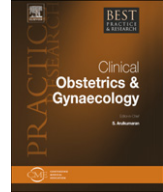




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8

### Issues in second trimester induced abortion (medical/surgical methods)

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Second trimester abortion remains a common procedure worldwide. Dilatation and evacuation (D&E) is the surgical method of choice, if the surgical expertise and facilities are available. Adequate cervical dilatation preoperatively is a prerequisite for a safe D&E. Medical abortion using misoprostol together with mifepristone is the medical method of choice. The recommended regimen is 200 mg mifepristone followed by 800 µg of vaginal misoprostol 36–48 h later. Subsequent doses of 400 µg of misoprostol can be given orally every 3 h up to a maximum of four more doses. Proper preoperative assessment would not only help to provide safe abortion treatment, but it also guides the choice of method. If the expertise and facilities of both methods are available, both methods should be discussed and offered to the patient so that the patient can make an informed choice.

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<sup>Q3</sup> Second-trimester abortion refers to the abortion performed between 13 and 28 gestational weeks. Abortion is one of the most common procedures done worldwide with an estimated 42 million induced abortions in 2003, compared with 46 million in 1995. The induced abortion rate in 2003 was 29 per 1000 women, of which, 48% of all abortions worldwide were unsafe, and more than 97% of all unsafe abortions were in developing countries.<sup>1</sup> Second-trimester abortions account for 11.2% of all abortions in the United States (USA) in 2005 and 9.7% in the United Kingdom (UK) in 2008.<sup>2,3</sup> In general, two-thirds of all major complications of abortions are attributable to those performed in the second

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45 trimester.<sup>4</sup> As the complication rate was much higher in abortions performed in the second trimester, it  
46 is important to facilitate the access to first trimester abortion to reduce the incidence of second  
47 trimester abortions, and to provide facilities for safe second trimester abortion in order to reduce the  
48 complication rates. However, the rate of second trimester abortions has remained the same in the  
49 recent decade.<sup>2</sup> In this article, the following issues on second trimester abortions are discussed: pre-  
50 abortion assessment and preparation, surgical methods, medical methods, patients with previous  
51 caesarean section and the factors affecting the choice of the method.

### 52 Pre-abortion assessment and preparation

53 To provide safe second trimester abortion, there should be careful pre-abortion assessment and  
54 preparation. A detailed history and careful physical examination should be performed to exclude possible  
55 medical disorders, risk factors for complications of abortion and to assess the gestational age of the  
56 pregnancy. If there is a discrepancy between the gestational age as estimated by the date of the last  
57 menstrual period and the uterine size, an ultrasound examination should be performed for accurate dating  
58 of the pregnancy. These will provide important information for the physicians and the pregnant women to  
59 choose the best-available treatment methods.<sup>5</sup> Counselling before abortion by appropriately trained  
60 personnel, such as nursing specialists and contraceptive counsellors, is also vital to reduce the risk of  
61 regrets and psychological burdens, and to plan for future contraception to decrease the chance of repeated  
62 abortions of unintended pregnancies. Proper assessment remains the most important way to reduce the  
63 chance of complications. Because of the possibilities of serious complications, second trimester abortions  
64 should be performed in facilities with easy access to blood transfusion and emergency laparotomy.

### 65 Surgical methods

66 Surgical abortion in the second trimester is the most common method in some countries such as  
67 USA and UK. Dilatation and evacuation (D&E) is the most common surgical method used for second  
68 trimester abortion. D&E was done in 98.6% of abortions between 13 and 15 weeks, 95.4% between 16  
69 and 20 weeks and 85.1% at 21 weeks or later in USA,<sup>2</sup> and 95% of abortions after 13 weeks in UK.<sup>3</sup>

70 Before D&E became the surgical method of choice in the 1970s, hysterotomy and hysterectomy,  
71 which are rarely done nowadays, were the only options for abortion after 17 weeks of gestation, other  
72 than medical methods. Hysterotomy, resembling a caesarean delivery on a pre-term uterus, consists of  
73 a laparotomy, incision on the uterus, removal of the product of gestation through the incision, together  
74 with the repair of the uterus. However, a low, transverse uterine incision is usually not possible, thus  
75 committing the patient to caesarean deliveries in future pregnancies.<sup>6</sup> This procedure is only per-  
76 formed when there is an obstruction of the cervix, either by uterine anomaly or by fibroid, or when the  
77 myometrium is too thin to safely manipulate instruments or to induce abortion. Hysterectomy should  
78 only be performed when there are other indications for hysterectomy.

