

Hepatitis C viral loads in the semen of HIV positive men during acute and chronic Hepatitis C infection

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Background

- Acute HCV infection in MSM is well described
- Sexual transmission of HCV is postulated
- The excess acute HCV infections among HIV positive men remains unexplained
- Are HIV positive men more likely to transmit HCV during acute HCV?
- HCV is present in extra-cellular fluid of semen (seminal plasma)
 - 11- 40% HCV viraemic men

Hypotheses

- HIV positive men with acute HCV infection are more likely to have detectable HCV RNA in seminal plasma than those with chronic HCV infections
- That if detectable, HCV viral load in seminal plasma is higher in HIV co-infection

Methods

- Substudy of Acute HCV cohort study
- Acute HCV definition
 - HCV RNA positive and anti HCV negative (with follow up)
 - HCV RNA positive with previous negative in 6 months
 - HCV RNA positive and ALT rise > x10 ULN (other causes excluded)
- Paired blood and semen samples
 - Baseline, 1 month, 6 months
- Control group HCV infection >6 months and not on HCV treatment

Methods virology

- HCV RNA quantification by in house RT-PCR
- Viral load lower limit of detection 10 IU/ml
- Process initially tested using HCV RNA spiked semen
- Internal control- Brome mosaic virus

Characteristics of study participants

- All HIV positive MSM
- All presumed to have acquired HCV sexually
- Median age years (range)
 - Acute cases 43 (35-47)
 - Controls 36 (26-46)

Results: acute HCV n=10

	Baseline VL (IU/ml)		1 Month (IU/ml)		6 months (IU/ml)	
	Semen	Plasma	Semen	Plasma	Semen	Semen
1	<10	950 000	<10	100 000	<10	5 000
2	<10	19 000	withdrew			
3	<10	11 000 000	27	5 600 000	14	5 900 000
4	<10	13 000 000	<10	<10 *		
5	<10	580 000	<10	52 000		
6	<10	170 000	<10	9 000		
7	<10	4 300 000	<10	<10 *		
8	<10	3 000 000	<10	17 000		
9	<10	<10 *				
10	<10	450 000				

* Acute HCV treatment

Results: chronic HCV n=10

	Baseline VL (IU/ml)		1 month VL (IU/ml)		6 month VL (IU/ml)	
	Semen	Plasma	Semen	Plasma	Semen	Plasma
1	150	12 000 000	80	13 000 000	230	22 000 000
2	<10	860 000	<10	590 000	<10	1 500 000
3	<10	12 000 000	<10	17 000 000	<10	17 000 000
4	37	20 000 000	<10	30 000 000	<10	43 000 000
5	<10	3 300 000	<10	1 300 000	<10	4 800 000
6	<10	97 000 000	<10	31 000 000	<10	16 000 000
7	<10	3 000 000	<10	300 000	<10	<10
8	<10	7 600 000	lost sample	2 700 00		
9	<10	2 700 000	withdrew			
10	<10	220 000	<10	1 700 000		

Results

- Detectable HCV RNA in semen
(excluding men opting for acute HCV treatment n=3)

	Cases	Samples
Acute HCV	1/9 (11%)	2/16 (12.5%)
Chronic HCV	2/10 (20%)	5/25 (20%)

- Quantification of detectable HCV RNA in semen
 - <30 IU/ml in acute cases
 - Range 37- 230 IU/ml in chronic cases

Limitations

- Small numbers n=20
- Acute HCV peak viral loads may have been missed

Conclusions

- No evidence that seminal HCV RNA viral loads were higher in acute HCV infection
- The majority of HCV seminal viral loads were undetectable
- When present, seminal HCV RNA viral loads were in very low quantities
- The increased transmission of acute HCV in HIV-positive men remains unexplained

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- Extra slides

Virology Methods 2

- Liquefy semen
- Divide into two aliquots
 - Process as neat
 - Diluted with 1:2 normal human plasma
- Centifugation 3000g for 20 min
- Supernatant taken
- Centifugation 3000g for 20 mins
- Extraction Biorobot MDX
- Extracted RNA amplified with HCV quantitative RT-PCR
- ABI Prism 7000/7500 Qiagen Quantitect Probe reagents