Antibiotics for incomplete abortion (Review)

May W, Gülmezoglu AM, Ba-Thike K

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ABSTRACT

Background
Unsafe abortions result not only in costs for acute care but may also be responsible for longer-term complications such as pelvic inflammatory disease, damage to reproductive organs, and secondary infertility. If effective, antibiotic prophylaxis at the time of the procedure can potentially prevent these adverse consequences.

Objectives
The value of routine antibiotics before surgical evacuation of the uterus in women with incomplete abortion is controversial. In some health centres antibiotic prophylaxis is advised; in others antibiotics are only prescribed when there are signs of infection. The objective of this review is to evaluate the effectiveness of routine antibiotic prophylaxis to women with incomplete abortion.

Search strategy
We searched the Cochrane Controlled Trials Register, Pubmed/MEDLINE, EMBASE and Popline. Date of last search: January 2007.

Selection criteria
Randomised trials comparing a policy of routine antibiotic prophylaxis with no routine prophylaxis were eligible for inclusion.

Data collection and analysis
Data extraction was conducted by two reviewers independently. Trial quality was assessed.

Main results
One study involving 140 women was included. A second well-conducted trial was excluded because of high losses to follow-up. No differences were detected in postabortal infection rates with routine prophylaxis or control. However, compliance with antibiotic treatment was also low.

Authors' conclusions
There is not enough evidence to evaluate a policy of routine antibiotic prophylaxis to women with incomplete abortion.

PLAIN LANGUAGE SUMMARY

Not enough evidence on routine antibiotics to prevent infection for women seeking care after incomplete abortion, but a single dose may be more suitable

Incomplete abortions cause many complications and the deaths of tens of thousands of women each year. Women who seek health care after an incomplete abortion usually come for problems from bleeding too much or infection. Antibiotics are generally given when there are signs of infection. The review of trials showed difficulties for women in continuing to take antibiotics and returning for care, so single dose antibiotics may be more suitable in these circumstances. The trials did not provide enough evidence to show the effects of routine antibiotics for women after incomplete abortion.

BACKGROUND

Unsafe abortion is a public health problem worldwide. The World Health Organization estimates that as many as 20 million abortions each year are unsafe and that 10% to 50% of women who undergo unsafe abortion need medical care for complications (WHO 1994). Approximately 13% of pregnancy-related mortality worldwide is due to unsafe abortion and the majority of these deaths (and morbidity) occur in developing countries where abortion is limited by law. 20-25% of all maternal deaths in Asia, 30-50% of all maternal deaths in Africa and Latin America and 25-30% of all maternal deaths in Russia are believed to be the result of induced abortion (Henshaw 1990, Popov 1991).

International meetings such as the United Nations International Conference on Population and Development (ICPD) held in Cairo in 1994 and the Fourth World Conference on Women held in 1995 in Beijing have urged governments to recognize and deal with the impact of unsafe abortion as a major public health concern.

Abortion-related maternal mortality and morbidity can be at least reduced by quality post-abortion care at all levels of the health care system. These levels include:

- the community level (with staff who have had basic health training, including traditional birth attendants)
- the primary level (with nurses, trained midwives, and in some cases, physicians)
- the first referral level (district hospitals)
- the secondary and tertiary levels (regional, national or teaching hospitals)(WHO 1995).

Quality post abortion care aims to strengthen the capacity of health institutions to offer three integrated components of care:

- emergency treatment for abortion complications
- post abortion family planning counseling and services
- links between emergency treatment and other reproductive health services (Population Rep. 1997).

Women who have had an unsafe abortion usually come to the health care facility with the following signs and symptoms:

- vaginal bleeding
- abdominal pain
- fever
- purulent or foul smelling vaginal discharge
- shock

The interventions which the health worker undertakes would depend on the level of health care facility, but at the primary level (with trained staff and appropriate equipment) or first referral level, the management would include:

- uterine evacuation
- initiation of antibiotic therapy
- initiation of intravenous fluid replacement
- oxytocics
- pain control (WHO 1995).

