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Journal of Women Health Care and Issues

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Review Article

Usefulness of Antibiotic Prophylaxis in Miscarriage Surgery for Induced Abortion and Retained Products of Conception: a Narrative Review

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Received date: August 05, 2022; Accepted date: September 13, 2022; Published date: October 10, 2022

Citation: Leonore Cloet, Kobe Dewilde, Thierry Van den Bosch. (2022). Usefulness of Antibiotic Prophylaxis in Miscarriage Surgery for Induced Abortion and Retained Products of Conception: a Narrative Review. J. *Women Health Care and Issues.* 5(6); DOI:10.31579/2642-9756/126

Abstract

Background: Miscarriage surgery is one of the most performed surgeries worldwide. Prophylactic antibiotics aim to avoid postoperative pelvic infection. Its use and benefit are well-known in induced surgical abortion, but far more ambiguous for miscarriage surgery for retained products of conception.

Objective: To investigate the usefulness of prophylactic antibiotics in miscarriage surgery for retained products of conception and induced abortion and evaluate the antibiotic regimen of preference.

Material and Methods: A comprehensive electronic literature search was conducted using PubMed, MEDLINE and Google Scholar. There were no specific inclusion criteria concerning study design, publication year, language, or study population.

Results: When evaluating the effectiveness of antibiotic prophylaxis for surgical intervention in induced abortion, 12 out of 19 studies showed a significant reduction on pelvic infection compared to the control group. There was no consensus regarding type and regimen of antibiotics. Five studies investigated prophylaxis in interventions for retained products of conception, of which 2 could show a significant effect.

Conclusion: There is evidence that antibiotic prophylaxis reduces the risk of pelvic infection. Single dose pre-operatively is favoured, for its effectiveness and patient compliance. Doxycycline and metronidazole are preferred, as for the type of antibiotics. There is limited evidence that antibiotic prophylaxis for surgical removal of retained products of conception or non-viable pregnancies might reduce the risk of pelvic infection.

Keywords: retained products of conception; induced abortion; miscarriage surgery; antibiotic prophylaxis; pelvic infection

Introduction

Globally there are an estimated 208 million pregnancies each year of which 10 to 20% end in spontaneous abortion [1]. Since miscarriage is often incomplete, surgical intervention may be required, making miscarriage surgery one of the most performed gynecological procedures worldwide [2]. When discussing miscarriage surgery, we need to acknowledge the difference between induced abortion and retained products of conception or non-viable pregnancies (previously defined as incomplete and missed abortion respectively). Spontaneous complete abortion does not require surgery in general, hence will not be discussed in this article.

A potential risk of miscarriage surgery is infection. Pelvic infection reportedly occurs in 1-4% of cases after surgical intervention for retained products of conception and may have long term consequences ranging from pelvic pain to dyspareunia, ectopic pregnancy, synechiae, and secondary infertility [3,4]. Finally, 13% (47 000) of maternal deaths are due to unsafe induced abortion practices, and this mainly because of infection [5].

The aim of prophylactic antibiotics in miscarriage surgery is to avoid pelvic infection, thereby preventing acute morbidity and mortality, as well as reducing the risk of infertility and extra-uterine pregnancies [2, 6].

Whilst antibiotic prophylaxis is often used in surgical interventions for induced abortion, data about its benefit in retained products of conception surgery, are less consistent [7]. Some guidelines do not recommend antibiotics based on a lack of data [8, 9], whilst others support its use based on hypothetical ground [10]. Also, the optimal antibiotic regimen remains uncertain [11].

An alternative strategy to prophylactic antibiotics, is the ‘screen-and-treat-strategy’. In the latter, only patients with proven infection are treated, therefore avoiding unnecessary use of antibiotics [6, 12].

In this review, we investigate the usefulness of prophylactic antibiotics in miscarriage surgery for retained products of conception and induced abortion and evaluate the eventual antibiotic regimen of choice.

Material and Methods

A comprehensive electronic literature search was conducted using PubMed, MEDLINE and Google Scholar. The search terms 'antibiotic prophylaxis', spontaneous abortion', 'retained products of conception', 'missed abortion', 'pelvic inflammatory disease', 'pelvic infection', 'post-abortal infection' and 'suction curettage' were used. Additional MeSH terms used in this search were the following: 'abortion, spontaneous', 'anti-bacterial agents', 'antibiotic prophylaxis', 'pelvic infection, prevention and control'. There were no specific inclusion criteria concerning study design, publication year, language or study population.

