit in terms of reduction in postpartum endometritis in women who received antibiotics following

uncomplicated vaginal birth. No clinical benefits were observed for other critical outcomes. The studies contributing data to the endometritis outcome were at high risk of bias because of lack of blinding, given that the diagnosis of endometritis in the studies was in part subjective.

Additionally, fever, a more objective measure, which was also included as part of the diagnosis of endometritis, was not different between intervention and control arms of the trial. The incidence of postpartum endometritis in the control population of the studies was 2.2%, suggesting that only a small proportion of women were at risk of endometritis. The number needed to treat to benefit (i.e. to avoid one case of endometritis) is 58. In view of the very low rate of endometritis and the fact that endometritis in itself is more of an early sign of severe pelvic infection when left untreated, unnecessary exposure of about 98% of women who are unlikely to develop this condition will negatively impact on public health in terms of increasing antimicrobial resistance.

Values and preferences

Health care providers and policy-makers in all settings are likely to place a high value on the potential negative public health impact of administering antibiotics to a very large proportion of women giving birth who are unlikely to develop peripartum infection. Mothers will also prefer to avoid the inconvenience and side-effects of antibiotic use. The panel is confident that there is no variation in this value among health care providers, policy-makers and mothers in low-, middle- and high-income settings.

Resource implications

The implementation of this recommendation is likely to save health care costs in settings were antibiotics are routinely given to women with uncomplicated vaginal birth. Additionally, adhrence to this recommendation could potentially contribute to signficant reduction in health care costs related to combating antimicrobial resistance in the larger population.

RECOMMENDATION 16

Vaginal cleansing with povidone-iodine immediately before caesarean section is recommended. *(Conditional recommendation based on moderate-quality evidence)*

REMARKS

- The recommendation of the use of povidone-iodine out of the common antiseptics was because it was the only agent tested in all randomized controlled trials that evaluated the review question.
- The GDG noted that the main clinical benefit (reduction in post-caesarean endometritis) demonstrated in the review was largely driven by women at higher baseline risk of infections (i.e. those who were already in labour and those with ruptured membranes). However, in consideration of the similarity in the statistical findings between subgroups and the entire study population, the group acknowledged that women at lower baseline risk of infection are also likely to benefit from the intervention.
- Due to the staining of surrounding tissues, vaginal cleasing in this context may be regarded as a potentially invasive procedure, and implementation might not be easy.
- The GDG considers further evaluation of the benefits in high-risk women and potential adverse effects (especially among women with ruptured membranes and those planning to breastfeed) a research priority. Additionally, the group considers it essential to identify the most appropriate timing of the intervention to achieve benefit with minimal harm and whether other antiseptic agents (e.g. chlorhexidine) have similar beneficial effects. The group noted that shorter application and contact time are likely to be associated with less maternal and fetal exposure. Therefore, the group suggested vaginal application of povidone-iodine very close to the start of caesarean section (e.g. following bladder catheterization) to mimimize the discomfort to the woman. The specified duration of vaginal cleansing with povidone-iodine in three of the seven included studies in the Cochrane review was 30 seconds.
- The use of a high concentration and/or repeated applications of povidone-iodine should be avoided to minimize maternal and fetal exposure and possible interference with the results of neonatal thyroid screening.