Among the above interventions, the effectiveness of manual vacuum aspiration (MVA) for uterine evacuation is well documented both in developed and developing countries (Greenslade 1993, Ekwempu 1990, Kizza 1990, Verkuyl 1993). In Ghana, non-physician providers at lower levels of the health care system, the midwives, have not only been trained but have now begun to provide post abortion care, which includes prophylactic amoxycillin (Billings 1998).

The use of antibiotics in septic abortion is well documented. Chow et al. (Chow 1977) compared the responses to therapy with either clindamycin alone or penicillin plus chloramphenicol in 77 patients with septic abortions in a randomised, double-blind study. It was found that aggressive management that included early uterine evacuation and broad-spectrum antibiotics effective against both aerobic and anaerobic bacteria was the key to reduced morbidity and mortality rates in treatment of septic abortion.

The use of antibiotics in individuals for induced surgical abortion is a controversial issue. Some authors have recommended periabortal antibiotics for surgical abortion (Blackwell 1993, Darj 1987, Grimes 1984) while others have advocated their use on women with a high risk of infection (Sonne-Holm 1981, Hemsell 1991, Heisterberg 1987). Sawaya, Grady, Kerlikowske and Grimes (Sawaya 1996) conducted a systematic review and meta-analysis of the data and concluded that there was a substantial protective effect of antibiotics in all subgroups of women undergoing therapeutic abortion. Penney et al.(Penney 1998) conducted a randomised clinical trial to compare two clinical management strategies for minimising the risks of infective morbidity after induced abortion . It was found that overall, women allocated to receive prophylaxis had lower rates of measures of short-term infective morbidity than those allocated to screen-and-treat. The above studies have been conducted on women coming in for induced surgical abortion in health care facilities, usually hospitals, under relatively “safe” and aseptic conditions.

Fawcus et al. (Fawcus 1997) in their study of the management of incomplete abortions at South African Hospitals found that antibiotics were prescribed for 49.5 % of women admitted with incomplete abortions. They found that antibiotic usage and blood transfusion were more common with increasing severity of the clinical presentation and a low haemoglobin level on admission.

The routine prophylactic use of antibiotics for women coming in with a presumed unsafe abortion is a question that still needs to be answered. In some countries, such as Ghana, Ethiopia and Nicaragua, prophylactic antibiotics are part of the post-abortion care package. In others, antibiotics are provided when there are signs and symptoms of infection.

In many settings, the objective of the intervention leading to unsafe abortion is an interference with intra-uterine contents so that either blood or products of conception pass through the cervical canal and vagina. It would therefore be a logical assumption that a common presentation of unsafe abortion is incomplete abortion and unless the woman attends a health care facility late with sepsis, the majority of these women will present with vaginal bleeding and pain. Although it is difficult to quantify what proportion of incomplete abortions are induced there is some evidence to support this assumption. In the South African Incomplete Abortion Study, 57.6 % (286/514) of women presenting with incomplete abortion and normal temperature (<37.3°C) were judged to have certainly, probably or possibly induced abortions by the clinicians looking after them (Jewkes 1997). Furthermore, also in the same study, 38.7 % of all incomplete abortion admissions were second trimester abortions (Rees 1997). This relatively high abortion rate in the second trimester of pregnancy suggests contribution of induced cases.

There is no uncertainty with regard to antibiotic treatment in septic abortion or in women with signs and symptoms of an infection. However, incomplete abortion is a frequent presenting form of unsafe abortion as well as "spontaneous abortions" and this is the case where, should antibiotic prophylaxis prove effective, a substantial amount of morbidity can be prevented. If not, scarce resources would be wasted.

Therefore, the present review aims to systematically search for and combine all evidence from randomised or quasi-randomised clinical trials to evaluate the effectiveness of the routine use of antibiotics for women with incomplete abortion in order to apply the best evidence currently available on which to base recommendations for clinical practice and further research.

OBJECTIVES

To determine, from the best evidence currently available, whether routine use of prophylactic antibiotics should be recommended for women with incomplete abortion.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

The types of studies that were considered for inclusion in this systematic review were randomised or quasi-randomised clinical trials.