Results

Only few papers evaluated antibiotic prophylaxis for surgical intervention in retained products of conception (RPOC), while most studies cover antibiotic prophylaxis for induced surgical abortion. Some studies included both RPOC and induced abortion. Other studies compared different type of antibiotics regimens to prophylaxis while other studies compared one type of antibiotic prophylaxis versus placebo.

Diagnostic criteria of pelvic infection were defined in the most articles as two or more of the following symptoms: temperature > 38 degrees, adnexal masses or tenderness on pelvic examination, purulent discharge or heavy bleeding, and/or leukocytosis [3,4,11,13-22].

	Antibiotic	Dose		Pelvic infection rates treatment group N(%)	Pelvic infection rates control group N(%)	Significance	p-value	Compared to
[6]**Brewer(1980)**	doxycycline	500 mg	single dose	1/1519 (0,07%)	8/1431 (0,56%)	yes	< 0,05	placebo
[23] **Krohn (1981)**	tinidazole	2 g	single dose	6/104 (5,77%)	11/106 (10,37%)	no	0,23	placebo
[24] **SonneHolm (1981)**	penicilline G pivampicillin	2 million IU 3x 350 mg	pre- and postop for 4 days	14/254 (5,5%)	26/239 (10,9%)	yes	0,03	placebo
[25] **Westrom (1981)**	tinidazole	2 g	single dose	10/102 (9,8%)	17/110 (15,4%)	no	0,22	placebo
[26] **Krohn (1986)**	sulbactam ampicilline	0,5 g 1 g	single dose single dose	4/145 (2,75%)	11/140 (7,86%)	no	0,053	placebo
[13] **Darj (1987)**	doxycycline	400 mg	single dose	8/380 (2,11%)	24/387 (6,20%)	yes	0,0047	placebo
[14] **Levallois (1988)**	doxycycline	300 mg	single dose	2/502 (0,40%)	15/497 (3,02%)	yes	0,001	placebo
[12] **Pennev (1998)**	metronidazole doxycyline	1g 2x 100 mg	single dose for 7 days	35/755 (4,64%)	54/791 (6,83%)	no	0,07	screen&treat
[15] **Heisterberg (1985)**	metronidazole	3x 400 mg	pre- and postop	2/51 (3,92%)	10/49 (20,41%)	yes	0,012	placebo
[27] **Larsson (1992)**	metronidazole	3x 500 mg	for 10 days	3/87 (0,03%)	11/87 (12,64%)	yes	0,001	placebo
[16] **Crowley (2001)**	metronidazole	2 g	single dose	12/142 (2,11%)	21/131 (16,03%)	yes	0,0001	placebo
[28] **Sorensen (1992)**	erythromycine	2x 500 mg	for 7 days	20/189 (10,59%)	30/180 (16,67%)	no	0,09	placebo
[29] **Nielsen (1993)**	ofloxacine	400 mg	single dose	20/149 (13,42%)	27/159 (16,98%)	no	0,39	placebo
[17] **Henriques (1994)**	ceftriaxone	2 g	single dose	4/108 (3,7%)	6/129 (4,7%)	no		standard treatment (ampicillin+metronidazole/ metronidazole+pivampicilline 3x/d for 4 days)
[17] **Henriques (1994)**	ceftriaxone	2 g	single dose	02/275 (0,7%)	10/274 (3,6%)	yes	0,05	no antibiotics
[18] **Larsson (2000)**	clindamycine	creme	3 days pre-op	29/650 (4,46%)	30/626 (4,80%)	yes	0,77	placebo
[19] **Caruso (2008)**	prulifloxacin	600 mg	1 day pre-op 2 days postop	4/158 (2,5%)	16/153 (10,5%)	yes	0,004	prulifoxaline 600 mg 3 days postop
[3] **Sawaya (1996)**	NOS; meta-analysis			155/2587 (5,99%)	267/2601 (10,27%)	yes	< 0,0001	placebo
[11] **Low (2012)**	NOS; Systematic review			203/3525 (5,75%)	330/3500 (9,43%)	yes	< 0,0001	

Table 1: Effectiveness of prophylactic antibiotics for induced surgical abortion

A. Effectiveness of prophylactic antibiotics for induced surgical abortion (cfr Table 1)

In a randomized controlled trial using a single dose of 500 mg oral doxycycline pre-operatively, Brewer et al. found a significant reduction in pelvic infection, with 1/1519 (0,07%) patients being affected in the treatment group, compared to 8/1431 (0,66%) in the placebo group (X^2=4,37) [6].

