Intentional Transplantation of Hepatitis C Positive Livers into Hepatitis C Negative Recipients- Report of the first Case Series in World

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Disclosures

• I have no financial relationships with commercial interests to disclose.

• My presentation does not include discussion of off-label or investigational use.
Background

- HCV prevalence in the world is 3% (200.000.000 people).
- 19.5% donors that are PHS increased risk in USA.
- 4.2% of donors HCV Ab positive and 2.4 % NAT positive.
- Outcomes of HCV+ livers are similar to HCV- livers transplanted in HCV+ recipients.
- Mortality wait list in US is 14% (UNOS).

Verna EC. Liver Transpl 2018 Jan;24(1):12-14
Opioid Epidemics and Utilization of HCV Livers in USA

Overdose donors

Figure 1.
First-time adult liver transplant recipients with HCV and HCV donor utilization since introduction of MELD-based allocation

Durand C. Ann Intern Med April 2018. doi 10.7326/M17-2451
Change in Paradigm

• First DAA FDA approval Dec 2013.

• Proven Efficacy even in the immunosuppressed patient (post-transplant) - end of 2015.

• Pangentotypic and high Success rate DAA treatment (>95%) 2016.
Establishing Protocol

• Discussion of the concept in our transplant meetings.
• Ethical committee consult.
• Hospital risk assessment/lawyers approval.
• Patient and family’s education/consent in several occasions.
• Documentation consent by hepatologist and transplant surgeon.
• No pre-transplant authorization from health insurance companies.
• Patients were informed there was a chance they would have to pay out-of-pocket for treatment if insurances denied treatment or if we were not able to obtain compassionate treatment funding.
• Final organ acceptance by two transplant surgeons.
• Final written consent at the time of transplant.
• Post-transplant follow-up protocol by ID and hepatology.
• Request insurance approval after first HCV test is positive (first week).
Indications

- **Recipients**
  - Adults
  - Patients were consentable (no significant encephalopathy).
  - No emergent transplant
  - High MELD recipient or low MELD with poor QOL (multiple admissions, refractory ascites, recurrent GI bleeding, etc).

- **Donors**
  - Whole livers
  - Liver Biopsy with no more than stage 1 fibrosis or significant steatosis.
  - Liver biopsy review by the transplant team.
April 2016: First case of Intentional Transplantation of HCV positive Liver into HCV negative recipient: Univ of Massachusetts. NYT cover page Oct. 6th 2016

Results

• From a total of 650 LTx (~ 30% PHS increased risk donors) in two patients there was non-intentional HCV transmission (genotype 1A and 4A/4C/4D).

• We intentionally used 5 livers that were HCV positive (2 viremic and 3 aviremic).

• No transmission in the 3 patients that received Ab + NAT- HCV livers after median follow-up of 239 days. Transmission in the 2 patients that received NAT+ HCV livers (both genotype 1A).

• No problems to obtain insurance authorization for DAA in patients that got HCV infection after receiving HCV+ livers.

• Successful treatment in all 4 patients that got HCV infection from the donors.
Our Cases of Non-intentional Transmission of HCV Positive Livers (Falsely negative NAT)

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<th>Case</th>
<th>Intentional Allocation</th>
<th>Age recip</th>
<th>Donor HCV Ab</th>
<th>Donor HCV RNA</th>
<th>HCV Genotype</th>
<th>Transmission Hep C</th>
<th>DAA Therapy</th>
<th>SR12 weeks</th>
<th>Follow-up post LTx (Days)</th>
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Our Series of Intentional Transmission of HCV
Hep C+ liver into Hep C- recipient

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Discussion
Case reports: Non-Intentional Allocation of HCV+ livers into HCV- recipients

• Several cases of non-intentional transmission of HCV have been reported when NAT test was not available (before 2005) and NAT tests that were falsely positive or done within the “window period”.

• Several of these cases were treated successfully with DAAs.

Tugwell BD. Annals Int Med 2005, 143:648
Shah AP. Transp Inf Dis 2017;19(2).
Case reports: Intentional Allocation of HCV+ livers into HCV- recipients

- Only four papers reporting intentional use of HCV+ livers into HCV-.
- Bari et al used 25 livers from HCV Ab positive NAT-. There was a transmission rate of 16%.
- Saberi and Campos-Varela used each one HCV NAT+ liver (viremic donors). Both recipients (genotype 1A and 3, respectively) were successfully treated.
- No abstract in ILTS and the Am Transp Congress 2018 (besides this one).

Saberi B. Liver Transpl 2018, 24:140.
Modeling Analysis of Transplanting HCV Positive Livers into HCV Negative Recipients

Limitations of the Allocation: HCV + into HCV -

- Ethical Dilemma: “Primum non Nocere”? vs. patient autonomy
- Cost of treatment (over $100,000 USD)
- Need for insurance authorization (no guarantee it will be covered).
- Relapses/resistance?
- Risk of fulminant hepatitis C (very rare).
- Potential higher risk of transmission of HCC (?)
- Risk of cholestatic hepatitis

Conclusions

• Risk of transmission of HCV Ab + NAT negative (aviremic) livers is low (0-16%).

• Risk of transmission of HCV Ab + NAT positive (viremic) livers is 100%.

• All reported cases of LTx from HCV+ into HCV- have cleared hepatitis C.

• Use of Hepatitis C positive livers (both aviremic and viremic) should be considered to expand the donor pool and decrease mortality on the waitlist.