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Incidence of uterine post abortion infection at Hospital de Clínicas de Porto Alegre. Is prophylactic antibiotic necessary?

Incidência de infecção pós-abortamento no Hospital de Clínicas de Porto Alegre. O antibiótico profilático é necessário?

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ABSTRACT

Objective: To identify the incidence of pelvic infection after miscarriage undergoing uterine evacuation in a tertiary hospital in southern Brazil and to compare with the international literature. **Methods**: we reviewed electronic medical records of the Hospital de Clinicas de Porto Alegre of all patients who underwent uterine evacuation for miscarriage between August 2008 and January 2012 were reviewed. We included all patients submitted to uterine curettage due to abortion and who had outpatient visits for review after the procedure. We calculated emographic and laboratory data of the study population, number needed for treatment (NNT) and number needed to harm (NNH). **Results**: of the 857 revised electronic medical records, 377 patients were subjected to uterine evacuation for miscarriage; 55 cases were lost to follow-up, leaving 322 cases that were classified as not infected abortion on admission. The majority of the population was white (79%); HIV prevalence and positive VDRL was 0.3% and 2%, respectively. By following these 322 cases for a minimum of seven days, it was found that the incidence of post-procedure infection was 1.8% (95% CI 0.8 to 4). The NNT and NNH calculated for 42 months were 63 and 39, respectively. **Conclusion**: The incidence of post-abortion infection between August 2008 to January 2012 was 1.8% (0.8 to 4).

Key words: Incidence. Infection. Pelvic infection. Abortion, spontaneous. Anti-bacterial agents/prophylaxis.

INTRODUCTION

It is estimated that 47,000 maternal deaths occurred each year worldwide between 1990 and 2008 due to abortion without safe practices, infection being the main cause[1]. Approximately 13% of maternal deaths are related to the performance of abortion with unsafe hygiene techniques[2]. One of the complications of this procedure is the post-abortion pelvic infection. The infection in the upper genital tract probably arises from the introduction or migration of bacteria through the uterine cervix[3]. This condition has its clinical short-term manifestation with the post-abortion syndrome, characterized by an acute pelvic infection[4], and on the long term, with sequelae and chronic pelvic pain, dyspareunia, infertility and ectopic pregnancy[5].

The use of antibiotic prophylaxis with oral doxycycline before the curettage procedure is recommended by the Society of Family Planning[6]. The half-life of doxycycline is four days[7] and theoretically there would be no need for a new prophylactic administration for a few days if curettage was rescheduled. However, the Ministry of Health of Brazil does not mention the use or not of prophylactic antibiotics for cases of abortion[8].

A 2012 meta-analysis on the use of antimicrobial prophylaxis before uterine evacuation in cases of abortion demonstrated that the prophylactic use of antimicrobials is effective in preventing infection of the upper genital tract after curettage; the incidence of post-abortion infection in the groups using universal prophylaxis was 2.1% (1.1 to 4)[2]. In this meta-analysis[2], it was warned that because of the heterogeneity of the studies this effect cannot be applied to all populations and needs to be revised in each location.

At the Porto Alegre Clinics Hospital (HCPA), a university tertiary hospital, universal antibiotic prophylaxis is not undertaken, since the incidence of post-abortion infection is not known; the primary objective of this study was to determine the incidence of post-abortion infection in women undergoing uterine curettage. The secondary objectives were: to calculate the demographic and laboratory data of the study population, the number needed for treatment (NNT) and number needed for harm (NNH).