Darj et al. showed a significant reducing effect on pelvic infection rates of a single dose of 400 mg of oral doxycycline 10-12 hours pre-operatively, with a RR of 0,33 (95% CI 0,15-0,73) [13]. Of the 800 women included in the

study, 32 were diagnosed with pelvic infection. Eight of them (2,1%; 8/380) had received prophylactic antibiotics, whereas the 24 (6,2%; 24/387) others did not.

A randomized controlled trial by Levallois et al. compared prophylactic 300 mg doxycycline with placebo in 999 patients undergoing induced surgical abortion. It confirmed a significant effect with 2/502 (0,44%) patients in the antibiotic group developing pelvic infection versus 15/497 (3,0%) in the placebo arm (p=0,001) [14].

A meta-analysis by Sawaya et al. showed an overall relative risk of 0,58 (95% CI 0,47-0,71) in developing pelvic infection in women receiving antibiotic therapy after induced surgical abortion (155/2587 (66%)), compared to placebo (267/2601 (10,33%)) [3]. In those with a history of PID, considered a high-risk-population, a summary RR of 0,56 (95% CI 0.37-0.84) was seen. In a low-risk population, without history of PID, there was a summary RR of 0,65 (95% CI 0,47-0,90).

In a double-blind randomized controlled trial, Heisterberg et al. compared the risk of pelvic infection in a group of patients receiving prophylactic metronidazole, in a regimen of 400 mg 1 hour pre-operatively, and 4 hours and 8 hours postoperatively, to a placebo group. A significant effect was shown with 2/51 (3,9%) infections in the prophylactic group in comparison to 10/49 (20,4%) infections in the placebo group (p<0,025) [15].

A double-blind randomized trial focused on women with bacterial vaginosis and compared the risk of pelvic infection after induced abortion when treated with metronidazole or placebo [16]. Metronidazole 3x500 mg was used for 10 days. In the treatment group 3/87 patients (3,45%) were diagnosed with pelvic infection, whereas infection was diagnosed in 11/87 (12.6%) patients of the placebo group (p<0,05).

A multi-centered randomized controlled trial by Crowley et al. (2001) compared the risk of pelvic infection after a single peri-operative dose of 2-gram metronidazole rectally to placebo, in women undergoing induced abortion and who were positive for bacterial vaginosis. Twelve out of 142 (8,5%) of the treatment group developed a pelvic infection, compared to 21/131 (16%) with a RR of 0,53 (95 CI 0,27-1,03) [16].

In a randomized trial, a group of 1672 women in Scotland undergoing induced abortion were allocated to either prophylaxis (metronidazole 1 gram rectally pre-operatively and doxycycline 100 mg twice daily for seven days) or a screen-and-treat-strategy [12]. Pelvic infection was seen in 4,6% of the prophylaxis group versus 6,8% of the screen-and-treat-strategy, not reaching a significant difference between the two strategies (RR 1,53; CI 0,99-2,36).

Henriques et al. investigated the effect of single dose ceftriaxone on pelvic infection, compared to a standard treatment in high- and low-risk patients [17]. Patients were considered high-risk when having a history of PID or STD, and their standard treatment was peroperative intramuscular ampicillin 1 gram and metronidazole 500 mg, followed by oral metronidazole 500 mg and pivampicillin 500 mg three times daily for four days. No significant effect was shown with 3,7% infections in the ceftriaxone-group and 4,7% in the standard treatment group.

On the other hand, the standard management for low-risk patients was no antibiotics. In the ceftriaxone-group 0,7% infections were diagnosed versus 3,6% in those who did not receive any antibiotics (p<0,05).

When comparing 500 mg of erythromycin twice daily for 7 days to placebo in a double-blind randomized trial, there was no significant difference in infection rates [28]. Pelvic infections occurred in 20/189 (10,6%) patients in the treatment group versus 30/180 (16%) in the placebo group (p= 0.13).

