

# An Unusual Case of Recurrent Severe Hypoglycemia in a Woman With Type 1 Diabetes Undergoing Medically Assisted Abortion

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## Presentation

A 32-year-old woman developed severe recurrent hypoglycemia after a medically assisted, first-trimester abortion. She had had type 1 diabetes since 1988, and the pregnancy was her first and planned. The patient's glycemic control had been good, with a preconception A1C of 6.3%. She was on a multiple daily injection insulin regimen and routinely counted carbohydrate. Unfortunately, she had a missed miscarriage at 11 weeks' gestation and opted for medical management. She was given mifepristone 800 µg.

After taking mifepristone, the patient noticed that she had numerous episodes of unexplained prolonged hypoglycemia. She had a significant and sudden drop in capillary glucose levels with no obvious trigger and very little warning within about 2 hours after taking mifepristone. Over the next 2–4 days, she continued to have multiple hypoglycemic episodes, mostly attributable to her rapid-acting insulin. However, her glycemic control started to settle down after 5 days, and her blood glucose levels subsequently stabilized in her target range with no hypoglycemia. She was seen in the diabetes clinic after this episode, when she reported the effects of the medical miscarriage treatment on her glycemic control. Her glycemic control has remained stable since, without any further episodes of unexplained hypoglycemia.

## Questions

1. What is the most likely cause for severe, prolonged hypoglycemic episodes after undergoing medically triggered abortion?
2. How likely is this effect of mifepristone?
3. What course of action or precautions should be taken for patients with diabetes who are undergoing medically assisted abortion with mifepristone?

## Commentary

Tight glycemic control is very important to improve pregnancy outcomes, but it also may be associated with an increased risk of hypoglycemia (1). Because it is well documented that severe hypoglycemia can lead to significant problems for pregnant women and is a major cause of maternal morbidity, pregnant women on intensive insulin therapy must be closely monitored, and the cause of any hypoglycemia should be identified and resolved promptly.

Although intensive insulin therapy is considered to be the major cause of hypoglycemia in this patient group (2), impaired hormonal counterregulatory responses have also been implicated as another important contributory factor (2–4). Pregnancy is considered to be a cause for diminished counterregulatory responses to hypoglycemia. Although reduced adrenaline, noradrenaline, and growth hormone responses have all been reported, sympatho-adrenal response is considered to be the most

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significantly affected of all counter-regulatory mechanisms (2,5–7). This may help to explain why there are reduced warning signs of hypoglycemia during pregnancy.

Because attempts to achieve tight glycemic control may not be the only factor increasing the likelihood of hypoglycemia during pregnancy (4,5), health care providers must be cautious and mindful of various other possible contributory factors to hypoglycemia. Other factors commonly considered to be contributing to this problem include pregnancy-related nausea and vomiting (7).

Early pregnancy is also considered to be a risk factor because severe hypoglycemia has been described to be three times more frequent in early pregnancy than in the pre-pregnancy period (7). The incidence of hypoglycemia is highest in gestational weeks 8–16 (8). A declining insulin requirement in the late first trimester of pregnancy in women with type 1 diabetes has been documented, and over-insulinization has been suggested as a contributing reason for severe hypoglycemia in early pregnancy (9). Fluctuating plasma glucose levels and a longer duration of diabetes might also contribute to a higher risk of severe hypoglycemia, whereas the number of mild hypoglycemic events per week, A1C, and the fraction of biochemical hypoglycemia do not predict severe hypoglycemia in these women (8).

Mifepristone is a steroidal anti-progesterone drug used for the medical termination of intrauterine pregnancy (10). It is also a glucocorticoid receptor antagonist and binds to the glucocorticoid receptor three times more strongly than dexamethasone, but it does not bind to the mineralocorticoid receptors (11). Because of its anti-glucocorticoid action, this drug may be associated with adrenal insufficiency and is contraindicated in people with adrenal insufficiency.

Mifepristone treatment does not lower the production of cortisol,

but rather antagonizes the effects of cortisol, such as increased blood glucose levels. Therefore, mifepristone was approved by the U.S. Food and Drug Administration in 2012 to control hyperglycemia in adults with endogenous Cushing's syndrome who are not candidates for surgery or who have not responded to surgery (10). Mifepristone has been shown to improve abnormal glucose metabolism, psychiatric symptoms, and somatic changes associated with Cushing's syndrome. Hypokalemia is the most commonly reported side effect (12,13).

Although the risk of hypoglycemia due to anti-glucocorticoid action is documented in the product literature (14), we could not find any previous reports about patients developing severe hypoglycemia after administration of mifepristone. There is also no available published research about the effect of this medication on the glycemic control of people with diabetes.

We believe the cause for the recurrent unexplained hypoglycemic episodes in our patient was multifactorial, with a possible contribution from mifepristone because of its anti-glucocorticoid action. The glucocorticoid receptor–blocking activity of mifepristone could explain why our patient had a sudden and rapid onset of hypoglycemia after taking this drug. We therefore hypothesize that, in this patient with type 1 diabetes who was on intensive insulin treatment and already had early pregnancy–induced counterregulatory responses, temporary mifepristone-induced reduction in glucocorticoid activity in the body might have contributed to recurrent prolonged hypoglycemia. Because the patient was discharged home on the same day she took mifepristone, we do not have any blood pressure recordings or measurements of serum electrolytes during the hypoglycemic episode that might have been associated with mifepristone.

## Clinical Pearls

- Because hypoglycemia in pregnancy could be multifactorial, it is mandatory for all health care professionals caring for pregnant women with diabetes to have a thorough understanding of hypoglycemia during pregnancy, and a particular understanding of the various risk factors so they can better counsel and educate these women to reduce the risk.
- Severe hypoglycemia in cases such as this are likely multifactorial and caused by a combination that could include intensive insulin therapy, reduced counterregulatory responses during pregnancy, and the anti-adrenal effect of mifepristone.
- Women with type 1 diabetes should be counseled about a potential risk of hypoglycemic episodes before medical management of miscarriage commences. Insulin doses will need to be adjusted accordingly.

## Duality of Interest

No potential conflicts of interest relevant to this article were reported.

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