Management of Diabetes in Patients with Cancer
Part 1
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Disclosure
Nothing to Disclose

Objectives

- Explain the relationship between diabetes and cancer.
- Identify ways to evaluate glucose control in persons with glycemic dyregulation and cancer.
- Describe the importance of evaluating the persons individual oncology treatment plan.
What we will cover:

- Relationship between diabetes and cancer
- Evaluation of glucose control
- Imaging
- Treatment options currently used
- Chemotherapy
- Immunotherapy
- Stem Cell transplant
- Surgery
- CART

A Little Bit About Us

The M.D. Anderson Diabetes program consists of 3 Diabetes Physicians and 5 Nurse Practitioners. We rotate between Inpatient and Outpatient duties. We see patients who are admitted with elevated glucose readings and in the outpatient clinic.

New Rates of Cancer in the US-2015

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Relationship between diabetes and cancer

Prediabetes: 2014 meta-analysis found
Increased risk of:
- Liver (highest)
- Endometrial
- Stomach
- Colorectal
- Pancreas
- Breast

Not associated with:
- Bronchus/Lung
- Prostate
- Ovarian
- Kidney
- Bladder


Type 1 Diabetes

Increased risk
- Pancreatic
- Liver
- Esophageal
- Colon

Increase mortality
- non-Hodgkin's Lymphoma

Type 1 Diabetes

Increased risk women
- Rectal
- Stomach
- Thyroid
- Brain
- Lungs
- Endometrial
- Ovarian

Increased risk men
- Kidney

Type 2 Diabetes

Increased risk
- Liver
- Pancreas
- Breast
- Colorectal
- Endometrial
- Gallbladder

Increased Mortality
- Liver
- Pancreas

Did you know?
Women with diabetes have a 6% greater risk to developing cancer?
**Evaluation of glucose control**

Hgb A1c
- Limited to those with a normal hematological profile.
- Is the patient anemic?
- Do they have a condition that will increase or decrease cell turnover?
  - Increased cell turn over will lead to artificially high levels
  - Decreased cell turn over will lead to artificially low levels
- Assess to see if they have received PRBC’s in the past 90 day
  - Results with be artificially low if transfused.
- Frequent transfusions in Leukemia and Lymphoma patients.

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**Evaluation of glycemic control**

Fructosamine
- Unaffected by RBC lifespan
- Protein dependent
- Monitor protein status
- Artificially elevated
  - Hypothyroidism or with cirrhosis
  - Artificially lowered
  - Liver failure, low serum albumin level, nephrotic syndrome, hyperthyroidism, high triglyceride levels, nonalcoholic fatty liver disease

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**Evaluation of glycemic control**

Finger stick blood glucose monitoring
- ISO 15197:2013 requires 95% of test fall within +/-15 mg/dl for glucose less than 100 mg/dl and 15% for glucose readings over 100 mg/dl
- There is no systematic post market Surveillance Program for BGMS once cleared by the FDA.
- No studies have been conducted to see if chemotherapy affects readings
- New Surveillance Program is “intended to protect people with diabetes from inaccurate, poorly performing BGMS products” it will provide an “independent assessment of the analytical performance of BGMS following clearance from the FDA as well as to generate information that can assist people with diabetes, health care providers, and payers in making educated selection of BGMS”.

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Wright, L, et al, Metrics Beyond Hemoglobin A1c in Diabetes Management: Time in Range, Hypoglycemia, and other Parameters
Diabetes Technology & Therapeutics 2017 19 (2) E18-26

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Journal of Diabetes Science and Technology 2016 10 (3) 697-707
Imaging

- PET Scans
  - No long acting insulin for 6 hours before testing
  - No short acting insulin for 4 hours before testing
  - Glucose must be under 200 mg/dl.
- MRI, CT and X-Ray
  - Must remove pumps and sensors
  - Per manufacturer recommendations
  - Please teach when doing training.
  - We had a patient from a Southern State that wore her pump into a MRI.

Treatment Options

Chemotherapy
Immunotherapy
Stem Cell Transplant
Radiation
Surgery
CART

Often there will be a combination of the above therapies
Chemotherapy

Neoadjuvant therapy: used to shrink tumors before surgery or radiation
Adjuvant: used to make sure all cancer cells have been eliminated after other treatments have been performed

Best practice is to review the complete individual treatment plan

There are many different and complex treatment options both with and without steroids.

"Steroids won’t affect your glucose...much"

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**Half-Life of frequently used steroids**

<table>
<thead>
<tr>
<th>Steroid</th>
<th>Half-Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>8-12 hours</td>
</tr>
<tr>
<td>Prednisone</td>
<td>16-22 hours</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>18-36 hours</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>36-54 hours</td>
</tr>
</tbody>
</table>

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**How steroids affect the glucose levels**

[Diagram showing how steroids affect glucose levels]
Chemotherapy Regimens

R-CHOP
• Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone.
  • Prednisone 100-120 mg on days 1-5 of each cycle.

R-EPOCH
• Rituximab, etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin.
  • Prednisone 100-120 mg on days 1-5 of each cycle.

