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Utility and Limitations of Human Chorionic Gonadotropin Levels for Remote Follow-up After Medical Management of Early Pregnancy Loss

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Abstract

Early pregnancy loss (EPL) can be treated medically with mifepristone followed by misoprostol, with sonographic confirmation of pregnancy expulsion. Alternative strategies that ascertain treatment success remotely are needed. We compared percent hCG decline with treatment success or failure between patients who received mifepristone pretreatment followed by misoprostol or misoprostol alone for EPL between 5 and 12 weeks of gestation to determine a threshold decline that might predict success. Early pregnancy loss treatment success was associated with a greater percentage hCG decline compared with treatment failure, but no threshold was able to predict success. Additional research is needed to understand hCG trends after medical management of EPL in order to develop reliable protocols for remote follow-up.

Precis:

Early pregnancy loss treatment success after medical management was associated with a greater human chorionic gonadotropin (hCG) decline than failure, but an hCG threshold decline to determine treatment success could not be defined.

Introduction

Mifepristone pretreatment for medical management of early pregnancy loss (EPL) improves efficacy compared to misoprostol alone (1, 2). Ultrasound is often used to confirm treatment completion, although ACOG acknowledges the role of serial serum hCG measurements

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when ultrasound is unavailable (3). However, guidance regarding schedule and interpretation of serum hCG measurements to confirm completion is not established.

Remote follow-up with hCG assessments after medical induced abortion is validated (4–7), but unlike the predictable hCG trends after medical abortion, hCG values observed with EPL vary widely (8). Published data exist for hCG patterns after EPL management with misoprostol alone, (9,10) however hCG decline following mifepristone pretreatment has not been published.

Methods

We conducted a planned secondary analysis of a randomized controlled trial comparing mifepristone pretreatment followed by misoprostol to treatment with misoprostol alone for EPL between 5 and 12 weeks of gestation which was approved by the Institutional Review Board at the University of Pennsylvania (NCT02012491) (2). We evaluated baseline serum hCG level on day of randomization to mifepristone or no pretreatment (one day prior to misoprostol administration). Follow-up hCG measurements were collected between 1–4 days after misoprostol administration, when treatment success was determined. We hypothesized that mifepristone pretreatment would accelerate hCG decline compared to misoprostol alone.

We described baseline hCG level and its relationship to gestational age (determined by ultrasound) with linear regression. We compared percentage decline in hCG at follow-up by success or failure using a Wilcoxon rank-sum test. We excluded participants with a rise in hCG after treatment, an indicator of treatment failure.

Results

Of the 233 participants, 184 (79.0%) had successful treatment, 100 (86.2%) in the mifepristone pretreatment arm and 84 (72.0%) in the misoprostol alone arm ($p<0.01$). At baseline, participants had a median hCG level of 11,225 mIU/mL (range 205–224,581), which did not differ by treatment group (10,949 95% CI (8,785–15,037) vs 11,434 95% CI (9,814–15,117), p=0.70) or by outcome of success or failure, 11,413 95% CI (9,958–14,765) vs 10,336 95% CI (8,806–16,351) mIU/mL, p=0.99), respectively (Appendix 1, available online at http://links.lww.com/xxx). Linear regression demonstrated that gestational age did not account for variation in baseline (natural log of hCG) ($R^2 = 0.04$) (Appendix 2, available online at http://links.lww.com/xxx).

We compared percent hCG decline across participants with treatment success or failure to determine a threshold decline that might predict success. With mifepristone pretreatment, we noted a median 82.2% 95% CI (78.8–84.2%) decline and 66.9% 95% CI (42.1–84.6%) decline in those with success and failure, respectively, a 15.3% 95% CI (6.1–36.6%) difference (p=0.02). With misoprostol alone, we saw a median 83.8% 95% CI (80.3–85.7%) decline and 47.6% 95% CI (36.0–53.6%) decline in those with success and failure, respectively, a 36.2% 95% CI (27.2–45.1%) difference ($p<0.01$) (Figure 1). The difference in declines for the mifepristone pretreatment 15.3% 95% CI (6.1–36.6%) was not significantly different from misoprostol alone 36.2 95% CI (27.2–45.1%), as the confidence

intervals overlapped. Percentage hCG decline did not depend on baseline hCG (p=0.36). We were unable to define a threshold that reliably predicted treatment success.

