Quality improvement project: A review of patients with historic Didanosine (ddI) exposure to ensure assessment for liver toxicity

H Coleman, R Kulasegaram

Guy's and St Thomas' NHS Foundation Trust

Background: Didanosine (ddI) exposure is known to cause liver injury ranging from mild and transient elevation of liver enzymes to hepatotoxicity including[1-2]:

- acute idiosyncratic liver injury
- lactic acidosis with steatosis
- hepatic dysfunction (LASH)
- non-cirrhotic portal hypertension

People living with HIV (PLWH) often now have well controlled HIV and as such may be seen less frequently.
It is important to maintain standards of care and identify cohorts of patients who require additional screening.

Aim: Review patients with historic ddI exposure and ensure assessment for liver toxicity:
100% of patients with platelet count <150 should have ultrasound liver/FibroScan

Method: A quality improvement project. All patients with ddI exposure were included. Patients not seen in the clinic since 2018 were excluded from the review. Results were collected from electronic patient records.

Didanosine (ddI)[3]
First licenced: 1991
Side effects: diarrhoea, nausea, vomiting, rash, Lactic acidosis, pancreatitis, peripheral neuropathy (25%)

Non-cirrhotic Portal Hypertension[4]
Diagnosis following exclusion of other secondary causes of liver disease

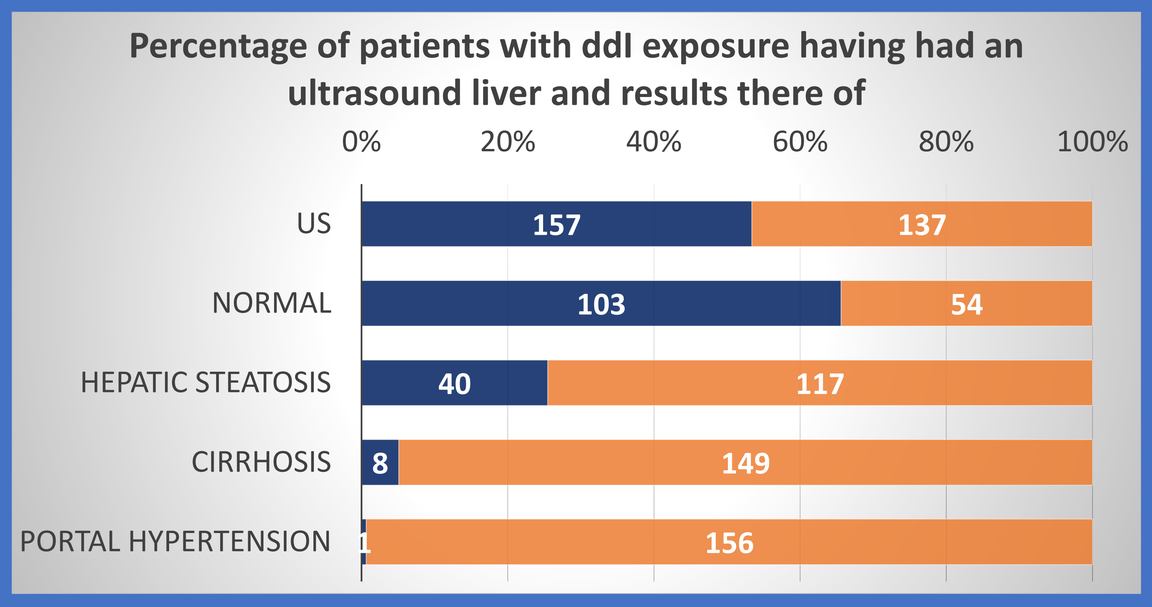
Clinical signs:
splenomegaly,
oesophageal varices,
ascites

Exclude: cirrhosis, viral hepatitis, non-alcoholic steatohepatitis, portal/hepatic vein thrombosis, other secondary causes of liver disease

Treatment: Treatment focus on prevention of complications related to portal hypertension

Results: **294 (~8%) out of our cohort of ~3800** patients had ddI exposure. Demographics and co-morbidities are listed below

Table 1			
	Number		Percentage
Median Age	57 years	Range 23-85	
Ethnicity	White	139/294	47%
	Black	121/294	41%
	Other/Unknown	34/294	12%
Median years since HIV diagnosis	25 years	Range 9-38 years	
Median exposure to ddI	3 years	Max 18 years	
Co-Morbidities	Hyperlipidaemia	117/294	40%
	Type II Diabetes	40/294	14%
	Peripheral neuropathy	39/294	13%
Viral Hepatitis	Hep B negative	272/294	93%
	Hep B Chronic	19/294	6%
	Hep B Cleared	3/294	1%
	Hep C negative	272/294	93%
	Hep C Cleared	22/294	7%



27% (78/294) had a FibroScan, average liver stiffness score was 5.1 KPa, and median CAPS 222 dB/m.

46 patients had a platelet count <150

43% (20/46) did not have ultrasound/Fibroscan assessment.

All patients within this group were hepatitis B/C negative.

Conclusion:

Although the majority of PLWH now have well controlled HIV, clinicians should be mindful of historical drug exposure. We have identified 20 patients with thrombocytopenia who require assessment with liver ultrasound.

The cohort of patient with ddI exposure have high rates of hyperlipidaemia, diabetes, peripheral neuropathy and have been living with HIV for many years.

Although ddI is no longer prescribed, patients may continue to live with toxicity from these early drugs. It is important trainees have an understanding of these drugs to guide holistic patient care as PLWH age.

Limitations of the project included using electronic patient records review (information not accurately documented; results available from 2003 onwards; transfer of care without information).

We plan to invite all identified patients for liver ultrasound assessment.

References:
1. Kovari, H., Ledergerber, B,. Peter, U., et.al. Swiss HIV Cohort Study, Association of Noncirrhotic Portal Hypertension in HIV-Infected Persons and Antiretroviral Therapy with Didanosine: A Nested Case-Control Study, *Clinical Infectious Diseases*, Volume 49, Issue 4, 15 August 2009, Pages 626–635
2. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Didanosine.
3. Didanosine(SPC) https://www.medicines.org.uk/emc/product/10500/smpc#gref
4. Schouten JN, Verheij J, Seijo S. Idiopathic non-cirrhotic portal hypertension: a review. *Orphanet J Rare Dis*. 2015;10:67. Published 2015 May 30. doi:10.1186/s13023-015-0288-8