Annotated Bibliography on Misoprostol Alone for Early Abortion

1. Aldrich T, Winikoff B. **Does methotrexate confer a significant advantage over misoprostol alone for early medical abortion? A retrospective analysis of 8678 abortions.** BJOG. 2007;114:555-562.

   A retrospective analysis of medical records compared the efficacy of four medical abortion regimens for termination of pregnancies of less than 56 days' gestation in 8678 women. Regimens analyzed were 2 doses of 800 mcg vaginal misoprostol alone, 50 mg/m^2 oral methotrexate plus 800 mcg vaginal misoprostol, 50 mg/m^2 oral methotrexate plus 800 mcg buccal misoprostol, and 50 mg/m^2 intramuscular methotrexate plus 800 mcg vaginal misoprostol. Success rates for the three methotrexate regimens were very similar (range 81.7 - 83.5%) and significantly greater than the success rate for the misoprostol-alone regimen (76.8%). Success was more likely for any of the three methotrexate regimens compared to the misoprostol-alone regimen (OR = 1.35). Success rates were lower with increasing gestational age.

2. WHO Research Group on Postovulatory Methods of Fertility Regulation. **Efficacy of two intervals and two routes of administration of misoprostol for termination of pregnancy: A randomised controlled equivalence trial.** The Lancet. 2007 369:1938-46

   This study tested four regimens of vaginal or sublingual misoprostol for induced abortion of gestations up to 63 days: three doses of 800mcg misoprostol given sublingually at 3-h intervals, vaginally 3h, sublingually 12h, and vaginally 12h. Treatment success was evaluated at 2-week follow up. Efficacy outcomes were analyzed for 2046 women, with complete abortion recorded in 84% (95% CI: 81-87) of the sublingual group and 85% (95% CI: 81-88) of the vaginal group when misoprostol was given at 3h intervals. In the 12h interval groups, the success rates were 78% (95%; CI:75-82) for sublingual and 83% (95%; CI:80-86) for vaginal administration. For vaginal routes, 3h and 12h intervals can be used; for sublingual administration the 3h interval is more successful, although side effects are increased.

3. Moreno-Ruiz NL, Borgatta L, Yanow S, Kapp N, Wiebe ER, Winikoff B. **Alternatives to mifepristone for early medical abortion.** Int J Gyn Obstet. 2007 96:212-218.

   This review analyzed prospective and controlled trials of misoprostol used alone or in combination with methotrexate for termination of pregnancies ≤63 days' gestation for misoprostol alone regimens, and <56 d for methotrexate regimens. Studies were included that were published since 1990 and if they included at least 100 women. Most misoprostol alone studies reviewed used a dose of 800 mcg vaginal misoprostol with 1-2 additional doses administered every 24 h. Success rates ranged from 84-96%. The median time for abortion completion ranged from 6-9h after the first dose. Most women completed their abortions within 3 days of the first dose of misoprostol. Studies analyzed employing methotrexate regimens commonly used a 50 mg/m^2 dose delivered intramuscularly followed by 800 mcg vaginal misoprostol 3 to 7d later. Efficacy ranged from 70-97% and was influenced by follow-up interval with longer intervals associated with higher success rates.

4. Salakos N, Kountouris A, Botsis D, Rizos D, Gregoriou O, Detsis G, Creatsas G. **First-trimester pregnancy termination with 800 mcg of vaginal misoprostol every 12h.** Eur J Contracept Reprod Health Care. 2005 Dec;10(4):249-254.

   This study tested the safety and efficacy of 800 mcg of misoprostol for pregnancy termination in 162 women with gestations between 50 and 63 days. Misoprostol was administered vaginally every 12 h for a maximum dose of 2400 mcg. Vaginal ultrasonography was performed 12 h after each dose to assess abortion status. Ninety-one percent of women had completed abortions at 36 hours. Sixty-eight percent of women had complete abortions at 12 h following the first dose while 18% and 5.4% of women had complete abortions twelve hours following the second and third doses, respectively. Mean time to expulsion was 8.5 ± 4 h. There was a significant decrease in hemoglobin from before to after treatment. Eighty-eight percent of women said they "had a very good opinion" or "good opinion" of the method. Eight-four percent of women stated that they would use the method again and 90% would recommend the method to a friend.

5. Blanchard K, Shochet T, Coyaji K, Ngoc NTN, Winikoff B. **Misroprostol alone for early abortion: An evaluation of seven potential regimens.** Contraception. 2005 Aug;72(2):91-7.