79 D&E refers to transcervical instrumental evacuation of the pregnant uterus at  $\geq 13$  weeks' gestation.  
80 The most common method of D&E involves preparation with cervical dilatation, aspiration of  
81 amniotic fluid with disarticulation and removal of the foetus through the prepared cervix using strong,  
82 elongated extraction forceps.

83 One variant of D&E is known as intact dilatation and extraction (D&X). According to the American  
84 College of Obstetricians and Gynecologists (ACOG) Statement of Policy on abortion, published in 2007,  
85 D&X included four elements: (1) deliberate dilatation of cervix, usually over a sequence of days; (2)  
86 instrumental conversion of the foetus to a footling breech; (3) breech extraction of the body excepting  
87 the head; and (4) partial evacuation of the intracranial contents of a living foetus to effect vaginal  
88 delivery of a dead but otherwise intact foetus.<sup>8</sup> There is no good evidence regarding which method is  
89 the better option, while a retrospective analysis revealed the safety of both methods.<sup>9</sup>

### 90 Complications

91 Complications of D&E include cervical injury, incomplete evacuation, bleeding, infection and  
92 perforation of the uterus. Adequate cervical dilatation before D&E can help reduce the risk of

99 complications. It was shown by various studies that the more the *Laminaria* is used resulting in  
 100 a decreased need for intra-operative cervical dilatation, the less likely it is to have complications such  
 101 as cervical injury or vaginal bleeding during D&E.<sup>10,11</sup>

102 Bleeding is the most common complication of surgical abortion in the second trimester. Its inci-  
 103 dence increases with gestational age.<sup>7</sup> The use of uterotonics, such as oxytocin, is commonly employed  
 104 to reduce the amount of blood loss of the procedures. However, its efficacy was not proved by any  
 105 prospective trial. A retrospective analysis over 8 years' data showed the effectiveness of uterine artery  
 106 embolisation as the sole method to control the haemorrhage due to disruption of fibroid, placenta  
 107 accreta and cervical lacerations.<sup>12</sup> There was also a case report of using tamponade with a large  
 108 intrauterine balloon to successfully manage intra-operative haemorrhage during D&E at 18 weeks of  
 109 gestation for foetal aneuploidy not resulting from uterine atony.<sup>13</sup>

110 Uterine perforation is another serious complication in second trimester surgical abortion, with the  
 111 incidence of 0.32%.<sup>14</sup> It was shown that the use of routine intra-operative ultrasound guidance during  
 112 D&E reduced the rate of perforation.<sup>15</sup>

### 113 Cervical dilatation for surgical abortion in the second trimester

114  
 115 To ensure a safe D&E, adequate cervical dilatation is vital, which could be acquired with either  
 116 mechanical or pharmaceutical agents.

117 One commonly used mechanical agent is *Laminaria*, which is a genus of brown algae. After dehydration  
 118 and sterilisation, the stem of the seaweed forms a thin rod. When it is inserted into the cervical canal, it  
 119 absorbs moisture and then expands, leading to the dilatation of the cervix. The major drawbacks include  
 120 the need for overnight placement for adequate dilatation and the lack of uniformity with unpredictable  
 121 dilatation in a natural product.<sup>16</sup> Lamigel, a synthetic osmotic dilator, is a sterile tent of dehydrated  
 122 polyvinyl alcohol impregnated with 450 mg MgSO<sub>4</sub>, which absorbs water and swells fourfold in diameter  
 123 after 4 h, with faster action than *Laminaria*. However, Skjeldestad et al. reported only about half of the  
 124 Lamigel remained in place after overnight insertion, whereas the other half was partially displaced or  
 125 completely expelled in first-trimester abortion.<sup>17</sup> Lamigel is effective for cervical ripening with insertion of  
 126 few hours in surgical abortion of gestations up to 16 weeks.<sup>18,19</sup> When used overnight, Lamigel is effective  
 127 up to 17 weeks of gestation.<sup>20</sup> Dilapan-S is a hygroscopic cervical dilator that is manufactured from an  
 128 aquacryl, a proprietary hydrogel. There are three different sizes available and the manufacturer recom-  
 129 mends overnight insertion for second trimester abortion with more than one dilator according to gesta-  
 130 tion. It continues to expand over 24 h, although it can achieve 10-mm dilatation after 2–4 h of insertion.  
 131 There are no published data on the direct comparison between Dilapan and Lamigel.

