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Efficacy and Safety of Bictegravir-Based Regimen in Pregnant Women Living with HIV: A Case Report

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Abstract

Bictegravir (BIC) is included in international guidelines as the first line of therapy for patients living with Human Immunodeficiency Virus (HIV), either as initial therapy or as a replacement for patients with prior antiretroviral therapy (ART). Due to limited efficacy and safety data, BIC is currently not recommended during pregnancy. Data on the safety and efficacy of BIC during pregnancy were unavailable at the time of drug approval. In our case, BIC/TAF/FTC was effective in suppressing viral load (VL) in pregnancy, and there were no reported safety issues for the mother or the baby.

Keywords

Bictegravir, human immunodeficiency virus, pregnancy

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Introduction

The Human Immunodeficiency Virus (HIV) causes a serious infection that targets the immune system. If HIV is not treated properly, it causes Acquired Immunodeficiency Syndrome (AIDS).[1,2] People who live with HIV are at high risk of immunosuppression and exposure to life-threatening opportunistic infections. HIV can be transmitted from a pregnant woman living with HIV to the infant during intrauterine life through the placenta, intrapartum when the infant is exposed to the mother's amniotic fluids, and postpartum via breastfeeding.[3] Intrauterine is the typical route of vertical transmission. With an unsuppressed viral load (VL) during pregnancy and insufficient maternal antiretroviral medication (ART), the risk of vertical transmission is increased.[4] To avoid vertical transmission, pregnant women should begin ART during their pregnancy.[5,6] The World Health Organization (WHO) and Human and Health Services (HHS) recommendations advocate monitoring HIV Ribonucleic Acid (RNA) Polymerase Chain Reaction (PCR) in pregnant women living with HIV regularly. At least four weeks before delivery, or at the latest at the time of delivery to recognize women who might be at risk for treatment failure and/or may deliver infants at higher risk of perinatal transmission.[7,8]

Bictegravir (BIC) is a second-generation integrase inhibitor antiviral agent that is generally well tolerated.[9] It is recommended in international guidelines as first-line therapy for people who have HIV, either as initial therapy or as a replacement for patients who have previously received ART.[10] Biktarvy is a brand name for BIC, which is co-formulated as a single tablet with Tenofovir (TAF) and Emtricitabine (FTC).[9] BIC is currently not recommended during pregnancy because of limited efficacy and safety

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data.[11] BIC/TAF/FTC has been approved in our country's regulatory affairs (Saudi Food and Drug Authority) and is accessible to HIV patients. Moreover, in childbearing female patients who will start on BIC/TAF/FTC in our hospital, a pregnancy test is ordered for them prior to starting and whenever there is a possibility of pregnancy during their course. We report a case of early-term delivery in a female with an unplanned pregnancy who became pregnant while receiving BIC/TAF/FTC in a tertiary care hospital in Saudi Arabia.

Case Presentation

This is a 42-year-old woman who was diagnosed with HIV in September 2020, with an HIV VL of 5738 and a CD4 level of 523. She was started on Raltegravir (RAL) and TAF/FTC because she was pregnant at that time. Previous to her HIV infection, she had two abortions. She delivered her first child via cesarean section in October 2020, and while waiting for the VL result, she was administered intrapartum intravenous Zidovudine. VL later proved to be undetectable after delivery. Raltegravir (RAL) and Tenofovir (TAF)/Emtricitabine (FTC) was discontinued in November 2020, and therapy was switched to BIC/TAF/FTC.

The patient was last seen in February 2021 and was constantly nervous, terrified, and crying for an unknown reason. She reported hair loss and an increase in appetite. The VL went undetected, and the CD4 was not found until the patient received the first dose of the COVID-19 vaccine in April 2021. The patient arrived at the infectious disease clinic in July 2021 after running out of medication and missing her appointment due to transportation issues. For two weeks prior to her arrival, she had been taking antiretroviral medication (ART) on alternate days. She also mentioned missing her period for the past two months and experiencing numbness in her arms and lower extremities. A pregnancy test was scheduled, and it came back positive, but she missed her follow-up appointments and continued to take BIC/TAF/FTC.

On November 3, 2021, a patient presented to the emergency department with labor pains in preparation for the birth of her second child. The patient stated that she was following her ART regimen and had not taken any medications in the previous year.

A cesarean section was performed because a membrane rupture occurred at 37 weeks of gestation and the VL was unknown. The patient tolerated the procedure and was transferred to the ward in stable condition. The VL went undetected, and after three days, the mother was discharged with BIC/TAF/FTC without complications. Because Zidovudine was unavailable in our hospital or near hospitals, prophylactic ART for perinatal HIV-1 transmission was not given.

Due to abnormal cardiotocography (CTG) and a ruptured membrane, an early-term baby girl was delivered through emergency cesarean section. She was born at 37 weeks gestation with a birth weight of 2430 g. The baby was in good condition upon birth, with Apgar scores of 7, 9, and 9 at 1, 5, and 10 min, respectively. This baby is classified as having low-risk prenatal HIV transmission because the mother's VL was not detected. The baby was taken to the Neonatal Intensive Care Unit (NICU) for observation. At birth, the vital signs were normal, with a heart rate of 158, a respiratory rate of 50, a temperature of 36.6, and an oxygen saturation of 93. Her blood samples obtained for laboratory tests after birth were completely normal, including HIV RNA VL, complete blood count, renal function, and liver function. The VL was undetectable. Table 1 shows the results of additional laboratory tests. The physical examinations were normal. For prophylaxis, zidovudine (4 mg/kg orally, twice day) was started, and breastfeeding was prohibited. The baby was admitted to the NICU for one day, then transferred to the nursery unit to be monitored for hyperbilirubinemia for three days before being discharged. The baby was discharged on oral Zidovudine for four weeks, with a follow-up appointment for the VL. However, the family did not bring the baby to the next checkups.

