Impairment of Renal Function associated with Tenofovir Therapy

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Introduction

• Tenofovir (TDF): nucleotide reverse transcriptase inhibitor (NRTI)

• Used in treatment of HIV and Hepatitis B

• Potential for accumulation of high concentration of TDF in renal tubular cells

• Impaired renal function first reported as side-effect in 2005
Aims of Study

To further investigate impact of TDF therapy on renal function in HIV positive patients, looking specifically at:

- Reversibility of renal impairment at 3 months post cessation of treatment
- Effect of HCV co-infection
- Confounding factors, such as concurrent protease inhibitor(s) therapy
Methods

- Renal function assessed retrospectively (eGFR and proteinuria) in HIV +ve patients (n=214) treated for >3 months with TDF at RIDU

- MDRD equation used to calculate eGFR from serum creatinine, age, race and sex

- Controls (n=162) had never received TDF

- Data analysed using SPSS version 19
Patient Selection

HIV Positive Cohort: N=376

GROUP 1
114 (who had ceased TDF therapy)
- eGFRs (at starting and stopping TDF)
- eGFRs at 3 months post TDF-cessation.

GROUP 2
100 (currently taking TDF)
- Current eGFRs

GROUP 3
162 (never taken TDF)
- Current eGFRs
Results: Mean eGFRs

**Group 1**
Before: 93.0 (+/- 21.1)
On stopping: 84.5 (+/- 32.1)
Post-cessation: 88.6 (+/- 30.1)

**Group 2**
103.0 (+/- 23.0)

**Group 3**
105.6 (+/- 26.35)
Results: Reversibility (Group 1)

- 26 patients died whilst receiving TDF. A further 2 patients died following in the 3 months follow-up.

- In 58/86 (67.4%) of patients, eGFRs did not return to baseline level by 3 months post-cessation.

- 30/86 (34.9%) did not return to within 10% of baseline eGFR at 3 months post-cessation.
## Results: Group 1

<table>
<thead>
<tr>
<th>CKD Stage*</th>
<th>GFR</th>
<th>Before TDF</th>
<th>On Stopping TDF</th>
<th>3 Months post-cessation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;= 90</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>60-89</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>30-59</td>
<td>4 (3.5%)</td>
<td>20 (22.7%)</td>
<td>9 (10.5%)</td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
<td>0</td>
<td>1 (1.1%)</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
<td>0</td>
<td>2 (2.3%)</td>
<td>1 (1.2%)</td>
</tr>
</tbody>
</table>

*NICE, Chronic Kidney Disease
Results: Proteinuria

- Median protein:creatinine ratio of 12 (IQ range 8.5-18) in group 2 compared to 10 (IQ range 7-15) in group 3

- No evidence of increase in proteinuria in patients receiving TDF
Results: HCV co-infection

- Did not impact the decline in renal function in any group

- Did not impact the reversibility of impairment of renal function (13/39 HCV +ve (33%) returned to baseline eGFR compared with 16/47 (34 %) HCV -ve)
Results: Confounding Factors

- Protease inhibitor therapy: no significant difference ($p>0.05$) in impairment of renal function or reversibility

- Duration of treatment, age, gender and ethnicity were not significant confounders ($p>0.05$)
Conclusions

• Results provide further support for previous studies \(^1,2\)

• The use of TDF is associated with impairment of renal function

• This impairment was not fully reversible in the majority of patients following cessation of TDF

• Further work required into benefits of treatment with TDF versus dangers of renal impairment.
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