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METHODS

Patients Analyzed

In this retrospective cohort study, we reviewed the medical charts of all patients who underwent uterine curettage for abortion at the Porto Alegre Clinics Hospital between August 2008 and January 2012. We included in the study all patients submitted to uterine curettage procedure due to abortion at the HCPA, with or without infection on admission, who had post-evacuation revision outpatient visits. The abortion cases were defined as gestational age d" 20 weeks, according to the last menstrual period or to obstetric ultrasound in the first quarter. All patients who had a diagnosis of miscarriage (according to the International Classification of Diseases – CID –O02.1, O03, O04, O05, O06, O07 and O08, with their subclassifications) were included. Cases of abortion with infection were not considered in the incidence of endometritis after curettage, but were considered to identify the laboratory (CBC, HIV, VDRL) and epidemiological profiles. The diagnosis of infected/septic abortion was made according to previously published criteria[9]. These data were verified by two independent investigators. In cases of doubts or discrepancies, a third researcher was consulted to reach consensus.

The post-abortion infection was defined by the presence of pelvic pain associated with at least one of the following signs or symptoms: increased vaginal bleeding as reported by the patient, fever (e" 37.8°C), bloody-purulent discharge flowing from inside the cervix, pain on mobilization of the cervix, adnexal pain, leukocytosis (> 14,000 leukocytes/mL) with or without increasing banded neutrophils, or the need to use antibiotics to treat pelvic infection identified in the first seven days after the procedure. Patients who used antibiotics to treat diseases other than pelvic infections, for example fungal vaginitis, low urinary tract infection, bacterial vaginosis, were not included as cases of post-abortion infection. The following variables integrated the standardized survey questionnaire: age at the time of curettage, race (white, indian, black, brown and yellow), hemoglobin (g/dL), total leukocyte count with differential, platelet count, serology for VDRL and HIV, level of schooling, and marital status.

Costs of medication

The different treatments for pelvic inflammatory disease have been reviewed in the literature[10,11]. Drug costs of prophylaxis (doxycycline) and treatment of pelvic inflammatory disease (doxycycline, azithromycin, ceftriaxone, clindamycin, gentamicin) were obtained from the websites of the Porto Alegre municipality (http://lproweb.procempa.com.br/pmpa/prefpoa/smf/usu_doc/_acs_ pe_085_12_medicamentos_humanos.doc) to calculate the cost of prophylaxis and treatment as described.

Ethical considerations and statistical analysis

This study was approved by the Ethics in Research Committee of the HCPA, under number 11-0248. The descriptive analysis with a confidence interval of 95%, the Mann-Whitney U test and the Fisher exact test were used for statistical analysis.

RESULTS

Of the 857 medical records of patients who were hospitalized in the Department of Gynecologic Emergency of the HCPA between August 2008 and January 2012, 378 cases were excluded because they were not submitted to curettage due to abortion. Of the 322 cases of uterine curettage without infection who were followed-up, six were identified with post-curettage pelvic infection (1.8% – 95% CI 0.8 to 4). Of the 87 cases that came with clinical / laboratory diagnosis of infected abortion, three had endometritis after curettage (3.5% – 95% CI 1.2 to 9.9), all had persistence of placental remnants. Further details of this study are depicted in figure 1.

When comparing patients who were hospitalized with or without a diagnosis of infected/septic abortion, we found that patients presenting infected/septic abortion had

