

Second trimester medical termination of pregnancy: procedure, immediate complications and the risk of repeat termination

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Background: The preferred method for second trimester medical termination of pregnancy (MTOP) is use of a combination of mifepristone and misoprostol. The recommended time interval between these medicines has been 36 to 48 hours, but a more flexible interval would be of value. Increasing gestational age in cases of surgical termination of pregnancy (STOP) has been associated with an increased risk of complications, but little is known about these complications after MTOP. Moreover, despite the fact that one third or even half of the women who undergo termination of pregnancy (TOP) end up repeating the procedure during their lifetimes, data on repeat TOP after second trimester TOP has been missing.

Objectives: To assess the procedure of second trimester MTOP by comparing one- and two-day intervals between mifepristone and misoprostol administration and evaluating the risk factors of surgical evacuation. Health and reproductive health issues were also assessed, evaluating complications of MTOP and the risk of repeat TOP after second trimester TOP.

Material and methods: The study consisted of an open randomized prospective trial and registry-based nationwide cohort studies. The randomized trial included 227 women who underwent MTOP between gestational weeks 13–24. Two dosing intervals, of one (17–28 hours) and two days (41–45 hours) between mifepristone (200 mg) and misoprostol (400 mcg) were compared.

The epidemiological studies were performed using the Finnish Abortion Registry. Complications related to MTOP were sought from the Hospital Discharge Registry. The complications after first and second trimester MTOP were assessed in a cohort of 18,248 women who underwent TOP in Finland between 2003 and 2006. The risk of repeat TOP was assessed in a cohort of 41,750 women who underwent their first TOP in Finland between 2000 and 2005.

Results: The mifepristone–misoprostol interval trial showed that the one-day interval was associated with a slightly longer median induction-to-abortion time (intention-to-treat analysis: 8.5 vs. 7.2 hours, $p=0.038$). However, this induction-to-abortion time was markedly

longer with the one-day interval among women without previous vaginal deliveries (10.1 vs. 7.6 hours, $p=0.013$) and when gestational age exceeded 16 weeks (10.8 vs. 7.2 hours, $p=0.024$). On the other hand the rate of surgical evacuation was higher with the two-day interval (per-protocol analysis: 30/115 women, 25% vs. 40/112 women, 37%; 95% CI 0.3–24.1, $p=0.044$).

Multivariable analysis of the risk factors of surgical removal of the placenta showed that the two-day interval doubled the risk of surgical evacuation (OR 2.2; 95% CI 1.1–4.1), as did age above 24 years (OR 2.4; 95% CI 1.1–5.3). Previous curettage increased this risk fourfold (OR 4.4; 95% CI 1.7–11.7) and foetal indication for TOP even more (OR 6.1; 95% CI 1.1–34.4).

In the registry study, second trimester MTOP in comparison with first trimester MTOP increased the risk of surgical evacuation (adjusted OR 7.8; 95% CI 6.8–8.9), especially immediately after foetal expulsion (adj. OR 15.2; 95% CI 12.8–18.0). Second trimester MTOP also doubled the risk of infection (adj. OR 2.1; 95% CI 1.5–2.9). Furthermore, in the registry-based study in which risk factors of repeat TOP after first and second trimester primary TOP were compared, second trimester TOP was shown to be an independent risk factor of repeat second trimester TOP (HR 3.8; 95% CI 2.9–5.1) and repeat TOP after 16 weeks of gestation (HR 5.0; 95% CI 3.3–7.7).

Conclusions: Both one- and two-day dosing intervals between mifepristone and misoprostol are suitable for second trimester MTOP, but women with no previous deliveries and those whose gestation exceeds 16 weeks may benefit from the longer interval. Compared with first trimester MTOP, second trimester MTOP is associated with an increased risk of retained placenta, which leads to a risk of surgical evacuation and/or infection. Previous curettage of the uterus increases this risk of retained placenta. As second trimester TOP is also a risk factor of repeat TOP, especially later in pregnancy, special focus on the safety and efficacy of the method is needed.