132 Prostaglandin (PG) analogues, specifically the PGE1 analogue, misoprostol, are often used as an  
 133 alternative or an adjuvant for cervical ripening. Various routes of administration were studied.  
 134 Adequate cervical preparation was achieved in 32 women between 14 and 16 weeks of gestation with  
 135 600 µg of buccal misoprostol 2–4 h prior to D&E.<sup>21</sup> A randomised, double-blinded, controlled trial  
 136 comparing 400 µg of vaginal misoprostol, given 3–4 h preoperatively, with overnight *Laminaria* at  
 137 13–16 weeks of gestation showed that significantly faster procedures and greater preoperative dila-  
 138 tation were achieved with *Laminaria* than with misoprostol. More patients in the misoprostol group  
 139 required additional manual dilatation.<sup>22</sup> Edelman et al. reported a randomised trial of preoperative  
 140 cervical preparation with overnight *Laminaria* and either buccal placebo or 400 µg buccal misoprostol  
 141 approximately 90 min before second trimester surgical abortion. It showed misoprostol treatment did  
 142 not improve the initial mean dilatation achieved with *Laminaria* alone in either gestation of 13–  
 143 15-week or 16–20-week groups, while a sub-analysis of gestations 19 weeks or more demonstrated  
 144 significantly greater dilatation in the misoprostol group. Subjects receiving misoprostol reported  
 145 significantly more cramping than those receiving placebo.<sup>23</sup>

146 Mifepristone, an antiprogesterin, though not widely available in many countries, is a potentially effective  
 147 cervical ripening agent. Its use together with misoprostol, either orally or sublingually, was proved to be  
 148 more effective, in terms of the average cervical dilatation and shorter operative time than misoprostol in  
 149 either route alone.<sup>24</sup> However, mifepristone is expensive and not available in many countries. Therefore,  
 150 from the available data, the preoperative insertion of intracervical tents appears to be the method of choice  
 151  
 152

in dilating the cervix before D&E in pregnancies less than 19 weeks. In more advanced pregnancies, the combined use of intracervical tents and misoprostol may be more appropriate.

### Medical abortion

Medical abortions in the second trimester are widely employed worldwide, especially where surgical expertise is not available. The popular methods three decades ago include the use of intra-uterine instillation of hypertonic saline, rivanol or hyperosmolar urea. As these methods are invasive and may be associated with serious complications such as disseminated intravascular coagulation, they are seldom used nowadays<sup>25</sup> although they are still used in some developing countries, such as Uzbekistan, as reported by Kapp et al. A randomised trial reported by Kapp et al. showed that when compared with misoprostol alone, the use of intrauterine hypertonic saline plus a PG F2 analogue was associated with a significantly longer procedure time and significantly more complications, such as retained placenta and haemorrhage. Both providers and patients gave a higher procedural satisfaction score to the misoprostol method and the authors suggested adopting the misoprostol method.<sup>26</sup>

Oxytocin is frequently used as an induction agent at term gestation and its use in second trimester abortion has also been studied. A prematurely terminated randomised trial showed a significantly shorter induction-to-delivery interval and a higher induction success rate in the group using misoprostol 600 µg followed by 400 µg every 4 h for five doses, compared with the escalating dose-concentrated oxytocin infusions plus vaginal misoprostol 400 µg, then 200 µg every 6 h and then 100 µg.<sup>27</sup> Another regimen of 200 mg of mifepristone orally between 36 and 48 h before the vaginal administration of 800 µg of misoprostol, together with amniorrhhexis and intravenous oxytocin infusion was studied in a descriptive study with 428 women of gestation between 19.1 and 25.6 weeks. Complete abortion occurred in 90.4%, while 9.6% of patients required D&E with a uterine rupture in one woman with a previous caesarean section noted.<sup>28</sup>

### Medical abortion with PGs

A breakthrough in the field of medical abortion is the development of PGs and their analogues. The natural PGs were less effective than their analogues and their use was also associated with a higher incidence of side effects. PGF analogues were also associated with a high incidence of gastrointestinal side effects and they were often given intra-amniotically to reduce the incidence of side effects. They are now mostly replaced by the PGE analogues.

