Cancer treatment and diabetes

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Diabetes and cancer

- Cancer and its treatment also poses challenges to managing diabetes
  - Surgery
  - Altered appetite
  - Cachexia
  - Artificial Nutrition
  - Weight Loss / Gain
  - Nausea and Vomiting
  - Palliative Care
Cancer treatments and diabetes

- Steroids
- mTOR inhibitors
- PI3 Kinase Inhibitors
- Others
Steroids

- Widely used in oncology
  - As part of chemotherapy regimes
    - Lymphoma
    - Myeloma
  - To improve tolerability of chemotherapy
  - To manage symptoms of cancer
    - Reduce inflammation (brain, spine metastases)
  - To manage side effects eg immunotherapies
Steroid induced hyperglycaemia

– Multiple mechanisms
  – Increased hepatic gluconeogenesis
  – Insulin resistance – reduced insulin stimulated glucose uptake
  – Increased lipolysis, leading to intracellular lipids
  – Reduced insulin secretion
Risk factors

– Pre-existing diabetes
– Those at increased risk of diabetes (obesity, family history, previous gestational diabetes, PCOS)
– Impaired fasting glycaemia or glucose tolerance
– At risk on Diabetes UK Risk Calculator
Your risk explained

These are the risk factors that you can’t change, so focus on the things that you can change or maintain.

<table>
<thead>
<tr>
<th>Age</th>
<th>Points</th>
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<tbody>
<tr>
<td>49 or younger</td>
<td>0</td>
</tr>
<tr>
<td>50 - 59</td>
<td>5</td>
</tr>
<tr>
<td>60 - 69</td>
<td>9</td>
</tr>
<tr>
<td>70 or older</td>
<td>13</td>
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Gender

<table>
<thead>
<tr>
<th>Gender</th>
<th>Points</th>
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<td>Male</td>
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<tr>
<td>Female</td>
<td>0</td>
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Ethnicity

<table>
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<th>Ethnicity</th>
<th>Points</th>
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<tbody>
<tr>
<td>Only white European</td>
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<tr>
<td>Oth</td>
<td>8</td>
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</table>

Relatives with diabetes

<table>
<thead>
<tr>
<th>Approach</th>
<th>Points</th>
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</thead>
<tbody>
<tr>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
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</table>

These are the risk factors that you can change. Even small changes can help reduce your risk.

<table>
<thead>
<tr>
<th>Waist measurement</th>
<th>Points</th>
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<tbody>
<tr>
<td>Less than 90cm (35.3in)</td>
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<tr>
<td>90 - 99.9cm (35.4 - 39.3in)</td>
<td>4</td>
</tr>
<tr>
<td>100 - 109.9cm (39.4 - 42.9in)</td>
<td>6</td>
</tr>
<tr>
<td>110cm (43in) or above</td>
<td>9</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>BMI</th>
<th>Points</th>
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<tbody>
<tr>
<td>Less than 25</td>
<td>0</td>
</tr>
<tr>
<td>25 - 29.9</td>
<td>3</td>
</tr>
<tr>
<td>30 - 34.9</td>
<td>5</td>
</tr>
<tr>
<td>35 or above</td>
<td>8</td>
</tr>
</tbody>
</table>

Low: 0 - 6
Increased: 7 - 15
Moderate: 16 - 24
High: 25 - 47
Definitions

- **Steroid induced diabetes**
  - New onset diabetes identified after starting steroids
  - May or may not resolve when steroids stop

- **Steroid induced hyperglycaemia**
  - Deteriorating glycaemic control in those with established diabetes after starting steroids
Patterns

– Depend on administration regime
– May be relatively mild impact on fasting glycaemia
– More dramatic effects of post-prandial levels, especially during day
– Onset can be within 4 hours
– Usually return to normal within 24 hours of stopping
Practical implications

- Need to monitor glucose both in those with diabetes and those at risk
- Fasting glucose may miss much of the effect
- Testing post-lunch or pre-evening meal more useful
- HbA1c no value in detecting effects of short steroid courses
Cancer drugs and diabetes

- Male, 60s
- Previous diabetes controlled on Metformin
- Colorectal cancer
- Commenced chemotherapy on d2 with Dexamethasone 4mg tds for 3 days

<table>
<thead>
<tr>
<th>Morning</th>
<th>Evening</th>
<th>Day</th>
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<td>8.6</td>
<td>8.3</td>
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<td>6.8</td>
<td>14.4</td>
<td>2</td>
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<td>10.1</td>
<td>26.1</td>
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<td>11.2</td>
<td>15.4</td>
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<tr>
<td>9.3</td>
<td>19.3</td>
<td>5</td>
</tr>
<tr>
<td>6.9</td>
<td>5.8</td>
<td>6</td>
</tr>
</tbody>
</table>
How would you treat?

1. Diet and exercise
2. Refer for structured education
3. Start Metformin
4. Start Gliclazide
5. Start Isophane Insulin
6. Start Mixed Insulin
7. Start GLP-1 analogue
8. Refer
How to treat:

– Difficult!!
– Oral Agents
  – Metformin useful if tolerated
  – Sulphonylureas - may only be needed whilst taking steroids
– Insulin
  – Once daily AM human
  – isophane isnulin
  – BD Mixed Insulin
  – Basal Bolus
How common?

- Surprisingly little data
- Perhaps because rarely do blood tests at time of peak risk
- Bournemouth Study
  - 39 Patients, after 5 cycles 8 had glucose in diabetes range and 6 with impaired glucose tolerance
- RMH Data (same regime)
  - 14% developed steroid induced diabetes

Hickish et al JNCI 2009
Other effects

- Putative effects of hyperglycaemia on effectiveness of chemotherapy
- Small studies have suggested increased toxicities eg neuropathy, but not consistent
Hyperglycaemia in newer cancer agents

– How are adverse events reported?

– Common terminology Criteria for Adverse Events – CTCAE Grade 1-5 (5=Death)

– Define either:

– Hyperglycaemia – cut offs of glucose level that do not correlate with diagnostic criteria for diabetes OR

– Impaired Glucose Tolerance – define by need for treatment

– Questionable how relevant these are to long term treatments
mTOR Inhibitors

- mTOR inhibitors (Everolimus) used to treat
  - Renal Cell Cancer
  - Breast Cancer
  - Neuroendocrine tumours
- >10% develop Grade III Hyperglycaemia (Glucose >13.8 mmol/l)
- Meta-analysis
  - RR 3.06 for any hyperglycaemia and 7.80 for high grade hyperglycaemia
mTOR Inhibitors

- Greatest risk in those with pre-existing diabetes
- Try to establish normoglycaemia before treatment
- Standard algorithms suggested – but consider role of TZDs and SGLT-2 inhibitors
PI3K Inhibitors

- In advanced stages of trials for multiple cancers
- Unsurprisingly hyperglycaemia commonly reported – around 30% in Phase 1 studies reported to date
- Increased Insulin levels

Rodon et al Invest New Drugs 2014
Saura et al Clin Cancer Res 2014
Other cancer drugs and diabetes

- Streptozocin used in some pancreatic NETS
- Small molecule inhibitors of IGF-1 receptor in Phase 1 trials
- AKT Inhibitors
- Immunotherapies – rare cases of Type 1 Diabetes
Evaluation: Cancer Treatment and Diabetes

Please rate this session for relevance to you as a GP:

1. Poor
2. Fair
3. Good
4. Very good
5. Excellent