HIV and Women – a conundrum in the management of a HIV positive woman who conceived on Dolutegavir with deviation from guidelines

CAROLE KHAW\textsuperscript{1,2}, MARK BOYD\textsuperscript{1,2}
\textsuperscript{1}Adelaide Sexual Health Centre (formerly Clinic 275), Infectious Diseases Unit, Royal Adelaide Hospital, Adelaide, SA, Australia
\textsuperscript{2}School of Medicine, Faculty of Health and Medical Sciences, University of Adelaide, Adelaide, SA, Australia

BACKGROUND

> In May 2018, the World Health Organization (WHO) issued a statement regarding the potential safety in Women living with HIV (WLHIV) using Dolutegavir (DTG) at conception.
> Preliminary unscrched analyses of an ongoing observational study in Botswana (Tepamo study) found 0.94% (0.37% to 2.45%) incidence of neural tube defects in infants of Botswana women conceiving on Dolutegavir compared to 0.12% (0.07% to 0.21%) incidence in infants born to women taking other cART at conception.
> This resulted in interim guidelines (DHHS and EACS) recommending that DTG should not be used in pregnant women in the 1st trimester and that women on Dolutegavir be switched to other cART pre-conception.

CASE PRESENTATION

> 35 year old African woman who immigrated to Australia in 2001 on a diplomatic visa at age 17.
> HIV (Clade C) was diagnosed in 2003.
> HIV acquisition was either through sexual transmission or from a blood transfusion following a termination of pregnancy in Africa.
> CD4 nadir was 54.
> Initiated on Combivir and Elavirenz soon after diagnosis.
> Was also commenced on Bactrim prophylaxis.
> Experienced considerable side effects from her J cART - hallucinations, depression and lipodystrophy.
> Persisted with her medications for 3 years.
> Ceased all cART and all medical contact in 2006.
> Returned to medical care early 2008 following her marriage.
> Her viral load then was 1497 copies/mL and CD4 count 71(7%).
> Recommended on cART - Kivexa and Kaletra.
> Also given Azithromycin and Bactrim prophylaxis because of her low CD 4 count.
> Viral load became undetectable by June 2008.
> Viral rebound late 2008 due to poor adherence, diarrrhea, psychological aspects.
> Monitored over the next year - Viral load ranged from low 700's to low 3000's - CD4 counts remained below 100.
> Early January 2010 – switched from Kivexa/Kaletra to Kivexa/boosted Atazanavir.
> Initially compliant with medications.
> By the end of 2010, viral load was undetectable with improved CD4 counts of 283 (23%).
> Unfortunately, lost to follow up again.
> January 2014 – re-presented.
> HIV viral load was 9060.
> Genotype was fully susceptible.
> Admitted to having issues of adherence - taking medications 50% of time only.
> Re-en: quite depressed.
> Admitted to having struggled with her diagnosis.
> Had shared her diagnosis with very few people over the years.
> August 2014 - referred to the first author who had monitored her progress.

> Switched to Truvirum - May 2016 - tolerated very well.
> Since commencing on Truvirum remained viral load undetectable - CD4 counts improved to the 300s and 400s.
> Discussion regarding conceiving and having children.
> Discussion regarding switching antiretrovirals at that time according to guidelines.
> Did not want to be on more tablets and was very happy with her STI of Truvirum.
> Mirena removed February 2018 - commencement on Folic acid.
> 18th of May 2018 - statement from WHO in Geneva - potential safety concerns of Dolutegavir at conception (Tepamo study at Botswana).
> At that time - patient had not fallen pregnant yet.
> Another long discussion occurred in view of this news with considerable concerns in both provider and patient.
> Several switch options were discussed in detail but patient was not keen.
> Patient’s decision to continue Truvirum as she had fully compliant with no side effects, had been fully suppressed and felt she was fully informed.
> She conceived in June 2018.

OUTCOME

> Patient monitored closely by multidisciplinary team throughout pregnancy.
> Pregnancy was unremarkable with normal morphological scans.
> February 2019 - Delivery by Lower Utterine Section Caesaran section (LUSCS) due to fetal distress.
> Healthy baby boy.
> Baby was given IV Lidasoune.
> Intention to breast feed but baby was eventually bottle-fed.
> Patient had remained viral load suppressed and to date the baby has remained HIV negative.

SIGNIFICANCE

> The case in particular demonstrated the importance of individualized, woman-centered approach to care.
> Despite some guideline recommendations at the time, the patient’s voice and right to self-determination was critical.

TSEPAAMO

DTG Exposure at Conception Associated With Smaller Increase in Incidence of Neural Tube Defects in Updated Analysis

10th IAS Conference on HIV Science, July 21-24, 2019; Mexico City, Mexico

Conclusions

> NTD prevalence among women who received DTG at conception – lower than initially signalised BUT still slightly higher than other exposure groups.\textsuperscript{11}
> Data as of March 2019: 0.1% DTG vs 0.1% non-DTG ART - estimated difference: 0.20% to 0.27%.
> Clinical and policy recommendations should consider the small but significant increased risk of NTD with DTG in context of other factors –
> considerable benefits of DTG
> lack of comparable data for other ARVs
> unknown risk factors of ART exposure in utero
> Based on current findings and additional surveillance reports,\textsuperscript{13} WHO released updated recommendations. Reconfirmation of use of DTG-based ART as preferred first and second-line therapy.\textsuperscript{24}
> Committee emphasized need for continued monitoring of NTD prevalence and patient counselling/shared decision-making.

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Health Central Adelaide Local Health Network

3. Farnet, JR 2019, AIDHA M2019/002
4. MPRO ART Policy Rev. 2019