   This study tested seven regimens of oral or vaginal misoprostol for pregnancy termination up to 56 days' LMP. In phase I of the study, women were randomized to 1 of 3 misoprostol regimens (Arm 1: 4x400 µg po every 3 hrs, n=36; Arm 2: 2x800 µg po every 6 hrs, n=24; or Arm 3: 1x600 µg pv, n=40). In phase II, women were randomized to 1 of 2 regimens (Arm 4: 2x800µg po every 3 hrs, n=35, or Arm 5: 1x800 µg pv, n=25). In phase III two regimens were consecutively tested (Arm 6: 800 µg pv wetted with saline repeated after 24 hrs if intact gestational sac, n=51, and Arm 7: 2x800 µg pv wetted with saline every 24 hrs, n=50). None of the oral regimens had an efficacy rate higher than 50%. Arms 6 and 7 (800mcg pv) were the most effective (80%; CI:67-89 and 66%; (CI:52-78) respectively) and had lower rates of continuing pregnancy and incomplete abortion. At least 86% of women in each arm reported abdominal pain or cramps. All regimens were found to be acceptable despite low efficacy in 5 of the regimens.

6. Billings D. **Misoprostol alone for early medical abortion in a Latin American clinic setting.** Reproductive Health Matters. 2004 12;(24 Supplement): 57-64.

   Report of clinical experience of 2,900 women using 3 doses of 800 mcg vaginal misoprostol administered at 24 h intervals. Seventy-six percent had complete abortions at 72 hours using one, two, or three doses of misoprostol. A higher percentage of women aborting at 4-7 weeks of pregnancy had complete abortions (77%) than those at 8-10 weeks of pregnancy (70%). Data obtained on the first 78 women attending follow-up visits demonstrated a high level of satisfaction with the method.

7. Borgatta L, Mullally B, Vragovic O, Gittinger E, Chen A. **Misoprostol as the primary agent for medical abortion in a low-income urban setting.** Contraception. 2004 Aug;70(2):121-6

   This retrospective chart review reports the outcome of early medical abortion in 440 women with pregnancies with gestational age of 8 weeks or less. Women received two doses of 800 mcg vaginal misoprostol; the first dose was administered by a provider at the clinic and the second dose by the woman at home 24 h later. Of the 410 women with documented outcomes, 90.8% had a complete abortion (95% CI: 88-94), 9.2% had uterine aspiration (11 cases, 2.7% were medically indicated) and the remainder had incomplete or no follow-up. Among 57 women who reported the date and time of tissue passage, the mean time to abortion was 8.5 h (95% CI: 6.5-13h).

8. Carbonell JL, Rodriguez J, Velazco A, Tanda R, Sanchez C, Barambio S, Chami S, Valero F, Mari J, de Vargas F, Salvador I. **Oral and vaginal misoprostol 800 mcg every 8 h for early abortion.** Contraception. 2003 Jun;67(6):457-462.

   This study evaluated the efficacy and safety of 800 mcg misoprostol every 8 hours for 24 hours for medical abortion; the treatment was repeated if abortion did not occur in the first 24 hours. The first misoprostol doses were always self-administered into the vagina; the second and third doses could be administered orally or vaginally depending on the amount of bleeding. Four-hundred and fifty-two women with gestations between 36 and 63 days LMP were recruited into the study. Complete abortion occurred in 409/452 (90.5%; 95% confidence interval [CI] 87%, 93%) patients. Vaginal bleeding lasted 15.9 +/- 4.4 days.

9. Singh K, Fong YF, Dong F. **A viable alternative to surgical vacuum aspiration: repeated doses of intravaginal misoprostol over 9 hours for medical termination of pregnancies up to eight weeks.** BJOG. 2003 Feb;110(2):175-80.

   One hundred and fifty pregnant women with pregnancies up to eight weeks of gestation who requested medical abortion were given an initial dose of 800 mcg of vaginal misoprostol. A further dose of 400 mcg was repeated every 3 hours for a maximum of three doses. The complete abortion rate, defined as successful cases that did not require vacuum aspiration, was 84.7% and 96.0% at 15 days and 43 days after initial administration of vaginal misoprostol. The mean duration of vaginal bleeding was 11.7 days (SD, 4.7).The mean interval between first dose of misoprostol and the onset of expulsion of products of conception was 8.1 hrs (SD 6.3).