Nielsen et al. compared the risk of pelvic infection in women receiving ofloxacin 400 mg 90 min prior to intervention, to placebo [29]. Patients were divided in two groups: those with (N=308) and those without (N=765) a history of PID. In the former group, 20 out of the 149 (13,4%) patients receiving ofloxacin developed pelvic infection, compared to 27/159 (17%) in the placebo group (p=0.39). In the group without a history of PID, 35/376 (9,3%) of the antibiotics group were diagnosed with pelvic infection, versus 46/389 (11,9%) patients in the placebo group (p=0.26). The differences did not reach significance in any of the groups.

A double-blind randomized study by Larsson et al. assessed the use of vaginal clindamycin on pelvic infection rates after induced surgical abortion, compared to placebo [18]. The first group had a pre-operative treatment for three days with clindamycin cream 2%. Of them, 29/650 (4,5%) were diagnosed with pelvic infection, versus 30/626 (4,8%) in the placebo group (p=0,68). In the subgroup with abnormal vaginal flora, using Nugent's criteria defined as bacterial vaginosis and intermediate flora, there was a significant lower risk of pelvic infection in the treatment group (RR: 4.2 (95% C.I. 1.2–15.9)).

A Cochrane systematic review including 19 randomized controlled trials showed that antibiotic prophylaxis in women undergoing induced surgical abortion is effective in preventing pelvic infection [11]. Fourteen of these 19 RCTs have already been aforementioned [12]–[16], [18], [27]–[33]. The five other studies will be discussed here. Krohn et al. conducted a double-blind randomized trial to investigate the effect of a single pre-operative dose of oral tinidazole 2 grams compared to placebo in preventing infections in patients undergoing first trimester abortion with vacuum aspiration [23]. Six out of 104 (5,8%) patients in the treatment group, and 11 out of 106 (10,4%) patients in the control group were eventually diagnosed with postoperative pelvic infection and needed antibiotic treatment. Results were not significant (p = 0,23).A single-blind randomized trial by Krohn et al. investigated the effect of a pre-operative single intravenous dose of sulbactam 0,5 gram and ampicillin 1 gram compared to placebo in preventing postoperative endometritis after first trimester abortion with vacuum aspiration [26]. Four of 145 (2,75%) patients in the treatment group and 11/140 (7,86%) in the control group developed endometritis. Results were not significant (p = 0,08).

Sonne-Holm et al. assessed the effect of antibiotic therapy on pelvic infection compared to placebo in a double-blind study in patients undergoing induced first trimester abortion [24]. Patients in the treatment group were given two million IU penicillin G, one hour pre- and three hours postoperatively, and additionally 350 mg pivampicillin three times daily for four days. Pelvic infection occurred in 14 out of 254 (5.5%) patients in the treatment group, and 26 out of 239 (10.9%) patients in the placebo group (p= 0,05).

In a double-blind study by Westrom et al., 212 patients undergoing induced first trimester abortion were allocated to either single pre-operative dose of 2 grams tinidazole, or placebo [25]. Patients who were positive for gonorrhea were excluded. Ten out of 102 (9,8%) patients in the treatment group, and 17 out of 110 (15,4%) in the control group developed febrile reactions with rectal temperatures above 38 degrees. There was no significant effect (p = 0,22).

Caruso et al. conducted a randomized controlled trial in 466 patients undergoing induced first trimester abortion to assess the effect of prulifloxacin in preventing postoperative pelvic infection [19]. Patients were randomized in three groups: one receiving 600 mg prulifloxacin for 5 days after surgery, another group receiving 600 mg prulifloxacin for 3 days postoperatively and the last group receiving 600 mg prulifloxacin one day pre-operatively and two days postoperatively. Respectively 16 (10,4%), 11 (7,10%) and four (2,53%) patients developed symptoms of pelvic infection. Results were significant when comparing the first and last group (p=0,01).

In the Cochrane review, 203 out of a total of 3525 (5,875%) patients developed an infection in the study group, as compared to 330/3500 (9,42%) patients in the control group (RR 0.59 (95%CI 0.46 to 0.75)).

No recommendations were made regarding the most effective type of antibiotics and dosage regimen.