Types of participants

The types of participants were women attending a health care facility with incomplete abortion. The trialists' definition of incomplete abortion are accepted in principle. In general, these included:
- bleeding
- pain
- passing products of conception

Women with signs and symptoms of infection were not included. No gestational age limit was imposed as long as the pregnancy was considered as an abortion by the trialist(s).

Types of intervention

Any antibiotic regimen compared to a no-antibiotic group (placebo/nothing). Other interventions such as blood transfusion, dilatation and curettage/manual vacuum aspiration or other medications for pain could be part of the intervention as long as the study groups compared an antibiotic with placebo/nothing.

Types of outcome measures

Clinical outcomes were the ones of interest to the review. The list of outcomes included:
1. Post-abortion infections
2. Antibiotic treatment after abortion
3. Prolonged hospital stay
4. Post-abortal fever
5. Pelvic inflammatory disease (PID)
6. Admission to intensive care unit (ICU)

These outcomes were added to the table of comparisons only when there was data for entry from included trials.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

The search strategy for this review included:
1. ELECTRONIC SEARCHES:
a. MEDLINE: 1966 to 2007
b. POPLINE: search conducted by Popline (1964 - 2007)(126 citations identified)
c. EMBASE: 1986 to 2007. (52 citations identified)
2. Cochrane Controlled trials register with the following key words:
- Abortion - incomplete
- Antibiotics
- Abortion - induced
- Abortion + antibiotics

METHODS OF THE REVIEW

The trials identified with our search strategy were checked initially for: duplicates and relevance for the review by looking at the title and abstracts. If it was not possible to exclude a publication by looking at the title or the abstract then the full paper was retrieved.

The remaining trials after initial eligibility assessment were evaluated for inclusion. Both application of inclusion criteria and

the data extraction were made by two reviewers (WM and AMG) independently and differences were resolved by discussion. Trials were excluded if the loss to follow-up rate was greater than 30 % or there were unexplained imbalances between the comparison groups.

In addition to the clinical outcomes, systematic data extraction was carried out for each trial for the following variables:
1. Methodology: Random allocation techniques, blinding, post-randomisation exclusions and loss to follow-up. Trials were given a quality score for the concealment of allocation as described in: Mulrow CD, Oxman AD (eds). Cochrane Collaboration Handbook [updated 1 March 1997]. In: The Cochrane Library [database on disk and CDROM]. The Cochrane Collaboration. Oxford: Update Software; 1996-. Updated quarterly.

2. Demographics: Type of health care setting, city, country, total number of women included, and inclusion and exclusion criteria.

There were no language preferences in the preparation of this review.

DESCRIPTION OF STUDIES

One trial conducted in Zimbabwe (Seeras 1989) was included in the review. See characteristics of included trials section for more details.

METHODOLOGICAL QUALITY

The Seeras trial was well conducted. Although placebos were not used outcome assessments were blinded and random allocation was accomplished by sealed, opaque envelopes. One other trial (Prieto 1995) which was eligible for inclusion had to be excluded because of a loss to follow-up rate of 30.5 %. However, this trial was otherwise a well-conducted placebo-controlled trial and the loss to follow-up was balanced in the two arms of the trial. Details of this trial have been presented in the 'excluded studies' section.

RESULTS

Seeras (1989) found no statistically significant differences in postabortal sepsis rates between the treatment and control groups (Relative Risk [RR]: 1.36, 95 % Confidence Interval [CI]: 0.86 to 2.14). The treatment group received tetracycline capsules 500 mg four times a day for one week. The compliance to treatment was assessed through interviews with patients and counting the remaining capsules. Only 17.4 % took the capsules and even then, failed to follow the instructions properly. The excluded Prieto trial used intravenous doxycycline at curettage and also did not find any decrease in the rate of postabortal fever in the treatment group.

DISCUSSION

The results from the studies demonstrated problems with patient compliance when an antibiotic has to be given several times a day for a week or so. Seeras (1989) has suggested that a single dose antibiotic would be better for improving the compliance.

Prieto et al. trial (1995) very clearly illustrated the fact that patients were difficult to follow-up, and that this was more so in post abortion patients. Prieto et al. used a single-dose intravenous antibiotic to ensure compliance. Considering the problems with compliance in the Seeras (1989) trial and the difficulty in following these patients it is important that future studies of antibiotic prophylaxis in abortion use a single-dose regimen to ensure that the intervention is applied.