10. Zikopoulos KA, Papanikolaou EG, Kalantaridou SN, Tsanadis GD, Plachouras NI, Dalkalitsis NA, Paraskevaidis EA. **Early pregnancy termination with vaginal misoprostol before and after 42 days gestation.** Hum Reprod. 2002 Dec;17(12):3079-83.

    One hundred and sixty women seeking medical termination of a pregnancy of <56 days were given 800 mcg of vaginal misoprostol, repeated every 24 hours for a maximum of three doses. The overall complete abortion rate was 91.3%. In group A (gestation <42 days) complete abortion occurred in 96.3% of women, whereas in group B (gestation = 42-56 days) complete abortion occurred in 86.3% of women (P < 0.025). The two groups did not differ significantly with respect to side-effects (incidence of pain, bleeding, nausea, diarrhoea, fever and headache).

11. Jain JK, Dutton C, Harwood B, Meckstroth KR, Mishell DR Jr. **A prospective randomized, double-blinded, placebo-controlled trial comparing mifepristone and vaginal misoprostol to vaginal misoprostol alone for elective termination of early pregnancy.** Hum Reprod. 2002 Jun;17(6):1477-82.

    Two-hundred and fifty women with gestations < or = 56 days were allocated by a random number table to receive either 200 mg mifepristone orally or placebo followed 48 hours later by 800 mcg vaginal misoprostol. Administration of misoprostol was repeated every 24 hours up to three doses if abortion failed to occur. Abortion success was defined as complete abortion without the use of surgical aspiration. Successful medical abortions occurred in 114 out of 119 subjects (95.7%) after mifepristone followed by vaginal misoprostol and 110 out of 125 subjects (88.0%) after placebo and vaginal misoprostol.

12. Tang OS, Miao BY, Lee SW, Ho PC. **Pilot study on the use of repeated doses of sublingual misoprostol in termination of pregnancy up to 12 weeks gestation: efficacy and acceptability.** Hum Reprod. 2002 Mar;17(3):654-8.

    Fifty women requesting medical abortion at up to 12 weeks since LMP were given 600 mcg misoprostol sublingually every 3 hours for a maximum of 5 doses. The overall complete abortion rate was 86% (95% confidence interval: 74-93). The mean number of doses of misoprostol required was 4.1 +/- 1.1. Diarrhoea, fever and chills were the most common side-effects. The acceptability of this misoprostol regimen was 97.7% and 88.4% of the women would recommend it to others.

13. Tang OS, Ho PC. **Pilot study on the use of sublingual misoprostol for medical abortion.** Contraception. 2001 Nov;64(5):315-7.

    Sublingual administration of misoprostol was used by 25 women with first trimester, non-viable intrauterine gestation and by 18 women requesting mid-trimester termination of pregnancy. Twenty-three women (92%, 95% CI 75, 98) with first trimester, non-viable gestation had complete abortion after sublingual misoprostol. All women (100%, 95% CI 82, 100) requesting second trimester abortion aborted, with a median induction-to-abortion interval of 11.6 hours. Eight women (44.4%) required analgesia in the form of intramuscular pethidine.

14. Jain JK, Harwood B, Meckstroth KR, Mishell DR. **Early pregnancy termination with vaginal misoprostol combined with loperamide and acetaminophen prophylaxis.** Contraception. 2001 Apr;63(4):217-21.

    Two-hundred women with an intrauterine pregnancy < or =56 days gestational age were enrolled in the study. One-hundred participants (group 1) ingested 4 mg of loperamide and 500 mg of acetaminophen before the vaginal placement of 800 mcg of misoprostol moistened with 2 mL of saline. If abortion had not occurred, the same regimen was repeated every 24 hours (maximum three doses). One-hundred participants (group 2) from the same clinic who previously underwent the same misoprostol regimen without prophylactic medication served as a control group. The rate of successful abortion was not statistically significantly different between the two groups (group 1 93%, group 2 89%). The incidence of opiate analgesic use was statistically significantly less in group 1 (4%) compared with group 2 (16%) (OR 0.22, 95% CI 0.06-0.73, p=0.01). There was a significantly lower incidence of diarrhea in group 1 (23%) compared with group 2 (44%) (OR 0.38, 95% CI 0.20-0.73, p = 0.003).

15. Carbonell JL, Rodriguez J, Aragon S, Velazco A, Tanda R, Sanchez C, Barambio S, Chami S, Valero F. **Vaginal misoprostol 1000 micrograms for early abortion.** Contraception. 2001 Mar;63(3):131-6.

