

Claims of Detection of Misoprostol in Women Accused of Induced Abortion

Recent efforts to prosecute women for induced abortion have included allegations that misoprostol was found in the woman's blood. However, such allegations should be viewed skeptically. If a woman induces an abortion with misoprostol, depending on the dose and route, the average time between taking the drug and expelling the fetus is 6-8 hours in the first trimester and 10-20 hours in the second trimester.⁹⁻¹⁴ Suspicion of induced abortion with misoprostol generally occurs well after expulsion, meaning several hours of time have passed since the alleged misoprostol administration. During the intervening hours, the misoprostol is rapidly metabolized, and, depending on the interval between taking the drug and suspicion, it will likely be undetectable in a blood sample. If a claim is made that misoprostol was detected in blood, there are a few critical questions to ascertain if the allegations could be real:

1. What documentation was provided to confirm the laboratory finding?

There should be a laboratory report from an accredited lab specifying the procedure used, timing of sampling and testing, and specific amount detected.

2. What compound was found in the blood?

It is not possible to detect misoprostol itself in blood plasma¹ even at five minutes after an oral dose.² Misoprostol is rapidly metabolized into **misoprostol acid** which can be detected only by complex procedures. The measurement of misoprostol acid in the blood is called an "assay" for misoprostol acid.

3. Where was the blood tested?

In order to detect misoprostol acid in blood, a validated assay is necessary. There are very few validated assays available and even fewer that are commercially available.* Most of the facilities with the capacity to detect misoprostol acid in blood are in Europe and Asia.

4. When was the blood sample taken?

The indicator for misoprostol, misoprostol acid, has an elimination half life of 20-40 minutes. This means that after 20-40 minutes the substance has lost half of its pharmacologic activity. Depending on the dose and route by which the drug is taken, the peak plasma level achieved and the amount of time the drug remains detectable in the body will differ slightly.³⁻⁶ Given available detection techniques, a 600mcg dose of oral misoprostol is no longer detectable after six hours.² Higher peak plasma levels are achieved via the sublingual route and a slower decline is observed by the vaginal route, but regardless of the route of administration the short half life requires near immediate blood draw to reliably detect the misoprostol acid in plasma.

* Note: We contacted clinics cited in pharmacological studies of misoprostol acid, and they were unwilling to conduct analyses commercially

5. How was the blood sample managed?

Blood samples for misoprostol acid analysis must be carefully managed. Validated methods of measuring misoprostol acid include immediate centrifugation and freezing in liquid nitrogen and then maintenance of the sample at -10 to -20 degrees Celsius.^{2,5-7} Any subsequent transport of the sample is done via a cooler with dry ice.^{6,8} If the sample is left at room temperature, misoprostol acid should be analyzed within four hours.²

6. What type of analysis was used?

There are three validated techniques for detecting misoprostol acid in blood, each with a different lower limit of detection. To analyze blood, a gas-chromatography mass-spectrometry machine or alternatively a liquid-chromatography mass-spectrometry machine is required. Radioimmunoassay has the potential to detect other metabolites, thus it is subject to non-specificity.⁵

7. Is there a claim of misoprostol found in other body fluids?

For any other body fluid (fetal blood, urine, breast milk) the same issues of the lack of availability of assays, short half life, and onerous testing procedures apply. However misoprostol acid levels would be even lower in these other fluids and therefore would become undetectable sooner. Consequently, claims of misoprostol detected in most body fluids should be further questioned.

CLAIMS THAT MISOPROSTOL WAS FOUND IN BLOOD OR OTHER BODY FLUIDS ARE SUSPECT AND SHOULD BE THOROUGHLY SCRUTINIZED.

FOR ADDITIONAL INFORMATION PLEASE CONTACT: PUBINFO@GYNUITY.ORG

References:

1. Schoenhard G, Oppermann J, Kohn FE. Metabolism and pharmacokinetic studies of misoprostol. *Dig Dis Sci* 1985;30:126S-8S.
2. Zou Y, Chen X, Song B, Zhong D. Determination of misoprostol acid in human plasma by liquid chromatography coupled to tandem mass spectrometry. *J Chromatogr B Analyt Technol Biomed Life Sci* 2007;852:122-7.
3. Tang OS, Gemzell-Danielsson K, Ho PC. Misoprostol: pharmacokinetic profiles, effects on the uterus and side-effects. *Int J Gynaecol Obstet* 2007;99 Suppl 2:S160-7.
4. Khan RU, El-Refaey H, Sharma S, Sooranna D, Stafford M. Oral, rectal, and vaginal pharmacokinetics of misoprostol. *Obstet Gynecol* 2004;103:866-70.
5. Ziemann M, Fong SK, Benowitz NL, Banskter D, Darney PD. Absorption kinetics of misoprostol with oral or vaginal administration. *Obstet Gynecol* 1997;90:88-92.
6. Tang OS, Schweer H, Seyberth HW, Lee SW, Ho PC. Pharmacokinetics of different routes of administration of misoprostol. *Hum Reprod* 2002;17:332-6.
7. Khan R-U, El-Refaey H, Sharma S, Sooranna D, Stafford M. Oral, Rectal, and Vaginal Pharmacokinetics of Misoprostol. *Obstetrics & Gynecology* 2004;103:866-70.
8. Abdel-Aleem H, Villar J, Gulmezoglu AM, et al. The pharmacokinetics of the prostaglandin E1 analogue misoprostol in plasma and colostrum after postpartum oral administration. *Eur J Obstet Gynecol Reprod Biol* 2003;108:25-8.
9. Carbonell JL, Torres MA, Reyes R, Ortega L, Garcia-Gallego F, Sanchez C. Second-trimester pregnancy termination with 600-microg vs. 400-microg vaginal misoprostol and systematic curettage postexpulsion: a randomized trial. *Contraception* 2008;77:50-5.
10. 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;59:219-25.
11. Carbonell JL, Varela L, Velazco A, Tanda R, Barambio S, Chami S. Vaginal misoprostol 600 microg for early abortion. *Eur J Contracept Reprod Health Care* 2000;5:46-51.
12. Carbonell JL, Rodriguez J, Aragon S, et al. Vaginal misoprostol 1000 microg for early abortion. *Contraception* 2001;63:131-6.
13. Ngoc NT, Shochet T, Raghavan S, et al. Mifepristone and misoprostol compared with misoprostol alone for second-trimester abortion: a randomized controlled trial. *Obstet Gynecol* 2011;118:601-8.
14. Velazco A, Varela L, Tanda R, et al. Misoprostol for abortion up to 9 weeks' gestation in adolescents. *Eur J Contracept Reprod Health Care* 2000;5:227-33.
15. Garcia-Enguidanos A, Calle ME, Valero J, Luna S, Dominguez-Rojas V. Risk factors in miscarriage: a review. *Eur J Obstet Gynecol Reprod Biol* 2002;102:111-9.