Sputum culture conversion of diabetes/tuberculosis patients compared to age, gender and disease matched patients without diabetes in Virginia

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ABSTRACT

Background: Diabetes (DM) complicates TB treatment including a prolonged time to sputum culture conversion and increased risk of death compared to non-DM/TB patients. Since 2013 in Virginia, recommendations have been in place to perform early therapeutic drug monitoring (TDM) and dose correction for isoniazid and rifampin after 2 weeks of therapy for DM/TB patients. Further effort has been made to screen those without known DM by HgbA1c.

Methods: A retrospective study of the state TB registry was performed for patients initiating treatment in 2013-2014. DM/TB patients undergoing early TDM were compared to non-DM/TB patients by ±10 years, gender, and smear status. Subjects were included if they had diabetes or were identified as having any other immunosuppressing condition, or any first-line drug resistance. DM/TB and matched non-DM/TB patients were then assessed for the time to sputum culture conversion.

Results: 373 patients started treatment, of which 60 were DM/TB, 19 DM/TB patients met study criteria, including 10 (53%) men and 16 (84%) smear positive, and were compared to 19 matched non-DM/TB patients. DM/TB patients mean age was 61.5 years ±13.6 (p=0.02) compared to non-DM/TB controls of 58.7 ± 15.7. In DM/TB, the isoniazid mean C2hr (daily dosing) was 2.5 μg/ml ±1.8 and 12 (63%) were in range for dose increase, rifampin mean C2hr was 8.4 μg/ml ±6.8 and 8 (47%) in range for dose increase, and ribafutin C2hr of 0.57 μg/ml ±1.8 in one subject (within the expected range thus no dose increase). Mean time to sputum culture conversion in DM/TB patients was 36.0 days ±21.9 compared to non-DM/TB of 58.8 days ±34.6 (p=0.02), despite the majority of DM/TB having cavitary disease.

Conclusions: Early TDM for DM/TB may shorten the time to sputum culture conversion compared to age, gender and disease matched non-DM/TB patients. These findings warrant further controlled study.

OBJECTIVES/ METHODS

- Compare the time to sputum culture conversion in DM/TB compared to non-DM patients following programmatic recommendations for increased screening by HgbA1c of all TB patients and early therapeutic drug monitoring for DM/TB

- Retrospective cohort review of state TB registry and laboratory records.

APPROACH

Study period 2013-2014: N=60

| N=19 DM/TB included that received early TDM |

| N=19 non-DM/TB (HgbA1c≥6.5%) and/or chart eval |

Time to sputum culture conversion?

Sputum culture negative

Extrapulmonary TB

Any first-line drug resistance

Other immunosuppression (eg. HIV)

No early TDM

Early therapeutic drug monitoring for DM/TB

2hr serum concentrations for isoniazid and rifampin (only) at -2 weeks after initiation, with single dose increase (only) if below expected range

n=18 DM/TB

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mean C2hr</th>
<th>Below expected range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid (n=19)</td>
<td>2.5 μg/ml ±1.8</td>
<td>12 (63%)</td>
</tr>
<tr>
<td>Rifampin (n=17)</td>
<td>8.4 μg/ml ±6.8</td>
<td>8 (47%)</td>
</tr>
<tr>
<td>Rifabutin (n=1)</td>
<td>0.57 μg/ml</td>
<td>0</td>
</tr>
</tbody>
</table>

Therapeutic Drug Monitoring for DM/TB

TIME TO SPUTUM CULTURE CONVERSION

DM/TB patients was 36.0 days ±21.9

non-DM/TB of 58.8 days ±34.6 (p=0.02)

LIMITATIONS

- Need complete data on adjunctive DM treatment- specifically metformin use

- Need additional comparison to DM/TB that did not receive early TDM

- Awaiting final outcomes on total treatment duration

CONCLUSIONS

- Unexpectedly, early TDM for DM/TB may shorten the time to sputum culture conversion compared to age, gender and disease matched non-DM/TB patients

FUTURE STUDY

- Achieve more complete screening (and data capture) of all TB patients with HgbA1c to evaluate the initiative on larger scale

- Determine proportion of patients with DM or newly diagnosed DM by HgbA1c that were linked to DM care (and received metformin)

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REFERENCES

