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Antibiotic prophylaxis practices in cesarean section with focus on timing – a Danish national survey

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ABSTRACT

Introduction: The last Danish survey in 1995 on the antibiotic prophylactic practices in cesarean section found that there was no consensus between delivery wards. Since then national guidelines have been established. We therefore wanted to see if clinical practice regarding antibiotic prophylaxis had become more uniform.

Methods: In February of 2019 the delivery wards in Denmark (n=21) were contacted to answer an online questionnaire regarding type and dose of antibiotic prophylaxis used, timing of the administration, and differences between elective and emergency cesarean section.

Results: All twenty-one wards applied a single dose of 1500 mg Cefuroxime, a 3rd generation cephalosporin. Three wards (14%) administered antibiotic prophylaxis after cord clamping and eighteen (86%) prior to clamping, with nine (43%) wards having changed practice during the last 10 years. Three wards recalled the precise year for the change, six wards gave an approximate range of years, and five wards did not remember. The exact timing of the antibiotic varied from 0-60 minutes prior to incision, with sixteen (76%) wards reporting giving antibiotics usually 0-30 minutes prior to and of those, eleven (52%) immediately prior. All wards had the same prophylactic antibiotics principles for emergency and elective cesarean sections.

Conclusion: Most wards adhere to national guideline recommendations, but recollection was imperfect as to when changes in practices were implemented. We suggest that current and previous guidelines from hospitals in Denmark be stored in a national database, or more preferably that a national cesarean birth registry be established, accounting for the frequent local changes and interpersonal differences in clinical practice.

Keywords: Antibiotic Prophylaxis; Wound Infection Postoperative; Cesarean Section

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INTRODUCTION

Before the introduction of antibiotics, postoperative infection rates in cesarean deliveries were reported to be as high as 50% [1]. Presumably, with advancements in operative techniques, routine antibiotic prophylaxis, better hygiene and living standards, these numbers have plummeted [1]. In the mid 1990's, a Danish survey of the practices regarding surgical antibiotic prophylaxis in cesarean section, revealed that most of the by then 48 active delivery wards, did not give antibiotic prophylaxis routinely for elective cesarean section and only half of the wards gave antibiotic prophylaxis for emergency cesarean section [2]. Back then, only 27% of the wards reported to give antibiotic prophylaxis routinely prior to cord clamping.

The issue of whether it was safe for the infant to administer antibiotic prophylaxis prior to cord clamping has been a much debated issue [3], although there have been no studies that have shown short-term detrimental effects on the infant [4]. Since administration prior to cord clamping has been shown to reduce the risk of postoperative maternal infections after cesarean section, many guidelines started recommend this practice during the late 2000's [5–8], with the Danish guidelines published in January of 2012 [9]. However, it is unknown whether these recommendations are followed in clinical practice at Danish delivery wards.

We therefore wanted to investigate which antibiotic prophylaxis regimens were currently applied at delivery wards in Denmark and if there had been a change in the administrative timing of antibiotic prophylaxis after the publication of the national guidelines.

Question	Predefined answers.
Is there a difference in how you administer antibiotic prophylactic treatment for emergency and elective cesarean section?	-Yes -No -Do not know -Other
Which antibiotic do you use as a prophylactic for cesarean section?	-Cefuroxime 1.5 grams -Amoxicillin 2 grams -Other
Do you repeat the dose postoperatively?	-Yes once -Yes more than once -No -Other
Do you administer the antibiotics prior to cord clamping of the infant?	-Yes 30-60 minutes prior -Yes 15-30 minutes prior -Yes 15-60 minutes prior -Yes but with another time interval -No but immediately after cord clamping -No but at another time point after cord clamping -Other
When did your ward change clinical practice regarding antibiotic prophylaxis administration from "after" to "prior to" cord clamping?	-We have not changed practice -Do not know -Year: (write below, preferably the month of the year if possible or a range of years if uncertain)

Table 1: The list of relevant questions from the online questionnaire, translated from the original Danish to English. Respondents were also asked if they were responsible for the ward's antibiotic guidelines regarding cesarean section and how long they had worked at their department.