    Three-hundred women with gestations between 42 and 63 days LMP received 1000 µg vaginal misoprostol every 24 hours up to a maximum of three doses for abortion. Complete abortion occurred in 279/300 (93.0%, 95% CI 90, 96) patients. Mean expulsion time was 8.1 +/- 3.0 hours for those who aborted after the first misoprostol dose. Vaginal bleeding lasted 14.7 +/- 5.4 days. The frequencies of nausea and diarrhea were high.

16. Carbonell JL, Velazco A, Varela L, Tanda R, Sanchez C, Barambio S, Chami S, Valero F, Aragon S, Mari J. **Misoprostol for abortion at 9-12 weeks' gestation in adolescents.** Eur J Contracept Reprod Health Care. 2001 Mar;6(1):39-45.

    A group of 150 adolescents with gestations between 63 and 84 LMP days received 800 mcg of vaginal misoprostol every 24 hours, up to a maximum of three doses, for abortion. Complete abortion occurred in 126/150 (84.0%, 95% confidence interval 77-89) patients. The frequencies of nausea and vomiting were statistically significantly higher when compared to those obtained for adult females. Vaginal bleeding lasted for 13.2 +/- 3.8 days (median 13 days, range 1-22 days). The mean expulsion time was 8.0 +/- 3.4 hours (median 8 hours, range 1-14 hours) for all subjects who aborted after the first misoprostol dose.

17. Velazco A, Varela L, Tanda R, Sanchez C, Barambio S, Chami S, Valero F, Aragon S, Mari J, Carbonell JL. **Misoprostol for abortion up to 9 weeks' gestation in adolescents.** Eur J Contracept Reprod Health Care. 2000 Dec;5(4):227-33.

    One hundred and fifty adolescents with gestations between 35 and 63 days LMP received 800 mcg of vaginal misoprostol every 24 hours, up to a maximum of three main doses, for abortion. Complete abortion occurred in 133/150 (88.7%, 95% confidence interval 82-93) patients. The frequencies of nausea, vomiting and diarrhea were statistically significantly higher when compared to those obtained for adult females. Vaginal bleeding lasted for 12.7 +/- 5.7 days (median 12 days, range 1-23 days). The mean expulsion time was 6.8 +/- 2.4 hours (median 6 hours, range 3-14 hours) for those who aborted after the first misoprostol dose. The mean time for the return of menses, for those who aborted with misoprostol, was 34.7 +/- 3.4 days.

18. Ngai SW, Tang OS, Chan YM, Ho PC. **Vaginal misoprostol alone for medical abortion up to 9 weeks of gestation: efficacy and acceptability.** Hum Reprod. 2000 May;15(5):1159-62.

    This randomized study investigated the efficacy of misoprostol with water versus misoprostol alone for first trimester medical abortion in women at </= 9 weeks of gestation. Eighty women were randomly assigned to group 1 (water added to misoprostol) and group 2 (misoprostol alone). Vaginal misoprostol 800 mcg was given on days 1, 3 and 5. If the woman did not require vacuum aspiration during the period up to the return of first menstruation after medical abortion, the outcome was classified as complete abortion. The complete abortion rate appeared higher when water was added but the difference did not reach statistical significance. Gastro-intestinal side-effects were common but well tolerated in both groups. With an overall complete abortion rate of 85%, the method is probably not a clinically acceptable.

19. Carbonell JL, Varela L, Velazco A, Tanda R, Barambio S, Chami S. **Vaginal misoprostol 600 micrograms for early abortion.** Eur J Contracept Reprod Health Care. 2000 Mar;5(1):46-51.

    The objective of this study was to evaluate the efficacy and safety of the vaginal self-administration of 600 mcg misoprostol up to a maximum administration of three doses in a 24-hour period, one every 8 hours, for abortion up to 9 weeks' gestation. A group of 90 women with gestations from 35 to 63 days LMP participated in the study. All women who aborted received a single additional dose of 600 mcg misoprostol. Complete abortion occurred in 57/89 (64%, 95% confidence interval 53-74%) subjects. The mean expulsion time was 7.4 +/- 3.8 hours (median 7.2 hours, range 3-20 hours) for all women who aborted within the first 24 hours of the administration of misoprostol. Thirty-two cases failed to abort, 28 cases due to failure of the method, of which 24 had a negative cardiac rhythm after the third dose, and four cases due to the doctor's decision.