Sulprostone, a 16-phenoxo-w-17,18,19,20-tetranor PGE<sub>2</sub> methyl sulphonylamide, was used in the 1990s for second trimester abortion. It can be given intramuscularly. It was as effective as carboprost (15 methyl PGF<sub>2α</sub> analogue) but the incidence of side effects was less. However, it was withdrawn from the market due to its association with myocardial infarction caused by coronary spasm.<sup>29</sup>

The most commonly used PG analogues for second trimester abortion nowadays are the PGE<sub>1</sub> analogues, namely misoprostol (15-deoxy-16-hydroxy-16-methyl PGE<sub>1</sub>) and gemeprost (16,16,-dimethyl-trans-d2-PGE<sub>1</sub> methyl ester). Both of them are effective in second trimester abortion. A number of randomised trials have been conducted to compare these two analogues. A systematic review of six randomised trials on the use of vaginal misoprostol compared with gemeprost revealed similar efficacy, whereas misoprostol was associated with reduced narcotic analgesia requirement and surgical evacuation of the uterus.<sup>30</sup> However, different regimens of misoprostol were used in many of the trials included in this systematic review. There was evidence that the regimen of vaginal misoprostol 400 µg every 3 h is, in fact, more effective than the standard gemeprost regimen of 1 mg every 3 h. In a study comparing 400 µg of vaginal misoprostol every 3 h with 1 mg of gemeprost every 3 h, the induction-to-abortion interval was significantly shorter in the vaginal misoprostol group.<sup>31</sup> Another randomised trial comparing the same regimens of misoprostol and gemeprost also showed that women in the misoprostol group aborted earlier, while there was more pyrexia in the gemeprost group.<sup>32</sup>

There are additional advantages to using misoprostol over gemeprost. Misoprostol is cheap and stable at room temperature, while gemeprost must be stored below -10 °C. These properties make misoprostol particularly attractive in developing countries. Therefore, misoprostol is the PG of choice in medical abortion. However, in many countries, only gemeprost, but not misoprostol, is registered for

207 termination of pregnancy. While this should not prevent the off-label use of misoprostol in many  
208 countries, the patient should be fully informed and consent should be obtained from her before using  
209 misoprostol for termination of pregnancy.

## 210 Regimens of misoprostol

211  
212 Various regimens of using misoprostol have been studied.<sup>33</sup> A randomised trial compared three  
213 regimens of misoprostol: 200 µg misoprostol at 6-h intervals, 400 µg misoprostol at 6-h intervals and  
214 a loading dose of 600 µg misoprostol followed by 200 µg at 6-h intervals. The results showed that  
215 among these three regimens, the preferred regimen for intravaginal misoprostol was 400 µg at  
216 6-h intervals as it was associated with a shorter commencement to abortion interval than the 200 µg  
217 regimen and fewer maternal side-effects than the 600 µg loading dose regimen.<sup>34</sup> However, two other  
218 randomised trials showed that the regimen of vaginal misoprostol 400 µg every 6 h is less effective  
219 than vaginal misoprostol every 3 h. Both trials compared the regimen of 400 µg vaginal misoprostol  
220 every 3 h up to a maximum of five doses with the regimen of 400 µg vaginal misoprostol every 6 h up  
221 to a maximum of three doses in 24 h. Both trials showed significantly shorter induction-to-abortion  
222 interval in the 3-hourly regimen, with a higher incidence of fever in one trial.<sup>35,36</sup> Therefore, the  
223 3-hourly regimen was probably the most optimal.

224  
225 Although misoprostol was licensed for oral use, various studies showed that it is also effective when  
226 given by other routes. The intravaginal route of administration was shown to have a shorter induction-  
227 to-abortion interval compared with the oral route in a small prospective study, while the overall success  
228 rates were similar in the two groups.<sup>37</sup> Using vaginal administration of misoprostol alone was shown to  
229 have a significantly shorter mean induction-to-delivery interval ( $19.6 \pm 17.5$  h vs.  $34.5 \pm 28.2$  h,  $P < 0.01$ )  
230 and shorter length of hospital stay ( $32.3 \pm 17.3$  h vs.  $50.9 \pm 27.9$  h,  $P < 0.01$ ) when compared with oral  
231 administration. There was an increase in febrile morbidity in the vaginal group (25% vs. 6.7%,  $P = 0.046$ ).<sup>38</sup>  
232 The vaginal route was also showed to be more effective than the oral route after mifepristone priming.<sup>33</sup>  
233 There was also a reduction in the incidence of side effects. However, more women preferred the oral route.