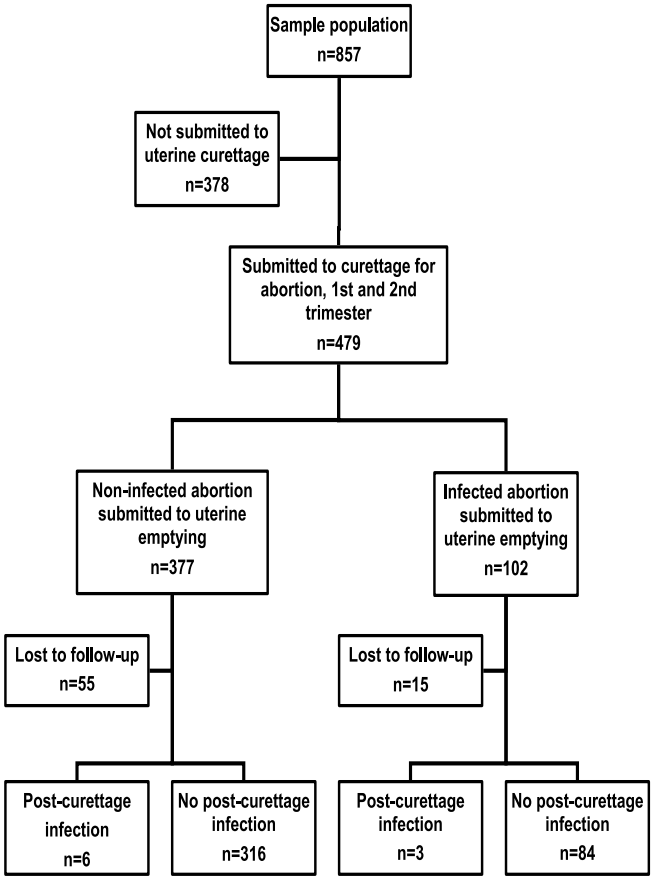

Figure 1 - *Flowchart of the study.*

a lower age compared with those who had no infection at admission, as well as a higher prevalence of HIV positive tests (Table 1). The costs of the prophylaxis and treatment of post-abortion infection in February 2013 ranged between R$ 17.64 and 31.85. (Tables 2 and 3).

DISCUSSION

The present study arose from the work of the group of the Cochrane Fertility Regulation, which suggests that the use of prophylactic antibiotics before uterine evacuation may not be effective in some populations and one should consider local epidemiological data[2].

Secondly, we aimed to identify the demographics of the population who presented or not with infected abortion at admission. We found that patients who were hospitalized with a diagnosis of infectious abortions were younger, with a higher prevalence of HIV infection (5.7%) and lower hemoglobin levels than those admitted without infection. No statistical difference was calculated for leukocyte levels, since the threshold of 14,000 leukocytes/mL was part of the criteria for infected abortion.

One should acknowledge the limitations of this study. Being a historical cohort study, and the study population consisting mostly (about 70%) of white and unmarried women, the generalizability of the data may be limited. The loss of 14.5% to follow-up could increase the incidence of post-curettage infection by 16%, which seems unlikely.

The incidence of 1.8% (95% CI 0.8 to 4) of post-curettage endometritis within a period of seven days after the procedure is within the limits of the incidence found in three European studies using prophylactic antibiotics[10-12]. In

Table 1 - Characteristics of the study population.

Characteristic	No infection at admission n=322	Infection at admission n= 87	*P*
Age-years	29 (14 a 47)	26 (15 a 43)	0.0008*
Race - n (%)			
White	254 (79)	67 (77)	
Black	50 (15)	15 (17)	
Brown	18 (6)	5 (6)	
Status - n (%)			
Married	85 (26.3)	10 (11.5)	
Divorcee	10 (3.1)	1 (1.1)	
Separated	3 (0.9)	0	
Single	222 (68.9)	75 (86.3)	
Widow	2 (0.8)	1 (1.1)	
HIV - n (%)			
Reagent	1 (0.3)	5 (5.7)	0.002**
No reaction	295 (91.6)	75 (86.3)	
Unavailable	26 (8.1)	7 (8)	
VDRL - n (%)			
Reagent	2 (0.6)	2 (2.3)	0.1**
No reaction	302 (93.8)	78 (89.7)	
Unavailable	18 (5.6)	7 (8.0)	
Hemoglobin (g / dl)	12.6 (7.2 a 14.4)	11.5 (6.7 a 15)	<0.0001*
Total Leukocytes	9020 (1410 a 13960)	15200 (4830 a 30940)	
Segmented	65 (32 a 87.5)	79.5 (42 a 94.1)	
Bands	0 (0 a 7)	0 (0 a 20)	
Eosinophils	1.5 (0 a 18.5)	0.6 (0 a 5)	
Basophils	0.2 (0 a 2.2)	0.1 (0 a 1)	
Monocytes	7 (0.4 a 13.9)	5 (0.3 a 11.3)	
Lymphocytes	25.2 (8 a 54.1)	10 (2 a 33)	
Metamyelocytes	0	0 (0 a 3)	
Myelocytes	0	0 (0 a 5)	
Platelets (x103)	245 (114 a 427)	231 (19 a 497)	0.17*