20. Bugalho A, Mocumbi S, Faundes A, David E. **Termination of pregnancies of <6 weeks gestation with a single dose of 800 microg of vaginal misoprostol.** Contraception. 2000 Jan;61(1):47-50.

Women with < or =42 days of amenorrhea, pregnancy confirmed by ultrasound, received 800 mcg of vaginal misoprostol once and were observed for 1 week. The gestational sac was measured before misoprostol administration, and 24 hours and 7 days afterward. After 1 week, those who had not aborted received a second dose of 800 mcg. Those who had not aborted by 24 hours later were treated by vacuum aspiration of the endometrial cavity. Twenty-four hours after treatment, 71.8% had aborted, and 87.1% aborted 3 days after treatment. After the second dose, 7 days later, the cumulative abortion rate reached 92.1%. None of the subjects who aborted required curettage or vacuum aspiration. The main complaints were pain (84.5%), nausea (21.4%), and headache (17.5%).

21. Jain JK, Meckstroth KR, Park M, Mishell DR Jr. **A comparison of tamoxifen and misoprostol to misoprostol alone for early pregnancy termination.** Contraception. 1999 Dec;60(6):353-6.

A clinical trial was conducted with a study group of 150 healthy women with pregnancies of </=56 days gestational age who desired pregnancy termination. Subjects were randomized to ingest either 20 mg of tamoxifen (group 1) or placebo (group 2) twice daily for 1 day, followed 48 hours later by vaginal administration of 800 mcg of saline-moistened misoprostol. This dose of misoprostol was repeated 24 hours later and 8 days later if an abortion had not occurred. Complete abortion occurred in 709 (93.3%) in group 1 and 68 (90.7%) in group 2. There was no difference in either group between earlier (</= 49 days) and later (50-56 days) gestations. The mean duration of uterine bleeding was 7.9 days and 8.2 days in group 1 and group 2, respectively. In group 1, 94.3% who aborted bled for <14 days, and in group 2, 95.6%.

22. Tang OS, Wong KS, Tang LC, Ho PC. **Pilot study on the use of repeated doses of misoprostol in termination of pregnancy at less than 9 weeks of gestation.** Adv Contracept. 1999; 15(3):211-6.

Twenty women at a gestational age of less than 9 weeks were given 800 mcg of vaginal misoprostol as an initial dose followed by 400 mcg of vaginal misoprostol every 3 hours for 4 doses. Fourteen women (70%, 95% confidence interval: 48, 85%) had a complete abortion. Two women (10%) had a missed abortion, and two (10%) had an ongoing pregnancy. Two women (10%) had an incomplete abortion. The interval between the first dose of misoprostol and the passage of tissue mass was 25.3 +/- 34.4 hours (median: 15 hours).The duration of vaginal bleeding was 23.6 +/- 20.4 days (median: 14 days). Side-effects were mild.

23. Jain JK, Meckstroth KR, Mishell DR Jr. **Early pregnancy termination with intravaginally administered sodium chloride solution-moistened misoprostol tablets: historical comparison with mifepristone and oral misoprostol.** Am J Obstet Gynecol. 1999 Dec;181(6):1386-91.

One hundred women at </=56 days' gestation received 800 mcg misoprostol intravaginally using sodium chloride solution-moistened tablets. The dose was repeated 24 hours later if a gestational sac persisted on ultrasonographic examination. These 100 subjects (group 1) were then matched with 100 subjects who had received 600 mg mifepristone followed by 400 mcg misoprostol orally as part of a large multicenter American trial (group 2). In 88 of the 100 women in group 1 and 94 of the 100 women in group 2, abortion occurred and a surgical procedure was not required. Abortion rates were not influenced by gestational age in either group. Prostaglandin-related side effects of fever and chills, vomiting, diarrhea, and uterine pain were all significantly higher in group 1. Excessive uterine bleeding was uncommon in both groups, and no subjects received blood transfusions.

24. Ozeren M, Bilekli C, Aydemir V, Bozkaya H. **Methotrexate and misoprostol used alone or in combination for early abortion.** Contraception. 1999 Jun;59(6):389-94.