Which antibiotic and dose do you use as prophylaxis for cesarean section?				
	Cefuroxime	21/21	100%	
	1500 mg	21/21	100%	
Is there a difference between how you administer antibiotic prophylaxis between elective and intrapartum cesarean section?				
	No	18/21	86%	
+	Emergency CS: antibiotics are given as soon as possible	1/21	5%	
+	Emergency CS: repeat antibiotics postpartum for 1 day	1/21	5%	
+	Emergency CS: antibiotics are given during surgery	1/21	5%	
Do you repeat the antibiotic dosage postpartum?				
	No	16/21	76%	
+	For hyper-acute CS: One extra dose Cefuroxime in addition to Metronidazole	1/21	5%	
+	For hyper-acute CS: Treatment for 1 day postpartum	2/21	10%	
+	If there are signs of infection prior to emergency CS: repeat dosage	2/21	10%	
When did your hospital change to giving antibiotic prophylaxis after cord clamping to giving prior to cord clamping?				
	No change in practice	7/21	33%	
	Do not know	5/21	24%	
+	Prior to 2010	1/21	5%	*
+	2010-2015	7/21	33%	
+	2016-2019	2/21	10%	*
How long have you (or the one you are responding on the behalf of) been working at your current department?				
	No change in practice	7/21	5.1 yrs	*
	Do not know	7/21	6.1 yrs	*
	Remembers year or range of years	8/21	8.1 yrs	

Table 2: Summary of select responses to the questions from table 1. CS = Cesarean section. When respondents filled out a commentary to a question, those answers are marked with a +. Discrepancies between respondents from the same delivery ward are marked with an *, reflecting there being a total of 22 responses (numerator) but only 21 departments (denominator) to the last question.

MATERIALS AND METHODS

During the annual obstetric guideline meeting for the Danish Society of Obstetricians and Gynecologists in January of 2019, a contact person for all the 21 obstetric wards active in Denmark in 2019 volunteered to answer an online questionnaire. Each doctor was then sent an e-mail with a link to an online questionnaire (Google Analytics). For every question, there were predefined possibilities of answers, with the option to answer "other" and write a comment (see table 1). The only exception to this, was that respondents were asked to write the year and month, or a range of years if the precise period could not be recollected, for the change in practice regarding antibiotic prophylaxis prior to or after cord clamping. Answers by means of comments, were collated into groups were possible.

RESULTS

All 21 labor wards answered the questionnaire, and all reported to routinely use 1500 mg Cefuroxime as an intravenous prophylactic antibiotic for emergency- as well as planned cesarean section (table 2). We did not specifically ask for information on treatment algorithms for overweight patients, but nine wards by own initiative noted that for these patients they doubled the dose of Cefuroxime to 3000 grams.

The majority reported to give antibiotics prior to cord clamping (n = 18/21, 86%) with only three wards administering antibiotics after cord clamping. The average number of yearly births in 2018 for hospitals administering antibiotics prior to cord clamping was 3,010 representing 96% of all births in a hospital (n = 54,190 / 56,193) and the average for those administering antibiotics after cord clamping was 2,003, with no university hospitals in the latter group. Of those giving antibiotics prior to cord clamping, only eight wards gave antibiotics routinely at least 15 minutes prior to incision. Eleven wards reported administration anywhere from less than 15 minutes, down to as little as "at incision", with most reporting it was at the discretion of the anesthetist (see Figure 1).

A third of the wards changed their prophylactic antibiotic practice from *after* to *prior to* cord clamping within the last 10 years (n = 9/21), but many did not recall when they changed their practice (n = 5/21). Only at three wards did the respondent recollect a specific year for when the change had happened.

