Treating Patient, Not Disease: People-Centered Approach

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Hepatitis C screening and treatment among DR-TB patients in Armenia

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Background

- Hepatotoxicity is common during multidrug resistant tuberculosis (MDR-TB) treatment
- Hepatitis C (HCV) associated with increased toxicity [1,2]
- Previously, treatment of hepatitis C was not possible in patients with active tuberculosis
- New treatments for hepatitis C with direct acting antivirals (DAA) may be given during tuberculosis treatment

=> important to identify patients with Hepatitis C disease who may benefit from this treatment

1: Lomtadze N et al. (2013) Hepatitis C Virus Co-Infection Increases the Risk of Anti-Tuberculosis Drug-Induced Hepatotoxicity among Patients with Pulmonary Tuberculosis. PLoS ONE 8(12): e83892. INT J
2. Lee et al. Frequency and risk factors of drug-induced liver injury during treatment of multidrug-resistant tuberculosis TUBERC LUNG DIS 20(6):800–805 Q 2016 The Union http://dx.doi.org/10.5588/ijtld.15.0668

Objective

Assess the prevalence of hepatitis C in MDR-TB patients in Armenia with a view to introduction of direct acting antivirals as required

Context

Armenia

- High burden of MDR-TB
- MSF supported MDR-TB treatment since 2005
- Hepatitis C (HCV) testing in MDR-TB patients non-systematic 2005-2015:
  - Patients with risk factors or hepatotoxicity
  - 6% per year (range 2-8%)

Methods

- **Target population for screening**:
  - patients receiving conventional MDR-TB treatment
  - with or without new molecules

- **HCV testing algorithm**
  - HCV serological testing
  - If HCV antibody testing positive
    - PCR testing and genotyping
    - Fibro-scan

Results (1) – Hepatitis C prevalence

	N (%)
Total screened	**208**
HCV serology positive	62 (62/208, **29.8%**)
HCV serology positive tested with PCR	58 (58/62, 93.5%)
HCV serology positive tested with PCR positive	40 (40/58, 69.0%)
HCV genotypes	
• 3a	19 (19/40, 47.5%)
• 1b	14 (14/40, 35%)
Overall HCV (PCR positive)	**40/208 (19.2%)**

Results (2) – factors associated with positive hep C serology: univariate

	Hep C positive n, (% *)	p-value
Gender		
Male	55 (32.9)	<0.047
Female	7 (17.1)	
Age in 2016 (years)		
< 35	6 (10.2)	
≥ 35	56 (37.8)	<0.019
Previous prisoner		
No	35 (20.8)	
Yes	23 (71.9)	<0.001
HIV status		
Negative	31 (28.2)	< 0.015
Positive	8 (61.5)	
DST at treatment initiation		
MDR	5 (14.7)	
Pre-XDR Inj	5 (26.3)	
Pre-XDR FQ	5 (21.7)	
XDR	11 (64.7)	<0.002

* % of subgroup that was HCV positive

Treatment of hepatitis C with DAAs

Priority patients for treatment with DAAs

- Patients with hepatotoxicity during MDR TB treatment
- Genotype 3- high risk to progress disease quickly
- HIV patients once viral load is undetectable
- Patients with F3-F4 stage of fibrosis

Exclusion criteria

- Pregnancy
- Detectable HIV viral load
- Age below 18
- Advanced/terminal diseases

Treatment

	N (%)
Total started Rx with DAAs (Dec 2016-Jan 2018)	**26**
Number of cases DAAs fully overlapping MDR-TB Rx	15 (**58%**)
Number of cases DAAs introduced after MDR-TB Rx	11 (42%)
Number of cases with MDR-TB with new drugs	16 (**62%**)
Number of cases with MDR-TB without new drugs	10 (38%)

Characteristics of the cohort treated with DAAs N-26

Genotypes	
3a	18 **(69%)**
1b	7 (27%)
2	1 (4%)

Stage of fibrosis	
F0-F1	15 **(58%)**
F2	2 (8%)
F3	4 (15%)
F4	5 (19%)

HIV status	
Pos	4 (15%)
Neg	22 **(85%)**

Treatment regimens and duration N-26

Regimen	Number of cases, %	Duration by weeks
SOF+DCV	17 (65.4%)	12
SOF+LDV	5 (19.2%)	12
SOF+DCV+RBV	4 (15.4%)	24

SOF: Sofosbuvir (400 mg tablets): 400 mg x 1 per day

DCV: Daclatasvir (30 or 60 mg tablets): 30-90 mg x 1 per day

RBV: Ribavirine (200mg tablets): 400-600mg x 2 per day

Outcomes of treatment with DAAs

Eligible for PCR at end of treatment* N-23	
HCV PCR Positive	4
HCV PCR Negative	17
HCV PCR not performed	**2**
Reason HCV PCR not performed	technical problems
Eligible for SVR 12 (HCV PCR 12 weeks post end of treatment) N-13**	
HCV PCR Positive	1
HCV PCR Negative	10
HCV PCR not performed	**2**
Reason HCV PCR not performed	left the country

* Viral load is tested at the end of DAA treatment

** Sustained Virological Response is tested at 12 weeks after end of DAA

Conclusion

- High proportion of the MDR-TB patients in this cohort had Hepatitis C

⇒ **Testing for active hepatitis C should be systematically performed at baseline on all patients with MDR-TB from regions with high prevalence of Hepatitis C**

- Treatment for hepatitis C should be considered in patients unable to tolerate MDR-TB treatment due to hepatotoxicity or high risk of cirrhosis

⇒**DAA compatible with MDR-TB treatment and preliminary results showed good tolerability and results**

Future perspectives and challenges

- HCV screening for all TB cases-not only MDR-TB
- HCV treatment for all TB cases-not only MDR-TB
  - during TB if hepatitis C treatment is a priority
  - after TB treatment (if Rifampicin included in their TB treatment)
- Address availability and access to DAAs
  - price and registration
- Develop a simple and affordable patient- centered model of care for hepatitis C treatment in TB patients
  - Include support for alcohol and drug addiction

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