A total of 108 subjects who had requested elective termination of pregnancy and medical abortion at 9 weeks gestation or less were randomized into three groups. Group 1 took 50 mg/sq. m IM methotrexate on day 1, and a second dose was given if the human chorionic gonadotropin level had increased by 50% of the initial level on day 4. Group 2 took 800 mcg vaginal misoprostol on day 1 and a repeat dose was given if ultrasound showed a gestational sac on day 4. Reexamination was done on day 7. Group 3 took 50 mg/sq. m IM methotrexate, which was followed 3 days later by 800 mcg vaginal misoprostol; subjects were reexamined on day 7. In group 1, complete abortion occurred in 69% of the subjects; in group 2, in 58% of the subjects; in group 3, in 89% of the subjects. Vaginal bleeding in subjects who successfully aborted began within 16 +/- 4 days in group 1 after

the first dose, and within 24 hours in 18 (86%) of the 21 subjects in group 2 and 27 (84%) of the 32 subjects in group 3 after the misoprostol dose. The drugs caused no serious or prolonged side effects.

25. Carbonell Esteve JL, Varela L, Velazco A, Tanda R, Cabezas E, Sanchez C. **Early abortion with 800 micrograms of misoprostol by the vaginal route.** Contraception. 1999 Apr;59(4):219-25.

    A group of 720 volunteer subjects with gestations from 35 to 63 days received 800 mcg of vaginal misoprostol every 24 hours up to a maximum of three doses for abortion. Complete abortion occurred in 644 of 720 (89.4%, 95% CI 87, 92) subjects. The mean decrease in hemoglobin was statistically significant (p = 0.0001). There were 14 subjects with clinically significant decreases in hemoglobin, but only two required transfusions. Vaginal bleeding lasted 6.7 +/- 3.9 days, spotting 8.1 +/- 4 days, and total bleeding 14 +/- 5.3 days. Mean expulsion time was 8.0 +/- 3.4 hours.

26. Carbonell JL, Varela L, Velazco A, Tanda R, Sanchez C. **Vaginal misoprostol for abortion at 10-13 weeks' gestation.** Eur J Contracept Reprod Health Care. 1999 Mar;4(1):35-40.

    A group of 180 women with gestations from 64 to 91 days, self-administered 800 mcg of vaginal misoprostol every 12 hours for a maximum of three doses without performance of postexpulsion systematic preventive curettage. Successful abortion occurred in 153/180 (85%) subjects (95% confidence interval (CI) 79-90). The decrease of hemoglobin was statistically significant (p = 0.0001) but clinically unimportant: 12.1 mg/dl (SD 1.1) before treatment and 11.7 mg/dl (SD 1.1) afterwards. The mean expulsion time for patients who aborted after the first dose was 8.3 +/- 3.6 hours (median 8 hours, range 2-12 hours). Vaginal bleeding lasted 6 +/- 3 days, spotting 7 +/- 3 days and total bleeding 13 +/- 4 days. The median dose of misoprostol administered was 1780 mcg (range 1400-3000 mcg).

27. Carbonell Esteve JL, Varela L, Velazco A, Cabezas E, Tanda R, Sanchez C. **Vaginal misoprostol for late first trimester abortion.** Contraception. 1998 May;57(5):329-33.

    A group of 120 women with gestations from 64 to 84 received 800 mcg of misoprostol vaginally every 24 hours, for a maximum of three doses. Complete abortion occurred in 104 women (87%, 95% CI 79, 92); 87 women (73%; 95% CI 64, 80%) aborted after a single dose, 11 (9%; 95% CI 6, 16%) required two doses, and 6 (5%; 95% CI 2, 11%) received a third dose. The remaining 16 women (13%; 95% CI 8, 21%) underwent surgical abortion. Mean hemoglobin decreased from 12.2 mg/dl before treatment to 11.6 mg/dl after abortion--a difference that was statistically but not clinically significant. Side effects--which disappeared within 2 hours--included nausea (22%), vomiting (17%), diarrhea (54%), dizziness (25%), headache (19%), and chills (72%). Although 99% of subjects reported pelvic pain, only 10% requested an analgesic for pain relief. Vaginal bleeding persisted for a mean of 8 +/- 5 days, spotting 4 +/- 3, and total bleeding 12+/- 4 days.

28. Carbonell JL, Varela L, Velazco A, Fernandez C, Sanchez C. **The use of misoprostol for abortion at < or = 9 weeks' gestation.** Eur J Contracept Reprod Health Care. 1997 Sep;2(3):181-5.