234  
235 Because of the preference of women for the oral route, the alternative of sublingual admin-  
236 istration of misoprostol was investigated. A pharmacokinetic study showed that after sublingual  
237 administration, misoprostol was absorbed more rapidly than after vaginal administration and the  
238 peak serum level as well as the area under the time concentration curve of misoprostol acid, the  
239 active metabolite of misoprostol, were significantly higher than those after oral or vaginal  
240 administration. However, the serum levels of misoprostol acid were maintained for a longer period  
241 after vaginal administration than with oral or sublingual administration.<sup>39</sup> A subsequent study on  
242 the pharmacokinetics of misoprostol after either vaginal or sublingual administration of repeated  
243 doses of misoprostol every 3 h showed that after vaginal administration, the serum levels of  
244 misoprostol acid were slightly higher in the vaginal group after 3 h, if there was no significant  
245 bleeding. If there was significant bleeding, the serum levels of misoprostol acid declined despite  
246 repeated doses. This is probably due to the impaired absorption of misoprostol when there was  
247 significant bleeding. A prospective randomised trial of 120 women at 12–20 weeks of gestation  
248 comparing sublingual with oral misoprostol (400 µg every 3 h for a maximum of five doses)  
249 36–48 h after 200 mg of mifepristone showed no significant difference in the success rate at 24 h  
250 with 91.4% in the sublingual group and 85.0% in the oral group, but the median induction-to-  
251 abortion interval was significantly shorter ( $P = 0.009$ ) in the sublingual group. The incidence of  
252 fever was higher in the sublingual group. The incidence of other side effects was similar in both  
253 groups.<sup>40</sup> A randomised trial comparing the efficacy of vaginal or sublingual misoprostol showed  
254 that the abortion rate at 24 h was significantly higher in the vaginal group.<sup>41</sup> Another randomised  
255 controlled trial comparing vaginal administration versus sublingual administration by the World  
256 Health Organization (WHO) also showed a higher effectiveness in the vaginal route (85.9%) than  
257 sublingual administration (79.8%) in terminating second trimester pregnancies, but this result was  
258 mainly driven by nulliparous women at 24 h. Fever was more prevalent with vaginal adminis-  
259 tration.<sup>42</sup> The results of all these trials indicate that the most effective route for administration of  
260 misoprostol for termination of second trimester pregnancy was vaginal. Sublingual administration

can be considered if there is contraindication to the vaginal administration or if there is significant vaginal bleeding.

Mifepristone, an antiprogestone, is the only anti-progestin approved for induction of abortion. However, only 0.2% (2 out of 956) women aborted after mifepristone alone without gemeprost within 36 h in one review.<sup>43</sup> The low efficacy of mifepristone being used alone was confirmed by another descriptive study.<sup>44</sup> Since it can sensitise the uterus to the action of PGs, it is used nowadays mainly in combination with PGs in induction of second trimester abortion. The effectiveness as a combination regimen with the two PGE<sub>1</sub> analogues was well proven by various studies.<sup>40,45–47</sup>