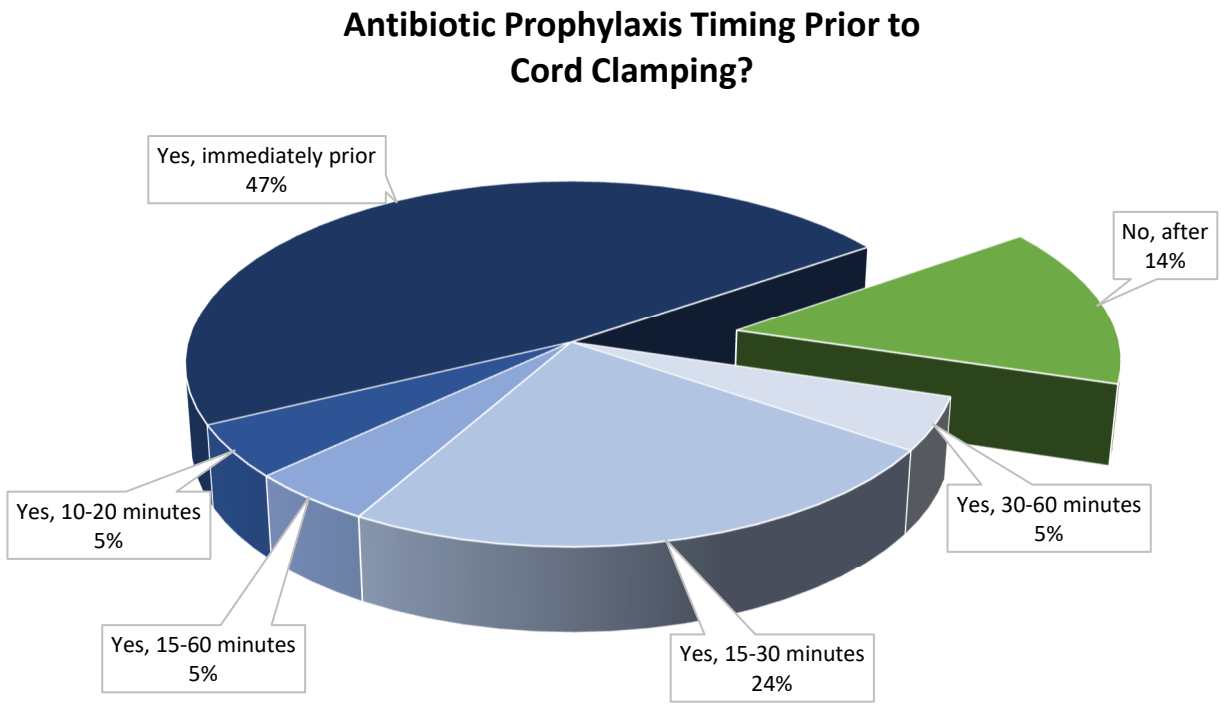

Figure 1: A chart pie diagram of equated answers for the question: "Do you administer the antibiotics prior to cord clamping of the infant?"
For the category "Yes, immediately prior" we have taken together any answers that can be equated to 0-15 minutes prior or at the anesthetist's discretion.

A few wards (n = 3/21) reported to repeat the antibiotic treatment within the first day after a hyper-acute cesarean section, with one department adding metronidazole to the treatment.

All respondents were either an authority on the subject or answered on their behalf, except for one ward where the answers where discussed and agreed upon by all the obstetricians. As seen in Table 2, responders who did not know when the change in practice took place, had been working for a shorter time on average at their department than those that could remember when the change was implemented; 6.1 vs 8.1 years.

At one ward two respondents answered to the questionnaire and the answers differed for three questions. One of the two respondents reported administration of antibiotics 5-10 minutes prior to incision with the other respondent reporting it was at the discretion of the anesthetist. One respondent reported that the department had changed their prophylactic antibiotic practice before 2010 and the other respondent reported that this happened between 2016 and 2019. These discrepancies are marked with an asterisk in Table 2 but were not included in Figure 1.

DISCUSSION

Most labor wards seemed to follow the recommendations of the Danish Society of Obstetrics and Gynaecology guideline [9] published in January of 2012. All wards used 1500 mg Cefuroxime as prophylactic antibiotics for all types of cesarean section, with the vast majority administering antibiotics prior to cord clamping. A third of the wards had changed their clinical practice regarding antibiotic timing at or after the time the guideline was published, indicating that the national guideline seemed to be a persuasive tool to uniform clinical practice. International publications and consensus was however announced prior to the publication of the Danish national guidelines [7,8].

The guidelines mention that a single dose given 30 minutes prior to incision is sufficient, but they also call this time period *the start of anesthesia*. This is the term that six wards used when describing timing of the antibiotic administration. However, in our experience this would mean that the timing was *at the anesthetist's discretion* and we therefore use these terms interchangeably. Further, at our department, the time from the start of the anesthesia procedure and until the start of the surgery is kept to a minimum, usually less than 15 minutes. We assume this is similar at other delivery wards in Denmark.