    A total of 175 women seeking elective abortion at < or = 63 days' gestation received 800 mcg of misoprostol vaginally. This dose was repeated at 48 and 96 h if abortion did not occur. Afterwards, up to three additional 600- or 400-mcg doses of misoprostol were administered if the uterus was not empty, as judged by ultrasound. Outcome measures included successful abortion (complete abortion without requiring a surgical procedure), side-effects and vaginal bleeding. Complete abortion occurred in 161/175 (92.0%; 95% CI 87-96%) subjects and 14/175 (8.0%; 95% CI 4-13%) cases failed. The immediate success rate was 77.7% with the first dose, 13.7% with the second dose and 0.6% with the third dose. The third dose of misoprostol showed very little efficacy. Vaginal bleeding lasted 5.5 +/- 2.8 days, spotting 5.7 +/- 3.1 days and total bleeding 11.2 +/- 3.0 days

29. Carbonell JL, Varela L, Velazco A, Fernandez C. **The use of misoprostol for termination of early pregnancy.** Contraception. 1997 Mar;55(3):165-8.

    A group of 141 women with pregnancies of less than 70 days LMP received up to 3 doses of 800 mcg of misoprostol vaginally every 48 hours. Failure was defined as the need for surgical abortion and success as the complete expulsion of the products of conception. In total, 132 cases (93.6%, 95% CI 89.4-97.8) aborted and 9 cases (6.4%) failed. With the first dose of 800 mcg, the success rate was 83%; with the second dose 9.9%; and with the third dose, 0.7 % (cumulative success was 93.6 %; 95% CI 89.4-97.8). The decrease in hemoglobin

was statistically significant (p = 0.001) but without clinical repercussions; before treatment: 11.95 mg/dl (SD 1.19) and after: 11.14 (SD 1.20). The third dose of misoprostol showed very little efficacy.

30. Koopersmith TB, Mishell DR Jr. **The use of misoprostol for termination of early pregnancy.** Contraception. 1996 Apr;53(4):238-42.

    Fifty-eight women with pregnancies less than 10 weeks gestation who desired pregnancy termination received varying dosages of vaginal misoprostol, either alone or in combination with laminaria or tamoxifen. The overall success rate for a complete abortion was 61%. The use of laminaria or tamoxifen did not affect success rates. Abortions occurred within 24 hours of administration of misoprostol. Side effects were minimal.

31. Bugalho A, Faundes A, Jamisse L, Usta M, Maria E, Bique C. **Evaluation of the effectiveness of vaginal misoprostol to induce first trimester abortion.** Contraception. 1996 Apr;53(4):244-6.

    Two doses, 200 and 400 mcg, of misoprostol, administered vaginally every 12 hours, up to four times, were tested in 101 and 133 healthy women, respectively, for interruption of pregnancies with 35 through 77 days of amenorrhea. The proportion of women who aborted increased with longer duration of treatment and was significantly higher with 400 than with 200 mcg (66 versus 46 percent at 48 hours). Abortions were classified as incomplete or complete, according to the presence or not of embryonic tissue in the uterine cavity, diagnosed by vaginal sonography. Vacuum aspiration was carried out in all cases not classified as complete abortion 48 hours after the initiation of treatment, or earlier in case of persistent bleeding or woman's request.

32. Creinin MD, Vittinghoff E. **Methotrexate and misoprostol vs. misoprostol alone for early abortion. A randomized controlled trial.** JAMA. 1994 Oct 19;272(15):1190-5.

    A total of 61 women who had requested elective termination of pregnancy and medical abortion at 56 days' gestation or less were randomized into two groups. Intramuscular administration of 50 mg of methotrexate per square meter of body surface area followed 3 days later by vaginal administration of 800 mcg of misoprostol (group 1) or the same dose of misoprostol given alone (group 2). The misoprostol dose was repeated 24 hours later if abortion had not occurred. Complete abortion occurred in 28 (90%) of 31 patients in group 1 and 14 (47%) of 30 patients in group 2 (P < .001). There were three treatment failures in group 1: two ongoing pregnancies (6%) and one incomplete abortion (3%). There were 16 treatment failures in group 2: eight ongoing pregnancies (27%), and eight incomplete abortions (27%). Methotrexate side effects were minimal. Misoprostol side effects were diarrhea in 18% and nausea and vomiting in 5%. In group 1, vaginal bleeding lasted 10 +/- 4 days and in group, 2 10 +/- 6 days.

