

been in place in our hospital for more than a decade and has resulted in zero infections for prolonged periods of time (unpublished results), this is a remainder that surveillance must not be relaxed. Timely detection of the cause of the outbreak in our hospital led to swift actions that prevented further cases. Despite negative cultures in cases, causality is strongly suggested by the following facts: (1) the presence of a common source in cases and its absence in non-affected patients, (2) the rapid onset of symptoms after exposure to the common source by the intravenous route (endotoxin in the infusate could have been the triggering event<sup>9</sup>), (3) the evidence of a pathogen recovered from the common source, (4) the evidence of breaches in the aseptic preparation of propofol infusions, (5) the extinction of the outbreak after reuse of propofol was stopped, and (6) the absence of sepsis cases before manipulation of propofol vials occurred.

Propofol infusate contamination remains an important risk factor for sepsis and bloodstream infections when aseptic practices are not followed in anesthetic procedures. We make a call for continued surveillance and education to prevent further cases, especially in outpatient settings.

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### Inadvertent dual therapy with dolutegravir and lamivudine in a pregnant patient living with HIV. A case report<sup>☆</sup>



#### Terapia dual inadvertida con dolutegravir y lamivudina en paciente embarazada con VIH. A propósito de un caso

All pregnant women with HIV infection should receive antiretroviral therapy (ART). It should be started early, regardless of their immunological and virological status. The aim is both to prevent transmission to the foetus or newborn (*perinatal transmission*) and to improve maternal health against the HIV infection.<sup>1</sup>

ART decreases the rate of progression of HIV infection by reducing the viral load in peripheral blood or by maintaining virological suppression (<50 copies/ml) once achieved. This significantly reduces the risk of perinatal transmission.<sup>2</sup>

Ioannidis et al. established a perinatal transmission rate of 1% in women whose HIV-1 viral load (VL) remained below 1000 copies/ml. The risk was reduced almost completely if suppression of maternal viraemia was also accompanied by antiretroviral prophylaxis.<sup>3</sup>

In pregnant women, the preferred ART regimens differ from those recommended for non-pregnant adults, due to the lack

of scientific evidence regarding efficacy and safety with some antiretrovirals in pregnancy. The recommendation is for ART based on triple therapy with combinations of *nucleoside analogue reverse transcriptase inhibitors* (NRTI) and *integrase inhibitors* (INI), such as raltegravir, or *protease inhibitors* (PI), such as ritonavir-boosted darunavir.<sup>4–6</sup>

We are reporting here the case of a 33-year-old woman from Morocco diagnosed with HIV-1 infection in 2011 in Greece. She was started on ART with ritonavir-boosted lopinavir (LPV/r) and a nucleoside analogue pair: emtricitabine/tenofovir (FTC/TDF). She was asymptomatic at diagnosis, with a CD4 nadir above 500 cells/μl (category A1). In 2017 the patient moved to Almería here in Spain and began follow-up at our centre.

Her adherence and tolerance to ART were good and she attended all her appointments without incident over the following three years, with optimal immunological and virological control. In March 2019, after stating that she had no desire to have children and with HBV serology negative, in order to minimise long-term toxicity, it was decided to simplify her ART to dual therapy with dolutegravir (DTG)+lamivudine (3TC). There was no virological failure before or after the switch.

In September 2019, she came to the clinic unexpectedly, 18 weeks pregnant. At that point, she was maintaining optimal immune control, with 544 CD4+/μl, and virological suppression (HIV-VL <20 copies/ml). It was decided to keep her on the same dual therapy, intensifying the obstetric checks, which had not detected any abnormalities or foetal malformations. Successive ultrasound

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and laboratory tests were optimal, with good immunological status and undetectable viral load in all determinations, including peripartum. The patient had a full-term pregnancy and normal delivery of a healthy newborn without perinatal transmission (progressive clearance of maternal antibodies in the newborn and undetectable HIV viral load). Universal recommendations were followed and she did not breastfeed.

In June 2020, the patient's dual therapy was optimised to a single tablet with DTG/3TC, without incident.

The guidelines of the world's main scientific societies consider DTG as one of the preferred agents. However, there is debate about recommending it in the first trimester of pregnancy and especially around the time of conception. We found different data in different studies. Zash et al. suggest increased risk of neural tube defects.<sup>7</sup> Zash et al., however, measured the rates of foetal and neonatal death, weight loss and preterm birth with DTG-based regimens started before or during pregnancy, and found them comparable to those of other antiretroviral regimens.<sup>8</sup> The World Health Organisation proposes DTG as the preferred first and second line treatment for all populations, including pregnant women and those with childbearing potential.<sup>9</sup>

There is an increasing amount of evidence on the safety and efficacy of dual therapy with DTG/3TC in patients with HIV infection, including the recommendation as initial ART in naïve patients after ruling out HBV coinfection.<sup>10</sup> The same regimen could be equally effective in pregnancy situations like the case we have discussed here. However, this needs to be demonstrated in well-designed studies.

Clinical practice guidelines recommend maintaining the ART taken prior to pregnancy in pregnant women with good immunological and virological control as long as it is compatible with the stage of pregnancy in which they are found and combinations with a high risk of toxicity are avoided.<sup>10</sup> This premise would be in line with the not-yet-proven safety and efficacy hypothesis of dual therapy with DTG/3TC in pregnancy. In the case we report here, the patient preferred to continue her ART, with which she was maintaining optimal immunological and virological control, despite our explaining to her the potential risks deriving from the limited experience of dual therapy in pregnancy.

After assessing the efficacy of dual therapy with 3TC + PI versus 3TC/ZDV + PI in a cohort of pregnant women who gave birth from 2006 to 2012 at the Pitié Salpêtrière Hospital (Paris, France), Gliga et al. suggest that the regimen based on 3TC + PI in dual therapy could control maternal viral load and prevent toxicities in both naïve and pretreated pregnant women.<sup>11</sup> Although the design and methodology of that study do not allow definitive conclusions in terms of practical application, it does lay down some bases for proposing the hypothesis of safety and efficacy of dual therapy in pregnancy which now needs to be demonstrated or refuted in well-designed studies.

We recognise that, with the scientific evidence available, the decision to maintain dual therapy in this case was controversial, although the positive experience and robustness of the DTG + 3TC regimen in other complex settings (such as naïve and pretreated patients with archived mutations)<sup>12,13</sup> could support the decision. Moreover, we must not forget that the patient herself preferred not to change her ART, which she had been both adhering to and tolerating well, and which she assured us she would not neglect during pregnancy, minimising the chances of perinatal transmission deriving from abandoning treatment.

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

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