### The use of cervical ripening agent

The use of misoprostol as a cervical priming agent for second trimester abortion, as a single dose of 50 µg of misoprostol given buccally for 30 min the evening prior to induction, was reported by one descriptive study, which included 19 women only. It showed that the median time from first dose of misoprostol expulsion was 9.4 h compared with the historical cohort of 14 h.<sup>48</sup> The insertion of a *Laminaria* tent 12 h before the administration of sulprostone has been shown to be effective in reducing the induction-to-abortion interval.<sup>49</sup> However, the *Laminaria* tent did not shorten the induction-to-abortion interval when the abortion was induced with vaginal misoprostol.<sup>50</sup> Mifepristone is a highly effective ripening agent. It can shorten the abortion process induced by PGs if it is given 36–48 h before the administration of PGs. Reducing the interval between mifepristone and PG to 24 h or less will lead to a significant increase in induction-to-abortion interval.<sup>51–53</sup> The dose of mifepristone can be reduced from 600 to 200 mg without loss of its efficacy.<sup>54,55</sup> Mifepristone 600 mg given 48 h before vaginal gemeprost was shown to be more effective in shortening the induction abortion interval than the *Laminaria* tent inserted 12 h before the administration of vaginal gemeprost.<sup>56</sup> Another randomised trial comparing mifepristone with *Laminaria* tent before vaginal misoprostol showed that the induction-to-abortion time was significantly shorter in the mifepristone arm (mean, 10 h vs. 16 h,  $P = 0.01$ ). Pain with cervical ripening was also significantly less in the mifepristone group than in the *Laminaria* group.<sup>57</sup> Therefore, the available evidence shows that mifepristone is the drug of choice for priming the cervix and uterus in second trimester medical abortion. Unfortunately, it is still not available in many countries.

### Recommended regimens

When mifepristone is available, the recommended regimen is 200 mg mifepristone followed by 800 µg of vaginal misoprostol 36–48 h later. Subsequent doses of 400 µg of misoprostol can be given orally every 3 h up to a maximum of four more doses.<sup>58</sup> Other PG analogues such as gemeprost can be used if misoprostol is not available. When mifepristone is not available, misoprostol can be used alone to induce abortion but the induction-to-abortion interval may be longer. Many regimens using misoprostol alone have been found to be effective. From the results of the various clinical trials, the regimen of 400 µg of vaginal misoprostol every 3 h up to a maximum of five doses appears to be an effective regimen without a very high incidence of side effects.<sup>33</sup> As a recent pharmacokinetic study showed that the absorption of vaginal misoprostol might be impaired in the presence of significant vaginal bleeding, misoprostol may be given orally or sublingually if the patient developed heavy bleeding. If the woman fails to abort after the completion of the first course of misoprostol, a second course of misoprostol can be given 12 h after the last dose of the misoprostol. Since the uterus is more sensitive to the action of PGs with increase in gestational age, a lower dose of PG or less frequent administration should be considered with pregnancies beyond 22 weeks. Medical abortion in pregnancies beyond 22 weeks may lead to the delivery of a potentially viable foetus. As recommended by the Royal College of Obstetricians and Gynaecologists (RCOG), intracardiac potassium chloride, one of the most commonly used foeticidal agents, should be used to induce foetal demise before medical abortion at  $\geq 22$  weeks gestation.<sup>58</sup> Potassium chloride is injected trans-abdominally under ultrasound guidance into the foetal cardiac ventricle or thorax. Digoxin, another commonly used foeticide, can be given by various routes, including injection into the amniotic fluid or other foetal tissues. Both agents were shown to be effective and safe.<sup>59,60</sup>

## 315 **Complication and risks**

316  
317 The most common side effects of PG analogues in second trimester abortion were nausea (64.7%),  
318 vomiting (22%) and chills (27.4%).<sup>61</sup> Fever was another commonly reported side effect, especially with  
319 misoprostol administration. The incidence was reported as 30–50% of women with 400 µg misoprostol  
320 every 3 h.<sup>31</sup> The probability of heavy bleeding requiring blood transfusion was 0.7%.<sup>44</sup>

321 A rare, but potentially life-threatening complication, is uterine rupture. Uterine rupture has been  
322 reported to occur in women undergoing second trimester abortion induced by either misoprostol or  
323 gemeprost.<sup>62,63</sup>

