

# Abnormal Uterine Bleeding in a Patient with Alcoholic Liver Disease

**Megan Kalata\***

Department of Obstetrics & Gynecology, Creighton University, Nebraska, United States

## Abstract

**Background:** Traditional medical therapies for the management of abnormal uterine bleeding cannot be used by patients with liver disease. Given that the incidence of liver disease is increasing among women in the United States, it is crucial to understand options for management among this high-risk population.

**Case Presentation:** This case presents a patient with acute-onset heavy vaginal bleeding in the setting of acutely decompensated alcoholic liver disease.

**Outcomes:** The patient was started on tranexamic acid for the management of her bleeding given her contraindication to typical medical management, such as oral contraceptives or IV estrogen.

**Recommendations:** In instances of acute vaginal bleeding for patients like the one presented here, tranexamic acid may be a safer, more appropriate option to bridge patients to the point where long-term management can be addressed for their underlying conditions.

**Keywords:** Uterine Bleeding; Alcoholic Liver Disease; Vaginal Bleeding; Estrogen; Oral Contraceptives; Tranexamic acid

\***Correspondence to:** Megan Kalata, MD/MPH, Department of Obstetrics & Gynecology, Creighton University, 7500 Mercy Rd, Omaha, Nebraska 68124, United States; Tel: 262-506-4127; E-mail: [megankalata@creighton.edu](mailto:megankalata@creighton.edu)

**Citation:** Kalata M (2023) Abnormal Uterine Bleeding in a Patient with Alcoholic Liver Disease. *J Womens Health Care Manage*, Volume 4:1. 142. DOI: <https://doi.org/10.47275/2692-0948-142>

**Received:** April 20, 2023; **Accepted:** May 12, 2023; **Published:** May 17, 2023

## Introduction

Women are becoming increasingly at risk for alcohol-related liver disease and its complications. Although liver disease still affects more men, younger women are driving the increase in deaths, a trend that has become amplified by the recent COVID-19 pandemic. Liver disease has the potential to impact the menstrual cycle through a variety of mechanisms, which is significant as approximately 4% of American women of reproductive age have severe alcohol use disorders [1]. Complications of substance use, such as coagulopathy, are more common in these instances and present an interesting management dilemma for women with acute vaginal bleeding, as evidenced by the following case.

## Case Presentation

A 23-year-old female presented to the Emergency Department with abnormal uterine bleeding. The patient reported a three-day history of heavy vaginal bleeding, changing 6-10 pads per hour for the last day and passing quarter and golf ball-sized clots. She also had abdominal pain that she described as being "like really bad menstrual cramps." She had tried acetaminophen and ibuprofen without relief. Her review of systems was positive for a 30-pound weight loss over the prior three months, which she attributed to loss of appetite, as well as lightheadedness, dizziness, nausea, vomiting, and one episode of hematemesis. Her review of systems was negative for syncopal episodes.

Notably, this patient had a history of alcohol dependence, with prior complications including alcoholic hepatitis and pancreatitis, both of which necessitated inpatient medical management. She reported drinking 6-12 shots of liquor per day and stated her last drink was approximately five hours prior to arrival.

Upon admission, the patient had stable vital signs. Her abdomen was mildly distended. A pelvic exam revealed a normal-sized uterus, closed cervical os, and a moderate amount of bright red vaginal bleeding. She was noted to have a hemoglobin of 9.3, which dropped to 6.6 over the course of several hours. Other labs of note included platelets of 35,000, AST 443, ALT 42, PT 13.5, PTT 29.3, and INR 1.2. Qualitative hCG was negative.

A CT abdomen/pelvis was obtained, which showed severe hepatomegaly and steatosis but was otherwise unremarkable. There was no evidence of intra-abdominal bleeding or hemoperitoneum. A transvaginal ultrasound was unremarkable, with no evidence of pelvic masses or distortion of the uterine cavity.

It was determined based on the above-mentioned workup that this patient's abnormal uterine bleeding was a result of her coagulopathy secondary to alcoholic liver disease. Given the etiology of this patient's vaginal bleeding, the decision was made to avoid estrogen and progesterone as a means to acutely stop her bleeding. Tranexamic acid was used to control the patient's acute blood loss anemia until she was



able to be stabilized and a long-term plan was made that could more appropriately address the underlying cause of her presenting symptoms.

## Outcomes and Implications

Liver disease, and subsequent death, in people of childbearing age, are increasing in the United States. According to the National Health and Nutrition Examination Survey, chronic liver disease was present in 10.4% of women ages 15-39 from 1988 to 1994 and increased to 24.9% between 2007 and 2012 [2]. The most common causes of liver disease in this population include nonalcoholic fatty liver disease and alcohol-related liver disease.