Hyper CVAD
• Cyclophosphamide, Vincristine, Adriamycin and dexamethasone.
  • Dexamethasone on days 1-4 and 11-14 on odd cycles
  • Rituximab weekly 21 day cycle
  • Dexamethasone 10 mg on days 1, 8, 15 and 21

Chemotherapy Regimens- Just a few more

• BR OP: PACLitaxel Weekly
  • Dexamethasone 10 mg each week

• GI Colon OP: irinotecan, 5-Fluorouracil, Leucovorin (Modified FOLFIIRI) [18 cycles]
  • Dexamethasone 10 mg day 1 of each 14 day cycle

• LEU OP/IP 'TI' with Hyper CVAD Regimen - Maintenance/Intensification
  • Prednisone 100 mg on days 1-5 of each cycle.

• LEU OP/IP - REduced Dose' Cyclophosphamide, DOrxorubicin, Vincristine and PredniSomE
  • Rituximab (MINI R-CHOP)
  • Prednisone 80 mg on days 1-5

• Palbociclib and Fulvestrant
  • No steroids

Phases of Clinical Trials

Animal and/or laboratory studies
Phase I (First use on human subjects)
• 15-30 patients

Phase II
• Fewer than 100 patients

Phase III
• 100-1000 patients

FDA Approval
Phase IV - after approval.
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**Examples of clinical trials**

2015-0069 Lenalidomide and OBINutuzumab with CHOP - 21 Day Cycle
• Methylprednisolone 80 mg on days 1, 8, 15 of each cycle

2015-0488 Enzalutamide and Weekly PACLitaxel - 7 Day Cycle
• Dexamethasone 4 mg on days 1 of each cycle

• MD Anderson conducts hundreds of studies

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**Immunotherapy**

• Immunotherapy works by stimulating the body’s own immune system to fight cancer cells.
  The cells can work too well causing autoimmune diseases
  • Encephalitis
  • Hormone gland problems
  • Thyroid, pituitary, adrenal and pancreas
  • Colitis
  • Pneumonitis
  • Hepatitis
  • Kidney failure and nephritis

Can cause Type 1 Diabetes with presentation of DKA at any time after the first dose is given.
• Check C-peptide with concurrent glucose; GAD-65 & Insulin autoantibodies
Immune checkpoint inhibitors

PDL-1 inhibitors
- Programmed Death-Ligand 1
  - Atezolizumab (Tecentriq)
  - Avelumab (Bavencio)
  - Durvalumab (Imfinzi)

PD-1 inhibitors
- Programmed Death Protein 1
  - Pembrolizumab (Keytruda)
  - Nivolumab (Opdivo)
  - Cemiplimab (Libtayo)

CTLA-4
- Cytotoxic T-Lymphocyte-associated protein 4
  - Ipilimumab

P13K-AKT-mTOR inhibitors
Associated with 13-50% incidence of hyperglycemia/new onset diabetes
- Everolimus/Afinitor
- Temsirolimus/Torisel
- Sirolimus/Rapamune

Stem Cell Transplant
- **Autologous**: Cells are collected from the patient’s own bone marrow
  - Little to no risk of rejection or GVHD (Graft Vs Host Disease)
- **Allogenic**: Cells are collected from a donor
  - Haploidentical (related usually 1st degree relative)
  - Matched unrelated donor
  - Increased risk of rejection or GVHD
### Pretreatment course can be complex

- Example: BEAM with Rituximab
  - Day -6 Dexamethasone
  - Day -5 Hydrocortisone
  - Day -4 Hydrocortisone
  - Day -3 Hydrocortisone
  - Day -2 Hydrocortisone
  - Day 0 Hydrocortisone 100 mg 30 minutes prior to transplant.

### Post-Transplant

- Decreased appetite and taste changes around day 4-5 post-transplant.
- Complications:
  - Increased bleeding
  - Anemia
  - Fatigue
  - Mouth sores
  - Acute Graft Vs Host Disease
    - Can occur anywhere in the body.
    - Most frequently GI, Skin and Liver
    - Often will start on high dose steroids 2 mg/kg
  - Chronic Graft Vs Host Disease
    - Can occur anywhere in the body.

### Radiation Therapy

- Used to decrease or destroy cancer cells
- Simulation used first
- Often requires multiple treatments
- Used alone or in combination with surgery and/or chemotherapy
Surgery

- Preventive - used to keep cancer from occurring (aka prophylactic surgery)
- Staging - determines the extent of the cancer
- Curative - removal of all of a cancer
- Palliative - improves quality of life; not a cure
  - Steroids are often given intraoperatively
  - Pasireotide given with pancreatic surgery

Chimeric Antigen Receptor T-Cell

CART

White blood cells (including T-Cells) are gathered through apheresis.

In the lab, the T-cells are separated and new DNA is introduced into the cell with a virus.

The new DNA causes a change to the receptors on the surface of the cell; they are now CAR T-cells.

The modified cells are allowed to multiply until there are millions of cells.

The modified cells are then infused back into the body.

The CART-cell receptors are attracted to the targets on the surface of cancer cells and kill the cancer cells.