Medical versus surgical methods for first trimester termination of pregnancy

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Prostaglandins alone seem to be less effective and more painful than surgical abortion. Evidence is inadequate on the acceptability and side-effects of the two methods. The medical approach avoids the use of anaesthetics; this and the possibility of using it as an outpatient procedure may offer an advantage in under-resourced settings.

RHL Commentary by Chien P and Thomson M

1. EVIDENCE SUMMARY

In this review (1) the upper limit for gestational age for first trimester pregnancy was limited to 14 completed weeks of pregnancy (98 days from the first day of the last menstrual period). Five single centre trials conducted in Europe and the USA (two trials in the United Kingdom, one trial each in Sweden, Denmark and the USA) and a multicentre trial conducted by the World Health Organization (WHO) that had recruited participants from 12 countries in Europe, Asia and Africa were included in this review.

Several different regimens for medical termination of pregnancy were used. The method for surgical termination of pregnancy used in these trials was vacuum aspiration. Two trials compared the use of prostaglandin alone with vacuum aspiration. Another trial compared mifepristone alone with vacuum aspiration. The combination of mifepristone and a prostaglandin was compared with vacuum aspiration in another two trials. The remaining trial compared the use of methotrexate and prostaglandin with vacuum aspiration.

Prostaglandin alone versus vacuum aspiration

There were two studies identified for the comparison between prostaglandin alone with vacuum aspiration limited to pregnancies up to 49 days of amenorrhoea.
The odds for the abortion process not completed by the intended method were significantly higher in the prostaglandin group compared with the vacuum aspiration group [pooled odds ratio (OR) 2.67, 95% confidence interval (CI) 1.06–6.75; heterogeneity P = 0.75]. There was not enough evidence to evaluate ongoing pregnancy rate following the abortion process (pooled OR 0.55, 95% CI 0.16–1.84; heterogeneity P = 0.48). In the WHO trial, pelvic infection tended to be more common in the prostaglandin group compared with the vacuum aspiration group, but the confidence interval was wide (OR 2.17; 95% CI 0.64–7.33). Vaginal bleeding lasted significantly longer in the prostaglandin group compared with the surgical termination group (weighted mean difference (WMD) 5.20 days; 95% CI 4.98–5.42).

Sixty four per cent of women allocated to the medical termination group said they would prefer the medical method for a future termination, whereas 36% of women in the surgical termination group said that they would choose the medical method in the small (n= 64) trial from Sweden.

The authors of the review concluded that prostaglandin used alone appeared to be less effective and more painful compared with surgical termination of pregnancy in the first trimester. Participants in the WHO study were recruited and randomized without prior confirmation of pregnancy. A pregnancy test was only performed on day of treatment and 54 (11%) patients were subsequently found to be not pregnant and therefore were excluded from the analysis. The exclusion of these patients can potentially result in an imbalance between the two groups studied.

Mifepristone alone versus vacuum aspiration

The review identified one trial that compared mifepristone alone with vacuum aspiration. This trial was conducted in Denmark and recruited 50 women with less than 43 days of amenorrhoea. These women received either 600 mg mifepristone orally at home or underwent a vacuum aspiration procedure under general anaesthesia.

The abortion process was more likely to be not completed by the intended method in the mifepristone group compared with the vacuum aspiration group, but the confidence interval was wide due to the small study sample size (OR 3.63, 95% CI 0.66–20.11). There was no reported ongoing pregnancy in either study group, but one patient sustained a uterine perforation in the vacuum aspiration group. Three patients in the vacuum aspiration group had a pelvic infection whereas there was no case of pelvic infection in the mifepristone group (OR 0.13; 95 CI 0.01–2.58).

Out of all the various regimens for medical termination of pregnancy used in the primary studies in this review, mifepristone alone appears to have the lowest efficacy (76%). This study is also markedly underpowered with its small sample size and no information was provided on the method in which the randomization sequence was generated.

Mifepristone and prostaglandin versus vacuum aspiration

Two trials – both conducted in Aberdeen, Scotland – were included in the review for this comparison.

The first trial recruited 363 women with gestational age up to 63 days (9 weeks) requesting a termination of pregnancy. The medical intervention was the administration of 600 mg of oral mifepristone followed by 1 mg gemeprost vaginal pessary 48 hours later. The surgical group underwent a vacuum aspiration procedure under general anaesthesia with all primigravidae having prior cervical priming with 1 mg of gemeprost vaginal pessary. The trial design was a patient preference trial with 96 women randomized to the medical intervention group and 99 to the surgical method. The remaining 168 women chose the intervention for their termination of pregnancy (95 chose the surgical method and 73 chose the medical method). The results were analysed with both the randomized and non-randomized women combined together according to the administered treatment as there was no significant difference between the women who chose their own interventions and those who were randomized to the treatments received. The advantage with this study design is the likely improvement in recruitment rate for the study and the possibility of studying the effect of
patient’s preference for the treatment intervention on the outcomes studied. The potential drawback is the
uncertainty over whether the randomization process could be preserved with subjects being allowed to choose their own interventions.