Incomplete abortion is a significant public health problem in many countries, as evidenced by the high proportion of patients with incomplete abortion admitted to gynaecology wards. Abortion-related complications contribute greatly to maternal mortality and morbidity in health facilities. The use of prophylactic antibiotics in induced abortion is a controversial issue. This is an area where evidence-based information is really needed, since it involves large numbers of women, and no existing standard treatment with both proven efficacy and cost-effectiveness.

There is no arbitrary indication as to whether or not prophylactic antibiotics should be given. The majority of research has been carried out in hospitals on women coming in for a surgically induced abortion. There is very little research on the routine use of prophylactic antibiotics in incomplete abortion. The few randomised clinical trials that have been conducted to date, however, do not provide the evidence that routine prophylactic antibiotics decrease the rate of post-abortal sepsis. However, the low compliance rate in the Seeras (1989) trial indicates that the intervention was not effectively tested either. The cost implications of recommending routine prophylactic antibiotics to women coming in with incomplete abortion should also be taken into account if routine antibiotic policy is to be pursued, and further work needs to be done in this area.

AUTHORS' CONCLUSIONS

Implications for practice

There is no evidence to either recommend or to abandon the use of prophylactic antibiotics in women with an incomplete abortion. Clinical judgment would need to be used by the health care provider.

Implications for research

There is a real and urgent need to find out whether antibiotics should be routinely used in cases of incomplete abortion. The policy and cost implications arising from this research will be tremen-

dous, and randomised clinical trials comparing antibiotics currently in use with no antibiotics are strongly recommended.

POTENTIAL CONFLICT OF INTEREST

None known.

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TABLES

Characteristics of included studies

Study	Seeras 1989
Methods	Randomised into two groups using sealed envelopes containing the treatment modality.
Participants	140 women admitted with a diagnosis of incomplete abortion to a tertiary care hospital inHarare, Zimbabwe. Included women with clinical evidence of an incomplete abortion; oral temperature not higher than 37°C; absence of a foul-smelling vaginal discharge; absence of abdominal tenderness, and a negative cervical excitation test
Interventions	Experimental: Tetracycline 500 mg four times daily for one week and evacuation Control: Evacuation
Outcomes	Postabortal sepsis based on the presence of at least 3 out of 5 parameters: 1) history of chills, fever, headache,or lower abdominal pain; 2) oral temperature of greater than 37°C; 3) abdominal tenderness; 4) positive cervical excitation test; 5) presence of a foul smelling vaginal discharge.
Notes	Post-experimental exclusions: None reported Loss to follow-up: 2 in EXPT and 3 in CNTRL On follow-up after one week, compliance was found to be very low. 82.6% had either not taken part of the whole course or the whole course. the 17.6% who did, failed to follow the instructions properly. The evacuation method was not mentioned. The author recommended the use of Doxycycline or any other antibiotic which is cheap and covers a wide range of organisms, administered as a single dose.
Allocation concealment	A – Adequate