Chronic liver disease can cause increased menstrual bleeding, both by direct effects on the hypothalamic-pituitary-adrenal (HPA) axis and by inadequate metabolism of estrogen and sex hormones, resulting in their accumulation [3]. Patients with alcoholic liver disease, specifically, have a blunted gonadotropin release relative to decreased levels of sex steroids and inadequate responses to stimulation by gonadotropin-releasing hormone (GnRH) agonists. Additionally, alcohol increases estrogen levels, which stimulates the growth of the endometrial tissue and subsequently heavier menses.

The impact of chronic liver disease, unrelated to alcohol, on the menstrual cycle is not as clearly understood. Among these women, two subgroups have been identified, those with hypogonadotropic amenorrhea and those with normal gonadotropins [4]. In one study, women in the hypogonadotropic group were significantly underweight, suggesting that malnutrition contributed to their amenorrhea. Patients with normal gonadotropins had increased levels of estradiol and testosterone compared with controls. This change in hormone levels alters the hypothalamic-pituitary-adrenal axis, leading to alterations in the menstrual cycle.

Traditional medical therapies for the management of acute abnormal uterine bleeding include prostaglandin inhibitors, oral contraceptive pills, progesterone, GnRH agonists, and IV estrogens for severe bleeding. However, these therapies each have reasons for which they may not be a suitable or effective choice for those with chronic liver disease. Prostaglandin inhibitors, such as NSAIDs, inhibit prostaglandins in the uterus, specifically  $PGF2\alpha$ , which has been found to have levels as high as three times greater in women with abnormal uterine bleeding [5]. However, they are metabolized by the liver and thus the ability to clear these drug metabolites decreases with worsening liver dysfunction. Due to decreased first-pass metabolism, prostaglandin inhibitors have higher bioavailability and a higher risk for toxicity. Additionally, in cirrhotic patients with portal hypertension, there is a risk of acute renal failure due to prostaglandin inhibition, which leads to decreased renal perfusion and reduction of glomerular filtration rate.

Oral contraceptive pills work by decreasing estrogen production and slowing the growth of endometrial tissue, thus making periods lighter. In patients with liver disease, estrogen can affect gene transcription in such a way that it increases plasma concentrations of clotting factors, making patients even more susceptible to thromboembolism. Furthermore, the reduction in hepatic excretory function induced by sex steroids can transform mild hyperbilirubinemia into frank jaundice, which can have complications as severe as encephalopathy or kernicterus.

Progesterone, often in the form of medroxyprogesterone or medroxyprogesterone acetate, inhibits the growth of the lining of the uterus and has also been used to control acute abnormal uterine

bleeding. However, it is also metabolized in the liver and can lead to transaminitis. Therefore, progesterone-based contraceptive methods are used in some instances but would not be ideal for patients with liver dysfunction [6]. While the use of hormonal contraception, such as oral contraceptive pills, has not affected disease progression in prior studies, there is no evidence for the effects of long-term use of medroxyprogesterone [7].

GnRH agonists, such as leuprolide, decrease the amount of menstrual bleeding, shorten the length of menstruation, and decrease clots. GnRH agonists induce hypo-estrogenism and endometrial atrophy, leading to lessened bleeding and improved hemoglobin [8]. They avoid hepatic metabolism so they may be an appropriate short-term agent for patients with liver disease. However, they are not recommended long-term as they can lead to bone demineralization and decreased high-density lipoprotein cholesterol. Traditionally, add-back therapy could be considered to avoid these long-term complications. However, add-back therapy, which typically includes a combination of norethindrone acetate and conjugated equine estrogens, would not be appropriate for patients with chronic liver disease.

Lastly, with prolonged bleeding, it has been suggested that the epithelial lining of the uterine cavity becomes denuded, leaving insufficient tissue for progestin action. IV estrogen induces a rapid return to normal endometrial growth as well as stimulates clotting at the capillary level. It is often the treatment of choice in patients with acute vaginal bleeding necessitating hospitalization. However, estrogen is not appropriate for patients with liver disease given its hepatic metabolism and previously mentioned complications.

With these considerations, the patient presented in this case was managed with tranexamic acid (TXA) in a dose of 10 mg/kg IV. The maximum dosing of TXA is 600 mg/dose every eight hours, and this patient received two doses of 530 mg eight hours apart, which stopped her profuse vaginal bleeding. TXA is a derivative of lysine that exerts its antifibrinolytic effect by reversibly blocking lysine binding sites on plasminogen, thereby preventing fibrin degradation [9]. Side effects most typically include mild symptoms of nausea, dizziness, or diarrhea.