	Antibiotic	Dose		Pelvic infection rates Treatment group N (%)	Pelvic infection rates Control group N (%)	Significance	p-value	Compared to
[20] **Prieto (1995)**	doxycycline	100 mg	single dose	8/120 (6,67%)	7/120 (5,83%)	No	> 0,05	placebo
[34] **Ramin (1995)**	doxycycline	200 mg	single dose	1/145 (0,69%)	4/144 (2,78%)	no	0,17	placebo
[7] **AIMS (2018)**	metronidazole doxycycline	400mg 400 mg	single dose	26/1700 (1,53%)	44/1704 (2,58%)	yes	0,03	
	metronidazole doxycycline	400mg 400 mg	single dose	68/1676 (4,06%)	90/1684 (5,34%)	no	0,08	
[4] **Seeras (1989)**	tetracycline	4x 500 mg	for 7 days	25/62 (40,32%)	23/78 (29,49%)	no	0,36	placebo
[21] **Titapant (2012)**	cefoxitin	1 g	single dose	0/40 (0%)	2/39 (5,13%)	no	0,3	placebo
[22] **Islam (2021)**	NOS; Systematic review			367/8138 (4,51%)	551/8040 (6,85%)	yes	< 0,001	

Table 2: Effectiveness of prophylactic antibiotics for retained products of conception

B. Effectiveness of prophylactic antibiotics for retained products of conception (RPOC) or non-viable pregnancies (cfr Table 2)

A randomized open-label trial by Prieto et al. failed to show a decrease in postoperative pelvic infection in the prophylactic intravenous 100 mg doxycycline-group. Eight out of 120 (6,6%) patients in the prophylactic group developed postoperative infectious morbidity, versus 7/120 (5,8%) controls (p>0,05) [20].

A randomized double-blinded prospective study by Ramin et al. compared the effectivity of a single dose of 200 mg doxycycline 30-60 minutes prior to curettage to placebo in preventing endometritis [34]. Endometritis was diagnosed in 1/145 (0,6%) in the study group and 4/144 (2,8%) in the control group (p=0,22). It was calculated that 700 patients would be needed to be able to reach statistical significance.

Morrill et al. reviewed eight randomized controlled trials on prophylactic antibiotics for induced abortion and RPOC, and one randomized trial including second-trimester dilation and curettage [35]. Results of pelvic infection rates when comparing prophylaxis to placebo, were ambiguous. Seven of the 9 studies have already been discussed in this paper [14], [17], [18], [20], [28], [32], [36]. One study was left out, since it focused on doxycycline serum levels and side-effects, but also because it included second-trimester dilation and curettage (Reeves et al. 2009).

The other study, by Lichtenberg et al., compared two different regimens of doxycycline after suction curettage, namely 100 mg twice daily for three or seven days [33]. There was no significant difference between these two regimens, but the requirement for sample size was not reached.

A Cochrane Review by May et al. about antibiotics for incomplete abortion could only include 1 RCT: by Seeras et al [38]. The latter did not show any statistically significant effect on sepsis rate, using 500 mg of tetracycline four times daily for a week [4]. Twenty-five out of 62 (40,32%) patients were diagnosed with pelvic infection despite antibiotic prophylaxis, versus 23/78 (29,5%) patients in the placebo group. Since the vast majority of the treatment group (82,6%) did not take the prescribed medication, the lack of significant reduction may be attributed to poor compliance. Therefore, the authors suggest a single-dose regimen, e.g., doxycycline, to overcome the issue of poor compliance.

In 2012, a randomized controlled trial by Titapant et al., investigated the effectiveness of cefoxitin in reducing the risk of endometritis in curettage for incomplete abortion [21]. One gram of cefoxitin was given 20 minutes pre-operatively in the study group, and 0,1 ml of vitamin B in the control group. Two out of the 79 cases (2,53%) developed endometritis, both belonging to the control group. The difference did not reach statistical significance, with a p-value of 0,24.