Summary - Misoprostol Alone for Early Abortion

Author	Sample size	Gestational age	Regimens	Efficacy
Aldrich T[1]	8678	< 56 days	800 mcg vag q24-48h x 2 50 mg/m^2 mtx oral + 800mcg buccal q48h 50 mg/m^2 mtx oral + 800mcg vag q48h 50 mg/m^2 mtx IM + 800mcg vag	76.8% 81.7% 83.5% 82.6%
WHO[2]	1021 1025	< 63 days	800 mcg vag x 3 q3h or q12h (tablets wetted w/water) 800 mcg sublingual x 3 q3h or q12h	85.0%/83.0% 84.0%/78.0%
Moreno-Ruiz NL[3]	2676 5177	<63 days <56 days	800mcg vag q24h up to 3 doses 50 mg/m^2 mtx IM + 800mcg vag 3-7days afterward	84-96% 70-97%
Salakos N[4]	162	50-63 days	800mcg vag q12h up to 3 doses	91%
Blanchard K[5]	261	< 56 days	Varying doses of oral or vaginal misoprostol	39-80%
Billings D[6]	2900	<70 days	800 mcg vag q24h up to 3 doses	76.4%
Borgatta L[7]	410	< 56 days	800 mcg vag q24h x 2	90.8%
Carbonell JL[8]	452	< 63 days	800 mcg vag q8h x 3 (self-administered)	90.5%
Singh K[9]	150	< 56 days	800 mcg vag plus 400 mcg q3h up to 3 doses	84.7%
Zikopoulos KA[10]	160	< 56 days	800 mcg vag q24h up to 3 doses	91.3%
Jain JK[11]	250	< 56 days	800 mcg vag q24 h up to 3 doses	88.0%
Tang OS[12]	50	< 84 days	600 mcg sublingual q3h up to 5 doses	86.0%
Tang OS[13]	25	< 84 days	Varying doses of sublingual misoprostol	92.0%
Jain JK[14]	100	< 56 days	800 mcg vag q24h up to 3 doses	89.0%
Carbonell JL[15]	300	42-63 days	1000 mcg vag q24h up to 3 doses	93.0%
Carbonell JL[16]	150	63-84 days	800 mcg vag q24h up to 3 doses	84.0%
Velazco A[17]	150	35-63 days	800 mcg vag q24h up to 3 doses	88.7%
Ngai SW[18]	80	< 63 days	800 mcg vag q48h up to 3 doses	85.0%*
Carbonell JL[19]	90	< 63 days	600 mcg vag q8h up to 3 doses (self-administered)	64.0%
Bugalho A[20]	--	< 42 days	800 mcg vag + 800 mcg vag 7 days afterward IFN**	92.1%***
Jain JK[21]	150	< 56 days	800 mcg vag q24h x 2 + 800 mcg 8 days afterward IFN	90.7%
Tang OS[22]	20	< 63 days	800 mcg vag + 400 mcg vag q3h x 4	70.0%
Jain JK[23]	100	< 56 days	800 mcg vag + 800 mcg 24 hours afterward IFN****	80.0%
Ozeren M[24]	108	< 63 days	800 mcg vag + 800 mcg 24 hours afterward IFN	58.0%
Carbonell JL[25]	720	35-63 days	800 mcg vag q24h up to 3 doses	89.4%
Carbonell JL[26]	180	64-91 days	800 mcg vag q12h up to 3 doses	85.0%
Carbonell JL[27]	120	64-84 days	800 mcg vag q24h up to 3 doses	87.0%
Carbonell JL[28]	175	< 63 days	800 mcg vag q48h up to 3 doses + 400-600 mcg IFN	92.0%*****
Carbonell JL[29]	141	< 70 days	800 mcg vag q48h up to 3 doses	93.6%
Koopersmith TB[30]	58	< 70 days	Varying dosages of vaginal misoprostol	61.0%
Bugalho A[31]	101 133	35-77 days	200 mcg vag q12h up to 4 doses 400 mcg vag q12h up to 4 doses	66.0%****** 46.0%******
Creinin MD[32]	61	< 56 days	800 mcg vag + 800 mcg 24 hours afterward IFN	47.0%

* The complete abortion rate appeared higher when water was added but the difference did not reach statistical significance.
** IFN = if necessary (i.e. woman had not yet aborted)
*** Cumulative abortion rate.
**** Misoprostol was administered in the form of sodium chloride solution-moistened tablets.
*****The third dose of misoprostol showed very little efficacy (0.6%).
******Abortion rate at 48 hours.

Note: Superscript numbers in chart refer to numbered articles on annotated bibliography.