The second trial was conducted on 486 women limited to 10–13 weeks of gestational age. The study design was a patient preference trial with 202 randomized to the medical group and 198 randomized to the surgical group. A total of 86 women were allocated to either medical or surgical termination method according to their preference. The medical group received 200 mg oral mifepristone followed by 800 ?g of vaginal misoprostol 36–48 hours later. If no products of conception were passed, a further two doses of 400 ?g of misoprostol were given either orally or vaginally at three hourly intervals. The surgical group underwent a vacuum aspiration procedure under general anaesthesia with all primigravidae undergoing cervical priming with 800 ?g misoprostol vaginally three hours before surgery. As in the above trial, the data were analysed with both the randomized and non-randomized women combined together according to the administered treatment.

The duration of vaginal bleeding was significantly longer in the medical group in both trials [weighted mean difference (WMD) 2.90 days, 95% CI 1.85–3.95 for the gestational ages up to nine weeks and WMD 3.00 days, 95% CI 1.60–4.40 for gestational ages between 10–13 weeks]. The amount of blood loss (assessed using a scoring system) was also significantly higher in the medical group for gestational ages up to nine weeks (WMD 1.90, 95% CI 0.05–3.75). For women with pregnancies of gestational ages between 10–13 weeks, pain from the procedure (OR 4.75; 95% CI 1.56–14.39), vomiting (OR 10.54, 95% CI 5.77–19.23) and diarrhoea (OR 15.87, 95% CI 7.38–34.15) were significantly more common in the medical group compared with the vacuum aspiration group.

Patient’s preference regarding the method for a future termination of pregnancy was reported in both studies. Seventy four per cent of women randomized to medical termination of pregnancy up to nine weeks gestation said they would prefer the same method of termination in the future, whereas 87% of women randomized to the surgical termination said they would prefer the same method for a future abortion. For women undergoing termination of pregnancy between 10–13 weeks gestation, 70% of women allocated to the medical group said they would prefer a similar option for a future abortion, whereas 79% of those assigned to the surgical group said they would chose the same method in the future.

Both studies were rated as high-quality studies in the review. The authors of the review concluded that vaginal bleeding lasts longer with medical termination of pregnancy (with both mifepristone and prostaglandin) compared with surgical termination, and this may be an important issue for women deciding on the preferred method for termination. The authors also highlighted that the data on pain following the procedure between the two groups may be difficult to interpret as women in the surgical group often received some form of routine analgesics in operation theatre as part of the procedure.

Methotrexate and prostaglandin versus vacuum aspiration

The review identified one small trial that made this comparison. This study had recruited 50 women with gestational ages up to 49 days to receive either 50 mg of methotrexate orally and 800 ?g of misoprostol vaginally 5–6 days later (n = 25) or manual vacuum aspiration and sharp uterine curetage (n = 25).

The proportion of women with the abortion process not completed by the intended method was higher in the medical group, but the confidence interval was wide (OR 4.57, 95% CI 0.47–44.17). As in the comparison between mifepristone and prostaglandin versus vacuum aspiration, the duration of vaginal bleeding (WMD 6.00 days, 95% CI 2.94–9.06) and pain resulting from the procedure (OR 153.00, 95% CI 8.12–2883.29) were significantly higher in the medical group compared with the vacuum aspiration group.
In this study, 63% of women allocated to the medical termination group expressed a desire for the same method of termination in the future, whereas 92% of women in the surgical termination arm said they would choose the same method in the future.

Both the method of randomization sequence generation and concealment of randomization were assessed to be adequate in this study.

2. RELEVANCE TO UNDER-RESOURCED SETTINGS

2.1. Magnitude of the problem

Induced abortion is one of the commonest gynaecological procedures performed around the world. It has been estimated that there are about 53 million abortions performed each year (2). In the United Kingdom, approximately 186 000 abortions are performed in England and Wales per annum and around 11 500 procedures per annum are performed in Scotland (3). Sadly, a significant proportion of the 53 million abortions are still performed in unsafe conditions, especially in developing countries. It has been estimated that approximately 13% of all maternal deaths in the world are attributed to the procedure having been performed in places where there is poor access to safe practice or the service is not available legally (4). Furthermore, complications arising from abortion procedures can also lead to subsequent morbidity with loss of fertility and the sequelae of chronic pelvic pain (5).

Since termination of pregnancy is such a common procedure, any attempt to reduce mortality and morbidity from this procedure can bring significant benefits to the quality of life for the women undergoing this procedure.