Data are median (range) or n (%)
** Mann-Whitney*
*** Fisher's Exact Test considering only with results available*

Table 2 - Cost to prevent one case of Pelvic Inflammatory Disease. Values of the drugs obtained from the Municipality of Porto Alegre 085/2012*

Medicine	Unit Value (R$)	Prophylaxis	Treatment Unit value (R$)	NNT	Final value to prevent one case of PID (R$)
Doxycycline	0.07/ 100mg pill	400mg 12h before surgery	0.28	63*	17.64
				91**	25.48
		500mg prior to surgery	0.35	63*	22.05
				91**	31.85

*NNT: number needed to treat based on the work of Brewer and Darj * 12 ** 13 and the incidence of infection in the HCPA.*
** Values of medicines obtained from the electronic address*
http://lproweb.procempa.com.br/pmpa/prefpoa/smf/usu_doc/_acs_pe_085_12_medicamentos_humanos.doc

Table 3 - Costs to treat one case of Pelvic Inflammatory Disease in an outpatient basis. Values of the drugs obtained from the Municipality of Porto Alegre 085/2012.

Drug	Treatment	Unit value (R$)	Final value to treat on case of PID (R$)
Ceftriaxone + Doxycycline[10]	Ceftriaxone 250mg IM + doxycycline 200mg/day for 14 days	Ceftriaxone 250mg-0.30 Doxycycline 100mg-0.07	2.26
Ceftriaxone + Azithromycin[11]	Ceftriaxone 250mg IM + 2 g Azitromicina	Ceftriaxone 250mg-0.30 Azithromycin 500mg-0.37	1.78
Gentamicin + Clindamycin + Doxycycline[10]	Gentamicin 240mg+ Clindamcin 2700mg IV for 3 days, followed by 10 days of doxycycline 200 mg daily*	Gentamicin 80mg-0.37 Clindamcin 600mg-0.99 Doxycycline 100mg-0.07	19.34

** Treatment with gentamicin and clindamycin has been used as a single daily dose at HCPA.*

a randomized study published by Darj *et al*. with 769 women where universal prophylaxis with doxycycline 400mg orally was compared with placebo, the number needed to treat would be 24 patients[12]. This represents a relative risk reduction of 66.9%. Brewer, in a randomized clinical trial with 2,950 women, identified an incidence of 0.1% (95% CI 0 to 0.4) of pelvic infection after curettage in the group who used prophylaxis (doxycycline 500mg orally on the day of curettage) and to 0.6% (95% CI 0.3 to 1.1) in the group using placebo. This represents an NNT of 203 women and a relative risk reduction of 88.2%[13].

These two studies[10,11] used universal prophylaxis compared with placebo and the incidence of uterine infection after the use of antibiotic were similar to those found in our study without the use of antimicrobials. The explanation for the low incidence of post-curettage infection at HCPA may be related to the criteria used to indicate therapy as the threshold of 14,000 leukocytes/mL.

With the values of relative risk reduction described by Darj *et al.*[12] (67%) and Brewer *et al.*[13] (88%), and the incidence of 1.8% in the HCPA, we could expect an absolute reduction of 1.1 to 1.6% of cases of infection after curettage, which would lead to a final incidence between 0.2 and 0.7% if we treated all patients with prophylactic antimicrobials. This would reduce the prevalence to a level below the confidence interval found in this study population. With that, we would have an NNT (NNT = 1/ Absolute Risk Reduction) between 63 and 91.