The Danish guidelines do not provide further discussion regarding the exact timing, but evidence from non-obstetric studies in general surgery indicates no difference in risk reduction as long as antibiotics are administered within 60 minutes prior to incision [10]. Cochrane reviews of women undergoing cesarean delivery have also not found an optimal period for administration prior to cord clamping, albeit in a smaller patient population [1,11]. However, for cesarean delivery there is concern that administration prior to cord clamping might cause long term harm to the infant microbiota [12]. In contrast to general surgery, there is usually only a delay of 1-5 minutes from the time of incision and until delivery. This then raises the question: will only a few minutes difference in administration result in a reported risk reduction of approximately 40% for either endometritis or surgical site infection in cesarean delivery? [4] The meta-analysis studying risk of surgical site infection after general surgery depending on timing of preoperative antibiotic prophylaxis, noted that there was a great heterogeneity between studies on the exact timing of antibiotics prior to surgery [10]. The exact post-incisional timing varied from immediately after to

a few hours after closing the incision. The studies that reported varying intervals for the antibiotic timing post-incision, seem to indicate that as more time passed from incision to administration of the antibiotics, the greater the risk of infection [13–15]. Contrary to the randomized trials included in the most updated meta-analysis, a recent large multi-center observational study conducted in Switzerland comprising 55,901 patients with prospective 30 day follow-up found no significant differences in risk of surgical site infection. Further, they showed that the timing interval either prior to or after cord clamping did not seem to have any clinically relevant effect either [16]. Further study into the consequences of timing of antibiotic prophylaxis is therefore needed.

Three wards did not adhere to the recommendation of antibiotic administration prior to cord clamping. We see two possibilities that can account for this: either those responsible for local clinical practice are not aware or they are not convinced of the recommendation's merits. Either way, it highlights that it might be advantageous to include representatives from as many wards as possible when composing national guidelines, to ensure nationwide uniform clinical practice. This will contribute to making sure different views on patient management are heard and key personnel will feel they have responsibility in realizing the recommendations.

A few wards offered comments on some additions to their antibiotic prophylaxis routines. Three wards reported that for hyper-acute cesarean sections (time to delivery <15 minutes) they extended the antibiotic prophylaxis with one or two extra doses postoperatively, or even added metronidazole. Meta-analyses have not found an effect of repeat dose of antibiotic prophylaxis for either elective or emergency cesarean section [17] but there could be some added protection from metronidazole [3], however with slight metronidazole accumulation in breastmilk [18]. The guidelines do not specifically address this subject, perhaps because hyper-acute cesarean sections are relatively rare. However, this lack of recommendation then opens up for differences in clinical practice, which other delivery wards may not be aware of. These differences can have consequences for research projects, if they are not taken into consideration. Even though the respondents in our study were recruited for being authorities on the subject, only three of the fourteen wards that had changed their practice were able to give a precise year for when the change in practice occurred. Most either did not remember or gave an approximate range of years, and in one instance two skilled respondents from the same department gave different answers.

The information regarding when changes in clinical practice take place, in general, can be valuable for both research and quality assessment. For the purposes of register-based research in Denmark, it might even be a good idea to keep track of obstetric delivery practices, for surgical, instrumentation and vaginal delivery methods at each labor ward. This could be done by establishing a database, where all wards submit their local guidelines regarding surgical procedures and antibiotic prophylaxis. A more ambitious project would be to either expand or establish a national registry of all obstetric patients and the details in clinical care. This could be achieved by establishing a Cesarean Birth Registry regarding key variables that vary with each cesarean section, such as exact timing of antibiotic prophylaxis, antibiotic dose, type of incision, suture technique used, use of single or double layered gloves and duration of the operation. Some of these variables could be made to be reported automatically from local electronic health records. That way, the frequent changes in local guidelines are accounted for and registered, and we will not need to rely on

the imperfect recollection of the institutions - as evident in this survey - for future research regarding the effects of implementing clinical changes.

CONCLUSION

All women routinely receive antibiotic prophylaxis for cesarean section in Denmark, with at least 1500 milligrams of Cefuroxime. Only three delivery wards administer antibiotic prophylaxis after cord clamping, with half the wards administering antibiotic prophylaxis immediately prior to cord clamping. Generally, the practices regarding antibiotic prophylaxis have become a lot more uniform in the past decades, perhaps in part due to national guidelines. We discuss if the actual clinical practice of antibiotic prophylaxis administration immediately prior to incision lives up to the guideline recommendations and current evidence.

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