Characteristics of excluded studies

Study	Reason for exclusion
Brewer 1980	The study was excluded since it was on women undergoing induced abortion
Brown 2003	Descriptive study - not RCT
Chow 1977	The study was on women with septic abortion.
Crowley 2001	Randomised double-blind placebo-controlled trial, but for women with bacterial vaginosis for induced abortion
Darj 1987	The study was excluded since it was on women undergoing induced abortion.
Foy 2004	Cluster RCT for induced abortion , not for incomplete abortion
Gebreselassie 2005	Descriptive study on magnitude of abortion complications in Kenya
Heisterberg 1986	The study was excluded since it was on women with a history of pelvic inflammatory disease undergoing first-trimester abortion.
Henriques 1994	Excluded since the study was on women admitted for legal termination of pregnancy at 12 weeks or less of gestation.
Hodgson 1975	The study was excluded since it was on patients undergoing first trimester abortions.
Levallois 1988	The study was excluded since it was on women who were seeking induced abortions.
Lichtenberg 2003	RCT but for surgical abortion, not for incomplete abortion
Miller 2004	Randomised trial, but on women with bacterial vaginosis
Penney 1998	Study excluded because it was on women undergoing induced abortion
Prieto 1995	This study had a high allocation concealment quality score (A); the generation of allocation sequence was reported and adequate; power calculation was done; and blinding of outcome assessment was presumably but not specifically done. There was no blinding of providers nor patients. However, the randomization schedule for each patient was not known by the examining physician at the time of the 2-week follow-up pelvic examination. Post-experimental exclusions and protocol deviation was not reported. However, there was a loss to follow-up of 30.5% which was 0.5% higher than the 30% which the reviewers had specified for the exclusion criteria, which was the reason for exclusion of the study. The study was conducted on 345 consenting women with an estimated gestational age of 6 - 14 weeks with an incomplete abortion at a tertiary care hospital in Texas, U.S.A. Exclusion criteria were: haemodynamically unstable; allergic to doxycline; had evidence of a septic abortion or urinary tract or pelvic infection. Interventions were Doxycycline 100 mg intravenously and suction curettage for the experimental group and normal saline and suction curettage for the control group. Follow up was after 2-3 weeks. Outcome assessed was infectious morbidity which was diagnosed if any two or more of the following symptoms were found: 1) low abdominal pain; 2) uterine, adnexal or cervical motion tenderness; 3) purulent leukorrhoea; 4) leukocytosis of more than 15,000/cu. mm.; or 5) fever above 100.4°F. The authors concluded that in their population of patients with incomplete abortion, prophylactic doxycycline did not decrease the rate of postoperative febrlle morbidity. This study was methodologically sound and the trial was done according to the protocol. If it had not been for the loss to follow-up which exceeded the reviewers' criteria by 0.5%, it would have been included.
Reeves 2005	Cost-effective analysis - not RCT
Sonne-Holm 1981	The study was excluded since it was on women having induced first-trimester abortions.
Spence 1982	The study was excluded since it was on women undergoing second trimester intraamniotic injection abortions.

ANALYSES

Comparison 01. Any antibiotic vs nothing

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 postabortion infection	1	135	Peto Odds Ratio 95% CI	1.61 [0.79, 3.26]

INDEX TERMS

Medical Subject Headings (MeSH)

*Abortion, Incomplete; *Antibiotic Prophylaxis

MeSH check words

Female; Humans; Pregnancy

COVER SHEET

Title	Antibiotics for incomplete abortion
Authors	May W, Gülmezoglu AM, Ba-Thike K
Contribution of author(s)	Win May had the idea, consulted with Metin Gulmezoglu for suitability for a Cochrane Review, contributed to the search, appraisal, analysis, the text of the review and is responsible for maintaining the review. Metin Gulmezoglu helped in the conduct of the review, contributed to the search, appraisal, analysis and the text of the review. Katherine Ba-thike read and commented on the text of the review.
Issue protocol first published	1999/2
Review first published	1999/4
Date of most recent amendment	21 August 2007
Date of most recent SUBSTANTIVE amendment	02 July 2007
What's New	The review has been updated in May 2001, July 2003 and July 2007. No new studies were included. The 2007 update includes new studies identified but excluded.
Date new studies sought but none found	22 January 2007
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	22 January 2007
Date authors' conclusions section amended	Information not supplied by author
Contact address	Dr Win May Scientist USC Division of Medical Education Keck School of Medecine, University of Southern California 1975 Zonal Avenue KAM 218 B

Los Angeles
California 90033
USA
E-mail: winmay@usc.edu

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GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Any antibiotic vs nothing, Outcome 01 postabortion infection

Review: Antibiotics for incomplete abortion

Comparison: 01 Any antibiotic vs nothing

Outcome: 01 postabortion infection

Study	Treatment n/N	Control n/N	Peto Odds Ratio 95% CI	Weight (%)	Peto Odds Ratio 95% CI
Seeras 1989	25/60	23/75		100.0	1.61 [0.79, 3.26]
Total (95% CI)	60	75		100.0	1.61 [0.79, 3.26]
Total events: 25 (Treatment), 23 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.32 p=0.2