The AIMS-trial was a randomized controlled trial investigating whether prophylactic antibiotics, defined as single dose oral doxycycline and metronidazole (400 mg each), used in low-resource countries effectively reduced the risk of pelvic infection [7]. Diagnostic criteria were defined as purulent or foul-smelling discharge, pyrexia, adnexal tenderness and leukocytosis more than $12x10^9$ per liter. The strict definition of PID required at least two of these characteristics, while the broad definition of PID required just one of these features and the clinical judgement for the necessity of antibiotics. When considering the broad criteria of PID, the results were not significant, with a risk of infection of 4,1% and 5,3% in the prophylactic group and placebo group respectively. However, when using strict criteria, there was a significantly lower rate of pelvic infection in the prophylactic group: 26/1700 (1,5%) versus 44/1704 (2,6%) patients respectively (RR 0,60 (95% CI, 0.37 - 0.96)).

A systematic review by Islam et al. studied prophylactic antibiotics in preventing pelvic infection in women with incomplete abortion [22]. In the overall group, 367/8138 (4,5%) patients receiving prophylactic antibiotics were diagnosed with pelvic infection, compared to 551/8040 (6,8%) in the control group (RR 0,72 (95% CI 0.58–0.90)). However, three studies focusing on the subgroup of women of low- and middle-income countries (N= 3579), did not show any significant effect. (RR 0,90 (95% CI 0,50-1,62). In 21 studies on women of high-income countries (N= 12599), there was a statistically significant effect of prophylactic antibiotics (RR 0,67 (95% CI 0,53-0,84). No recommendations concerning antibiotic dosage and regimen were made.

C. Choice of antibiotics

Several studies focused more specifically on the dosage regimen and type of antibiotics. Only studies comparing antibiotic regimens are included in this paragraph.

As discussed above, both oral doxycycline and metronidazole have proven to be efficient in miscarriage surgery for induced abortion [14], [36], [39].

A few studies focused on other regimens. In a meta-analysis by Heisterberg et al., based on 5 controlled clinical trials, penicillin and ampicillin reduced pelvic infection in women with a history of a pelvic inflammatory disease history [32], [36]. However, in women without a history of PID, imidazoles are more efficient in reducing PID.

As aforementioned, the Cochrane Review by Low did not make any recommendations regarding the most effective type of antibiotics and dosage regimen [11].

Herawati et al. conducted a retrospective study and evaluated the effects on the infection rates of 2 grams cefazoline pre-operatively and amoxicillin three times 500 mg postoperatively, administered in three regimens [40]. There were no significant differences between the three antibiotic regimens (p>0,05).

The systematic review by Islam et al. did not make any recommendations concerning dosage or regimen [38].

D. Screen-and-treat versus prophylaxis

An estimated 1% and 10% of patients attending a family planning clinic, are positive for N. Gonorrhea and C. Trachomatis respectively [41]. The isolation of Neisseria gonorrhea is associated with a three times elevated risk of post-abortal infection [42]. Several studies indicated that Chlamydia-positive patients have a significantly increased risk of pelvic infection after

induced abortion with rates from 10-20% in comparison to 1-8% in a Chlamydia-negative population [41]. An Australian study showed that there was a significant higher risk of pelvic infection after induced abortion in patients positive for bacterial vaginosis (10,8%) then in patients without anaerobic flora (4,5%) [43].

Osser et al. compared the rates of pelvic infection following induced abortion in Chlamydia-positive and -negative women [44]. Of the 1101 women undergoing curettage, 69/1101 (6,3%) were Chlamydia positive. Of these women, 16 (23,2%) and 10 (14,5%) were diagnosed with endometritis and salpingitis respectively in the first four weeks. In comparison, in chlamydia-negative women these rates were 59 (5.7%) and 5 (0.6%) respectively. These differencePenney et al. randomized women to either prophylactic antibiotics (metronidazole 1g prior to intervention and doxycycline 100 mg twice daily for seven days) or to the screen-and-treat-strategy. In the screen-and-treat group, adequate antibiotics was prescribed only if the culture came back positive [12]. Patients in the prophylaxis group had lower rates of pelvic infection (38/826 (4,6%)) than those in the screen-and-treat-group (58/846 (6,8%)), but no significance was reached.

Discussion

There is sufficient data supporting the use of prophylactic antibiotics for induced surgical abortion [3], [11], [13], [39], [41]. However, data on prophylactic antibiotics in surgery for retained products of conception, are far more ambiguous [2], [20].