Ethical Approval and Informed Consent

This report did not require ethical board approval because it did not contain any human or animal trials, and a consent form was obtained from the mother for the publication.

Discussion

During pregnancy, many physiological changes occur, causing in variations in the pharmacokinetic characteristics of ART.[11] We are reporting a case of HIV-positive pregnant women treated with BIC/TAF/FTC during their pregnancy in Saudi Arabia. The mother's VL was suppressed after delivery, and the baby was born healthy. HIV-integrase inhibitors are thought to be effective in lowering VL and as a first-line HIV

Table 1. Results of Laboratory Tests After Birth.

Laboratory Test	Result	Normal Lab Value
Platelet	208× 10^9/L	84 to 478× 10^9/L
Hemoglobin (Hgb)	15.5 g/dL	15 to 24 g/dL
White blood cells (WBC)	10.7× 103 cells/mm3	6 to 17× 103 cells/mm3
Red blood cell (RBC)	4.0 mill/mm^3	4 to 5.5 mill/mm^3
Hematocrit (Hct)	46.7%	44% to 70%
Bilirubin Total	111.4 mg/dL	< 12 mg/dL
Magnesium	0.75 mEq/L	5–2.5 mEq/L
Sodium	141 mEq/L	130–147 mEq/L
Chloride	112 mEq/L	95 to 105 mEq/L
Creatinine	0.59 mg/dL	0.03 to 0.5 mg/dL
Blood urea nitrogen (BUN)	1.6 mg/dL	2–20 mg/dL
Alanine aminotransferase (ALT)	11 units/L	6–40 units/L
Aspartate aminotransferase (AST)	69 units/L	30–150 units/L
HBV (dsDNA)*	Not Detected	-
HIV-1 (ssRNA)*	Not Detected	-

HBV: Hepatitis B virus; dsDNA: double-stranded DNA; ssRNA: Human immunodeficiency virus, single-stranded RNA.

treatment. Dolutegravir and Raltegravir-based regimens are currently considered effective and safe medications during pregnancy for HIV-positive pregnant women.[8] Bictegravir is presently not recommended during pregnancy due to limited efficacy and safety data in preventing vertical transmission.[11] Bictegravir is primarily metabolized by CYP3A4 and uridine diphosphate glucuronosyltransferase 1A1 (UGT1A1).[12] According to pharmacokinetic studies, medication clearances increase during pregnancy due to increased activity of CYP3A4 and UGT1A1. As a result, lower Bictegravir exposure is expected, which may raise the risk of treatment failure or vertical transmission.[13–15]

One recent study obtained the pharmacokinetics profile of two HIV-positive pregnant women. Before becoming pregnant, the first mother started taking BIC/TAF/FTC. In comparison, the second woman began taking BIC/TAF/FTC two months after pregnancy. The authors evaluated the levels of Bictegravir, including the 24-h area under the plasma concentration versus time curve (AUC 0-24), trough concentration (C-trough), and maximum concentration (C-max) in the two mothers during the third trimester and after delivery, to evaluate efficacy. In the first mother, the (AUC0-24) of Bictegravir was 37.9 h*mg/L, the (C trough) was 0.63 mg/L, and the (C max) was 3.82 mg/L. Third-trimester levels were 35%, 49%, and 19% lower than after six weeks of delivery, respectively. As a result, Bictegravir exposure decreases slightly in the third trimester. The VL, on the other hand, went undetected in the third trimester. The authors did not calculate the values because the second mother's pharmacokinetics profile remained incomplete. Nonetheless, the VL went undetected in the third-trimester. In our case, the VL was undetectable prior to pregnancy and for 12 h following delivery. The same study calculated the ratio of maternal blood to umbilical cord blood concentrations in the first mother 20 h after drug administration and 7 h in the second mother. The corresponding ratios were 1.49 and 1.42. Bictegravir may cross the placenta and reach the fetus based on these ratios. In this case, no vertical transmission occurred, and the baby was born normally.[16] Another case report for pregnant women who continued BIC/TAF/FTC throughout the second trimester and were able to maintain viral suppression until delivery.[17]

Rupture of the membranes near the end of a pregnancy can be caused by a variety of factors, including natural weakening of the membranes or contraction force, low socioeconomic conditions, previous preterm birth, and unexplained causes. These negative outcomes could be a result of a variety of factors, including BIC, but this cannot be proven.

Conclusions

In our case, BIC/TAF/FTC was effective in suppressing VL during pregnancy, and no maternal-infant safety concerns were reported. More research is needed to help us predict changes in the pharmacokinetics and safety of BIC/TAF/FTC during pregnancy. By adding data on the efficacy and safety of BIC use in pregnancy, we believe this case can help provide real-life experience using BIC/TAF/FTC for managing such complex cases.

Declaration of Conflicting Interests

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