Discussion

EPL treatment success after medical management was associated with a greater percentage hCG decline compared with treatment failure, but no threshold was able to predict treatment success. In addition, the percentage hCG decline appeared to differ across treatment arms, independent of treatment success, suggesting that hCG trajectory 1–4 days after expected pregnancy expulsion when using mifepristone pretreatment may be a less accurate measure of miscarriage completion than that observed after treatment with misoprostol alone. The potential role of mifepristone in modulating hCG decline should be studied further.

Percentage hCG decline 7, 14, or 30 days after treatment may be more applicable to clinical practice and yield better predictive accuracy, as observed with medical abortion (11). A later time point may be associated with greater decline and permit use of urine pregnancy tests for remote assessment. Clinical symptomatology including heavy bleeding, passage of tissue, or resolution of pregnancy symptoms may increase the utility of hCG decline to determine success or failure of medical management of EPL (12).

Evidence-based protocols for remote management of EPL are needed. Especially with easing FDA restrictions on in-person dispensation of mifepristone, remote EPL management has the potential to expedite care, reduce healthcare costs, and improve patient satisfaction.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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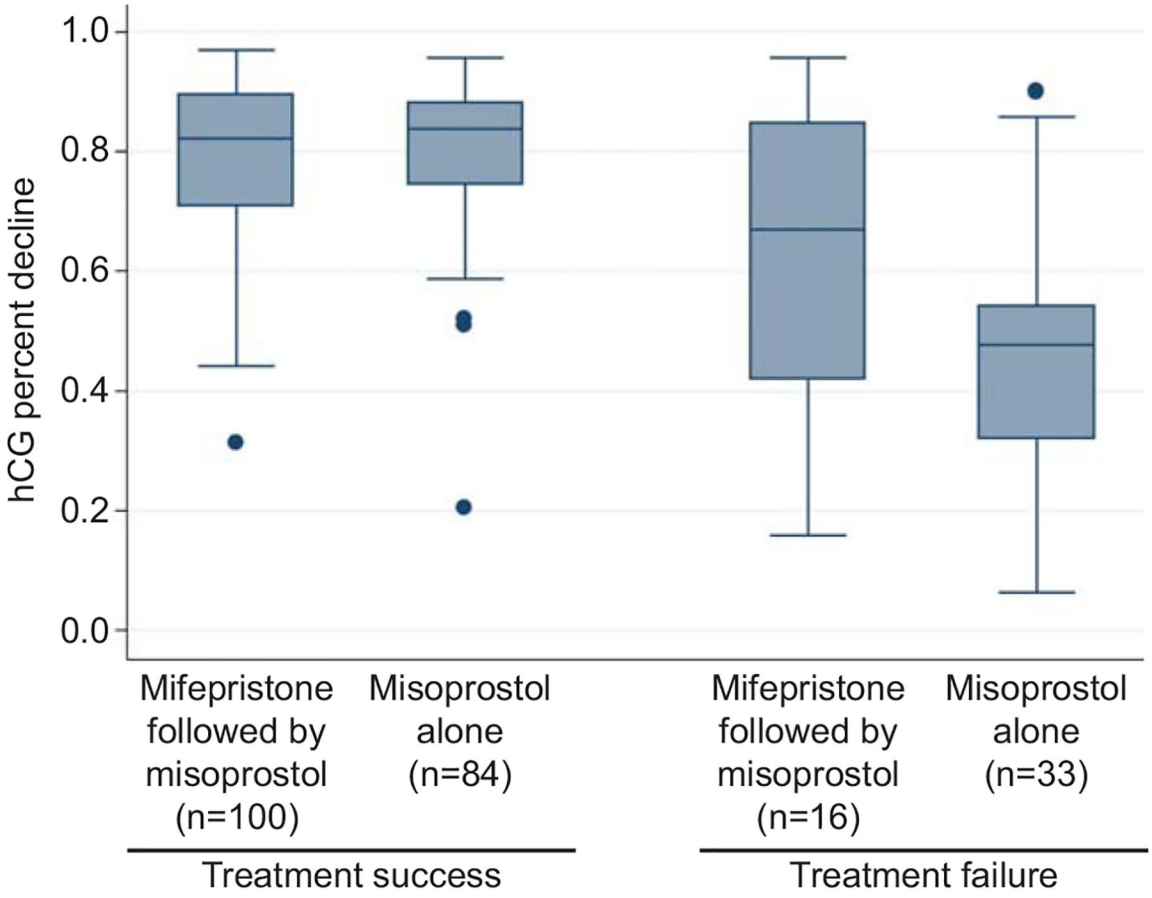

Figure 1:
Median human chorionic gonadotropin (hCG) (interquartile range).