## 325 **Pain relief**

327 Abdominal cramping is common during second trimester medical abortion. Since some women  
328 would perceive pain as a very important factor in choosing the method of abortion, pain relief during  
329 abortion is of utmost importance. There are various reports regarding pain relief for abortion. A recent  
330 double-blind randomised controlled trial compared 500 mg paracetamol with 400 mg ibuprofen for  
331 pain relief with the regimen of 600 mg mifepristone orally followed by 400 µg of oral misoprostol 48 h  
332 later for first-trimester abortion. The investigators found no significant difference in the complete  
333 abortion rates, the mean pain score after misoprostol and no significant difference in the time of onset  
334 of pain. However, there was a significant difference between the two groups in mean pain scores after  
335 administration of the respective analgesics, with the ibuprofen group achieving greater reduction in  
336 pain compared with the paracetamol group. In addition, the number of women who asked for second-  
337 line analgesia (dipyrone) was significantly higher in the group that received paracetamol (26.5%) than  
338 in the group receiving ibuprofen (6.2%).<sup>61</sup> A retrospective analysis on the use of 3–4-hourly intra-  
339 muscular diamorphine 10 mg in second trimester abortion between gestations of 12 and 20 weeks  
340 with the regimen of mifepristone and misoprostol showed that 76.2% of women needed diamorphine  
341 for pain relief, while 3.6% of women (14 out of 386) required more than two doses of 10 mg intra-  
342 muscular diamorphine administration.<sup>64</sup> The use of intramuscular pethidine injection and epidural  
343 analgesia were also reported in second trimester abortion or medical induction for foetal demise in  
344 second or third trimester in 24% and 28% of patients, respectively.<sup>65,66</sup> Therefore, non-steroidal anti-  
345 inflammatory drugs can be used for pain relief without affecting the efficacy of the PGs in medical  
346 abortion. However, it is expected that some women will need narcotic analgesics for pain relief.

## 348 **Post-abortion care**

350 After abortion of the foetus, the placenta is usually delivered soon afterwards. If the placenta is still  
351 not delivered after 1–2 h, an intravenous oxytocin infusion may be set up to facilitate the expulsion of  
352 the placenta. After delivery of the placenta, it should be inspected carefully to assess whether it is  
353 complete. If it is incomplete, evacuation of the uterus should be performed. After delivery of the  
354 placenta, the patient should be observed for a few hours to monitor the amount of vaginal bleeding.  
355 During this period, future contraception can be discussed with the patient and appropriate advice can  
356 be given before the patient is discharged from the hospital.

## 358 **Second trimester abortion in women with prior caesarean**

360 With the increase in the incidence of caesarean for delivery for various reasons, there is an increased  
361 demand on performing abortion in women with prior caesarean. The safety issue and the relationship  
362 with uterine rupture are of great concern. Both medical and surgical methods for second trimester  
363 abortion were shown to be effective and safe.

364 Both misoprostol and gemeprost were found to be safe in this aspect. A small observational study in  
365 Egypt of over 50 women with one prior caesarean delivery undergoing abortion between gestations of  
366 16 and 26 weeks showed the safety of the use of four doses of 200 µg of misoprostol applied vaginally  
367 every 4 h daily, with a 12-h nightly rest from misoprostol applications. The success rate of the regimen  
368 was 90% with no uterine rupture noted.<sup>67</sup> In a retrospective study using gemeprost 1 mg every 3 h for

a maximum of five pessaries over 24 h, the overall success rate of abortion within 72 h was 98.4% in women with one to three prior caesarean deliveries. There was one case out of 67 having heavy vaginal bleeding requiring emergency surgical removal of placenta and blood transfusion. One patient at 20 weeks pregnancy with two lower-segment transverse caesarean sections required hysterotomy due to uncontrolled vaginal bleeding and hysterectomy during the procedures due to unresponsive uterine atony.<sup>68</sup> A small case series of 15 women with one to two prior low transverse caesarean deliveries having second trimester abortion between gestations of 16 and 28 weeks revealed no uterine rupture without specifically describing the regimen. There was one uterine rupture among the two women with previous classical caesarean deliveries. The authors also performed a systematic review, which showed the incidence of uterine rupture was 0.4% in women with one prior low transverse caesarean delivery.<sup>69</sup> Another systematic review estimated that the risk of uterine rupture among women with a prior caesarean delivery undergoing second trimester abortion using misoprostol is 0.28% (95% confidence interval (CI) 0.08–1%) after pooling results of 16 studies, including 3556 patients with three uterine ruptures noted.<sup>70</sup> In the case series of 91 women, it was also shown to be safe to use *Laminaria* with D&E in women with one or several prior caesarean deliveries for second trimester abortion of gestations 17–24 weeks with no uterine rupture reported.<sup>71</sup>