TXA theoretically increases the risk of venous thromboembolism (VTE). However, there have been no reports of statistically significant increases in VTE in retrospective or case-control studies.<sup>10</sup> One of the largest drawbacks of this option is the cost associated with it. Furthermore, while TXA reduces menstrual blood loss, it does not address the underlying cause of dysfunctional uterine bleeding. Thus, in this and many patients, it is only a temporary solution.

## Recommendations

Long-term management of abnormal uterine bleeding in patients with alcoholic and non-alcoholic liver disease is most effectively addressed with a form of long-acting reversible contraception. Because copper intrauterine devices (IUDs) are non-hormonal, they can be used by patients with severe liver disease, including those with decompensated cirrhosis, whereas levonorgestrel IUDs and implants are avoided in patients with severe disease, Budd-Chiari syndrome, hepatocellular adenomas, and transplant recipients. Copper IUDs should be avoided in thrombocytopenia, heavy menses, or Wilson disease patients. A NuvaRing is also an acceptable option as it inhibits ovulation and reduces menstruation without undergoing first-pass metabolism. Lastly, if the patient no longer desires fertility, endometrial ablation or hysterectomy could be considered for definitive management.

Abnormal uterine bleeding in patients with chronic liver disease



can result from failure of the liver to regulate the production and breakdown of various hormones, disruption of the HPA axis, and impaired production of clotting factors. Abnormal uterine bleeding secondary to coagulopathy cannot necessarily be managed like other causes of abnormal uterine bleeding. This is significant because many types of liver disease result in altered menstrual cycles. Primary biliary cirrhosis, Wilson disease, non-alcoholic fatty liver disease, chronic hepatitis C, hemochromatosis, and alpha-1 antitrypsin deficiency are several examples. Tranexamic acid is an appropriate therapy for the acute management of abnormal uterine bleeding in these patients while providers work with patients on a longer-term basis to address the underlying causes. Because alcohol use disorder is increasing in the United States, future research is warranted to optimize current management strategies and minimize risks when caring for these patients.

### References

1. Morgan MY (1994) The prognosis and outcome of alcoholic liver disease. *Alcohol Alcohol Suppl* 2: 335-343.
2. Brady CW (2020) Liver disease in pregnancy: What's new. *Hepatol Commun* 4: 145-156. <https://doi.org/10.1002/hep4.1470>
3. Rachdaoui N, Sarkar DK (2013) Effects of alcohol on the endocrine system. *Endocrinol Metab Clin North Am* 42: 593-615. <https://doi.org/10.1016%2Fj.ecl.2013.05.008>
4. Cundy TF, Butler J, Pope RM, Saggarr-Malik AK, Wheeler MJ, et al. (1991) Amenorrhea in women with non-alcoholic liver disease. *Gut* 32: 202-206. <https://doi.org/10.1136%2Fgut.32.2.202>
5. Valimaki M, Pelkonen R, Salaspuro M, Härkönen M, Hirvonen E, et al. (1984) Sex hormones in amenorrheic women with alcoholic liver disease. *J Clin Endocrinol Metab* 59: 133-138. <https://doi.org/10.1210/jcem-59-1-133>
6. Connolly TJ, Zuckerman AL (1998) Contraception in the patient with liver disease. *Semin Perinatol* 22: 178-182. [https://doi.org/10.1016/s0146-0005\(98\)80050-5](https://doi.org/10.1016/s0146-0005(98)80050-5)
7. Centers for Disease Control and Prevention (2016) Reproductive Health: Injectables. Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, United States.
8. Aljaser R, Vilos AG, Abu-Rafea BA, Vilos GA (2021) Gonadotropin-Releasing hormone agonists are effective in long-term treatment of women with abnormal uterine bleeding and anticoagulant therapy: report of 3 cases and review of the literature. *Curr Obstet Gynecol Rep* 10: 38-43. <https://doi.org/10.1007/s13669-020-00276-y>
9. Sweet MG, Schmidt-Dalton TA, Weiss PM (2012) Evaluation and management of abnormal uterine bleeding in premenopausal women. *Am Fam Physician* 85: 35-43.
10. American College of Obstetricians and Gynecologists (2013) Management of Acute Abnormal Uterine Bleeding in Nonpregnant Reproductive-Aged Women. Committee Opinion Number 557. *Obstet Gynecol* 557: 1-6. <https://doi.org/10.1097/01.aog.0000428646.67925.9a>