When using a prophylactic medication, besides verifying its benefits, it is necessary to check for side effects (Number Needed to Harm-NNH). A meta-analysis demonstrated that the use of doxycycline as prophylaxis for leptospirosis produced side effects in 3%, resulting in an NNH of 39 cases in the study population[14]. Thus, for every two patients treated (NNT = 63; = NNH 39.), we would have about one side effect. These side effects, mostly nausea and vomiting, decreased if the medication is taken with food[15].

If we take into consideration the cost of prophylaxis (doxycycline) and of treatment of pelvic inflammatory disease (doxycycline, azithromycin, ceftriaxone, clindamycin, gentamicin) and the different forms of treatment for pelvic inflammatory disease, we can calculate the cost of prophylaxis and treatment, as described in tables 2 and 3. As can be seen, in February/2013 one would spend values between R$ 17.64 and 31.85 to save the costs of the treatment of pelvic inflammatory disease, which would be between R$ 1,78 and 19.34.

Another aspect to be considered is the incidence and severity of complications if the patient developed a post-curettage endometritis. The incidence of long-term complications for women not submitted to prophylaxis is 22% for miscarriage, 20% for dyspareunia and 10% for infertility. These data were obtained from a sample of 38 patients in Sweden [16], which is in agreement with data published by Ness et al. in a sample of 800 patients who were followed for over six months[17]. At this population, there were six cases of post-abortion infection in the population that received no pre-uterine emptying antibiotic. These patients were contacted after three years of the procedure and only one of them had a miscarriage in this new period. The other patients denied problems such as infertility, dyspareunia, or pelvic pain. Although these data are not part of the original study, it seems that these complications (about 17% of six cases) are in agreement with findings in the literature[18,19].

The last aspect to be calculated are the losses and costs related to absenteeism. These values would have to be deducted from the cost of prophylaxis, for example, R$ 17.64, but are complex calculations that are not part of the objective of the present study.

In conclusion, post-abortion infection between August 2008 and January 2012 was 1.8%. This data provides the basis for calculating the sample size for a randomized clinical trial for the formation of policies on routine use or not of antimicrobial prophylaxis in cases of miscarriage.

R E S U M O

Objetivo: *Identificar a incidência de infecção pélvica após aborto espontâneo submetido a esvaziamento uterino num hospital terciário do sul do Brasil e comparar com a literatura internacional.* ***Métodos:*** *Os prontuários eletrônicos do Hospital de Clínicas de Porto Alegre de todas as pacientes que foram submetidas ao esvaziamento uterino por abortamento entre agosto de 2008 e Janeiro de 2012 foram revisados. Foram incluídas no estudo todas as pacientes submetidas à curetagem uterina por abortamento e que tiveram consultas ambulatoriais de revisão após o procedimento. Os dados demográficos e laboratoriais da população estudada,* number needed for treatment *(NNT) e o* number needed to harm *(NNH) foram calculados.* ***Resultados:*** *Dos 857 prontuários eletrônicos revistos, 377 pacientes foram submetidas ao esvaziamento uterino por abortamento; 55 casos foram perdidos no seguimento, restando 322 casos que foram classificados como aborto não infectado na admissão. A maioria da população era da raça branca (79%); a prevalência de HIV e VDRL positivos foi de 0,3 e 2%, respectivamente. No seguimento desses 322 casos, num período mínimo de 7 dias, verificou-se que a incidência de infecção pós-procedimento foi de 1,8% (IC95%0,8 a 4). O NNT e o NNH calculado para 42 meses foi de 63 e 39, respectivamente.* ***Conclusão:*** *A incidência de infecção pós-aborto entre agosto de 2008 a janeiro de 2012 foi de 1,8% (0,8 a 4).*

Descritores: *Incidência. Infecção. Infecção pélvica. Aborto espontâneo. Antibiótico/profilaxia.*

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