Some studies suggest a significant reduction in infection rates in retained products of conception, when using oral doxycycline or metronidazole [14], [22], whilst others fail to show a significant effect of antibiotics [20], [21], [34]. The inconsistency in these trials is mostly due to a lack of sufficient sample size and of rigorous study design [2].

The most important and largest randomized controlled trial on this topic is the AIMS-trial and could only demonstrate a significant reduction in infections using strict diagnostic criteria for PID [2]. The participating countries in this trial included Malawi, Tanzania, Uganda and Pakistan. These specific countries were selected, since the researchers considered this clinical problem to be of particular importance in low- and middle-income countries [7]. Given the absence of similar studies in high-income countries, the issue whether these data can be extrapolated to other clinical populations has to be explored. In 2020, a study protocol for a systematic review and meta-analysis by Yu et al. was published. The researchers plan to investigate the effects of prophylactic antibiotics on the risk of pelvic infection in women undergoing surgery for incomplete spontaneous abortion [45]. This data could possibly lead to new insights.

The inconsistency amongst trials is also reflected in international guidelines, publishing different recommendations on the topic. RCOG and SCOG for example, do not recommend prophylaxis for retained products of conception due to the lack of robust data [8], [9]. ACOG on the other hand, extrapolating the findings on prophylaxis in induced surgical abortion, does advise antibiotics for this indication [10].

As for the type of antibiotics of choice for prophylaxis in miscarriage surgery, there is more consistency [14], [39]. Since infections after obstetrical surgical interventions are usually caused by endogenous flora or STD, the antibiotic prophylaxis should cover gram-negative, -positive and anaerobic agents. Therefore, the combination of doxycycline and metronidazole tend to be the preferred. Moreover, both antibiotic agents are relatively inexpensive, easily accessible, and allergies are infrequent [2], [46].

When comparing multiple versus single dose, the latter is to be preferred as to patient compliance [47]Given the plasma half-life of both doxycycline and metronidazole is over 10 hours, and given a curettage takes less than 30 minutes, a single dose may be considered sufficient [48], [49]. Therefore, antibiotic prophylaxis administered as a single dose pre-operatively is to be favored [46].

Another issue that remains uncertain, is whether a screen-and-treat-strategy should be preferred over universal prophylaxis. An advantage of a screen-and-treat-strategy is that only women who were tested positive would be treated, thereby avoiding unnecessary administration of antibiotics [41], [50]. Also, in screen positive women, the partner could be immediately treated as well, hence preventing re-infection [12]. A key study on this topic by Penney et al. failed to demonstrate a significant difference between prophylaxis and screen-and-treat [12]. The prophylactic regimen consisted of a ten-day course, and therefore should be considered therapeutic instead of prophylactic.

One of the downsides to the screen-and-treat-strategy is that more patients are at risk to be lost in follow-up, due to diagnostic delay, and hence won't be treated adequately. Also, to be successful, this strategy requires a vast organizational structure and thorough multidisciplinary communication [50]. Lastly, there may be a difference in population between women undergoing induced surgical abortion and those undergoing miscarriage surgery for retained products of conception. Women attending an abortion clinic may be more likely to match the high-risk profile for STD of being young with a lower socio-economic status and more likely to have a higher sexual risk behavior [38], [51]. Thus, for those specific patients a screen-and-treat-strategy could be considered more useful and cost-effective.

Importantly, antibiotic prophylaxis is applicable in asymptomatic patients. Clinical examination remains of utmost importance, to rule out infection already present at the time of intervention. In that case the patient should be treated according to local therapeutic protocol.

Conclusion

It is remarkable that there are few high-quality studies on one of the most performed surgeries worldwide. There is evidence that antibiotic prophylaxis for an induced abortion reduces the risk of pelvic infection. Single dose pre-operatively is favored, not only for its effectiveness, but also for patient compliance. As for the type of antibiotics, doxycycline and metronidazole are preferred. The role for the alternative screen-and-treat-strategy needs to be validated.

There is limited evidence that antibiotic prophylaxis for surgical removal of retained products of conception or non-viable pregnancies might reduce the risk of pelvic infection.

Further research should validate the benefit of prophylaxis in retained products of conception and clarify whether management should depend on the population profile.

Abbreviations: RPOC (retained products of conception)

Acknowledgements:

The authors declare no conflicts of interest. They received no specific funding for this work.

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DOI: 10.31579/2642-9756/126