#### How to choose the method

Both surgical and medical methods for second trimester abortion are safe and effective. However, the choice of the method very often depends on the availability of the surgical expertise in performing D&E as well as the preference of the physician in charge. The choice of the method greatly varies in different localities. For instance, in US, D&E is used in over 96% of second trimester abortions,<sup>2</sup> while in North Europe, namely Finland and Sweden, and China, almost all second trimester abortions were performed medically.<sup>72</sup> In a retrospective cohort study in US, where D&E was used in over 96% of patients, the overall complication rate was significantly lower in patients who underwent D&E than in patients who underwent medical abortion (4% vs. 29%;  $P < 0.001$ ). Medical abortions with misoprostol resulted in a lower complication rate than abortions with other medications.<sup>10</sup> There was one randomised trial comparing D&E with the modern medical method of mifepristone followed by misoprostol. However, the study was stopped prematurely at 1 year because of slow enrolment with only 18 women participating. The regimen of mifepristone–misoprostol abortion caused more pain and adverse events such as fever in three patients (33.3%). Three patients required surgical removal of the placenta in the mifepristone–misoprostol group for retained placentae, while one patient required suction curettage 6 days after abortion for retained products of conception.<sup>73</sup> A recent Cochrane review showed D&E was related to a lower combined incidence of minor complications than intra-amniotic instillation of PGF<sub>2α</sub> (odds ratio (OR) 0.17, 95% CI 0.04–0.65), as was the total number of minor and major complications (OR 0.12, 95% CI 0.03–0.46). The number of women experiencing adverse events was also lower with D&E than with mifepristone and misoprostol (OR 0.06, 95% CI 0.01–0.76). Although women treated with mifepristone and misoprostol reported significantly more pain than those undergoing D&E, efficacy and acceptability were the same in both groups.<sup>74</sup> However, there was only a single randomised trial comparing D&E with the mifepristone and misoprostol regimen and the number of patients in this trial was small. Therefore, further randomised trials with a larger number of patients are needed.

Specialised training and the maintenance of an adequate caseload are required to perform D&E safely. Inexperienced providers are advised to use medical methods.<sup>58</sup> From a survey of National Abortion Federation members (NAF) in North America and Australia, 72% of NAF clinics offer second trimester abortion services. The majority of second trimester providers are obstetricians/gynecologists (63%), male (62%) and at least 50 years old (63%). What raised their concern was the ageing of skilled practitioners, which may affect the future availability of second trimester abortion.<sup>75</sup>

If the surgical expertise of D&E is available, both surgical and medical methods should be offered to the women who request second trimester termination of pregnancy and let them make their own choice based on the information provided and their acceptance. However, if the surgical expertise for D&E is not available, medical treatment should provide a safe option in case of second trimester abortion.



## Conclusion

D&E is the surgical method of choice for second trimester abortion but it requires gynaecologists, who have been properly trained, appropriate instruments and adequate caseload to maintain the skill. The combination of mifepristone and misoprostol is the regimen of choice for medical abortion in the second trimester. Both D&E and the mifepristone/misoprostol medical abortion are safe and effective. The choice will depend on the availability of the appropriate facilities and expertise. If possible, the wish of the patients should also be taken into consideration.

Larger trials on the direct comparison of misoprostol with mifepristone versus D&E should be carried out to elucidate the choice of method to provide second trimester abortion. Although the combination of mifepristone and misoprostol is a safe and effective option, mifepristone is not widely available. Other potentially useful agents should be explored to provide alternatives for mifepristone.

### Practice points

- Proper preoperative assessment is a prerequisite for the provision of safe second trimester abortion, no matter which method is used.
- D&E is the method of choice for surgical abortion in the second trimester. Adequate preoperative cervical dilatation with intracervical tents with or without misoprostol is essential to reduce the risk of complications.
- To provide a safe D&E, adequate training of the gynaecologists is vital. It is also important to have the appropriate instruments and an adequate caseload to maintain the surgical expertise.
- The regimen of mifepristone followed by misoprostol is the method of choice for medical abortion in the second trimester.
- Misoprostol alone may be used if mifepristone is not available, although it is associated with longer induction-to-abortion interval and more side effects.
- Both surgical and medical methods, if available, should be discussed and offered to patients requesting second trimester abortion.
- If surgical expertise for second trimester abortion is not available, medical abortion with misoprostol with or without mifepristone should be offered.

### Research agenda

- Larger randomised trials on the comparison of medical abortion with misoprostol together with mifepristone and D&E.
- Trials on other agents potentially useful for medical abortion.

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