2.2. Applicability of the results

Of the four different regimens used for medical termination of pregnancy reviewed in this review, use of a combination of mifepristone followed by a prostaglandin 48 hours later is the most commonly used regimen at the present time (3). Given the clinical importance of this topic, it is surprising to find that the literature search for this review only retrieved two primary studies comparing the combination of mifepristone and prostaglandin versus vacuum aspiration. Of the two different gestational periods studied in these two studies, it is now widely accepted that the efficacy rate for the combination of mifepristone and prostaglandin is higher for gestational ages up to nine weeks than for the longer gestational period of 10–13 weeks (3). The prostaglandin employed in the study by Henshaw et al. (3) was vaginal gameprost pessary. This prostaglandin has now been replaced by vaginal misoprostol tablet owing to its cheaper cost. Indeed, the efficacy (defined as completion of abortion process without the need for surgical evacuation of uterus or suction termination of pregnancy) of 200 mg oral mifepristone followed by 800 μg vaginal misoprostol 1–3 days later for termination of pregnancy up to nine weeks gestation is at least 94% (6).

It is important to note that both the above primary studies on mifepristone and prostaglandin compared with vacuum aspiration were conducted in a well resourced and developed country. However, there is sufficient evidence from observational studies from under-resourced countries suggesting that the findings from the developed-country studies can be generalized to developing countries (7, 8).

The main advantage of the medical method over surgical termination of pregnancy is the potential avoidance of an anaesthetic and complications such as cervical laceration and uterine perforation. Furthermore, the whole procedure can be undertaken either at home or in an outpatient setting (9). In under-resourced settings, these features can be an advantage as the direct health-care cost is lower compared with the surgical option. The drawback with the use of mifepristone and misoprostol is the need to follow-up patients to ensure that the abortion process is complete. Because of the high efficacy, safety and benefits of medical termination of pregnancy with mifepristone and misoprostol, the proportion of pregnancies of up to nine
weeks’ gestation terminated with this method increased from 19% in 1996 to 55% in 2005 in a major teaching hospital in Dundee, Scotland (unpublished data).

2.3. Implementation of the intervention

There is evidence that it is beneficial to perform a routine ultrasound scan at the time when a patient is seen for the first time for a termination of pregnancy (10). The scan allows the determination of gestational age, which is important for advising the patient about the most appropriate method of termination. It also helps to diagnose multiple pregnancies, exclude/diagnose an ectopic pregnancy, diagnose a molar pregnancy and diagnose coincidental pelvic pathology, such as an ovarian cyst. The unavailability of this investigation may, however, be a limiting factor in a under-resourced setting.

Although the prostaglandin used in the original primary studies was either PGE2 or gameprost, it is clear that satisfactory efficacy can also be achieved with misoprostol (3). The use of misoprostol instead of PGE2 or gameprost will also reduce the cost of treatment especially in under-resourced settings.

There is sufficient evidence to show that the self-administration of these agents at home is feasible, safe and acceptable to patients. This approach will further open accessibility of the service and reduce the need to keep patients in hospital to provide a termination service (9).

A recent randomized controlled trial in Dundee has shown that the efficacy with the administration of 200 mg oral mifepristone followed by 800 ?g of vaginal misoprostol after six hours instead of the more conventional time interval of 48 hours can achieve an efficacy of 89% (11). The main advantage with this regimen is that the treatment can be delivered in one day as opposed to three days with the more conventional regimen. Although this efficacy rate is lower than that achieved with the 48-hour regimen, it can potentially improve the accessibility of the service, especially in developing countries where women may have to travel long distances to reach a clinic.

With regard to the need for follow-up of patients undergoing medical termination of pregnancy to ensure completeness of the abortion process, this is achieved in Dundee by keeping the patient on a day ward for six hours after the administration of misoprostol. If the patient can be verified to have aborted in the ward during this time interval, then the patient is discharged without any further follow-up. On the other hand, if the products of the pregnancy are not passed vaginally during this time interval, the patient is asked to return in two weeks for an ultrasound scan of the uterus. In under-resourced setting, such follow-up could be undertaken using a home pregnancy test 4–6 weeks after the administration of the mifepristone and misoprostol, instead of an ultrasound scan to ensure completeness of the abortion process.

3. RESEARCH

Future research should be conducted using the mifepristone and misoprostol protocol. There is a need to examine the different dosages, routes and timing of administration of these therapeutic agents to determine the most appropriate treatment protocol. There is also a need to evaluate whether repeated doses of misoprostol can further improve the efficacy of a single dose of misoprostol for termination of pregnancy up to nine weeks' gestation. Furthermore, head-to-head randomized comparisons between the combination of mifepristone and misoprostol with methotrexate and misoprostol should be undertaken to assess the efficacy of the later therapeutic regimen as mifepristone is not available and licensed for use in some countries where termination of pregnancy is not legally available.

References


Guest J, Chien PFW, Thomson MAR, Kossiem ML. Randomised controlled trial comparing efficacy of same day administration of mifepristone and misoprostol for termination of pregnancy with standard 36 to 48 hour protocol. *BJOG in press*.


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