Care Step Pathway - Type 1 Diabetes Mellitus (immune destruction of beta cells in pancreas)

Nursing Assessment

Look:
- Does the patient appear fatigued?
- Does the patient appear dehydrated?
- Does the breath have a sweet/fruity smell?
- Is the patient tachycardic?

Listen:
- Frequent urination?
- Increased thirst?
- Increased hunger?
- Increased fatigue?
- Confusion, altered level of consciousness with advanced cases

Recognize:
- Symptoms of diabetes
- Serum glucose levels
- Other immune-related toxicity (and any corticosteroids given)
- Infections

Grading Toxicity

Mild hyperglycemia
New-onset hyperglycemia glucose >ULN –200 mg OR history of type 2 DM with low suspicion of DKA

Moderate or worse hyperglycemia (Likely New-onset Type 1 Diabetes); No DKA
New onset fasting glucose >200 mg/dL or random blood glucose >250 mg/dL OR history of type 2 DM with fasting/random glucose >250 mg/dL; DKA workup negative

Moderate or worse hyperglycemia (Likely New Onset Type 1 Diabetes); DKA
New onset fasting glucose >200 mg/dL or random blood glucose >250 mg/dL OR history of type 2 DM with fasting/random glucose >250 mg/dL; DKA workup positive

Management

Overall Strategy
- Evaluate for symptoms of DKA in patients with new onset fasting glucose >200 mg/dL or random blood glucose >250 mg/dL OR history of type 2 DM with fasting/random glucose >250 mg/dL: excessive thirst, frequent urination, general weakness, vomiting, confusion, abdominal pain, dry skin, dry mouth, increased heart rate, and fruity odor on the breath
- If DKA is suspected, evaluate per institutional guidelines, including blood pH, basic metabolic panel, urine or serum ketones/anion gap positive. Consider C-peptide if urine or serum ketones/anion gap is positive
- If Type 1 DM is suspected, also consider anti-GAD, anti-islet cell antibodies
- High-dose corticosteroid* use for other immune-related adverse events may induce or exacerbate hyperglycemia; if corticosteroid-induced hyperglycemia is suspected, evaluate benefit: risk ratio of tapering corticosteroid for glucose control vs management of the immune-related adverse event

Mild hyperglycemia
- Continue pembrolizumab, nivolumab, or ipilimumab
- Monitor serial blood glucose at each dose
- Institute diet/lifestyle modification
- If necessary, provide antidiabetes medication per institutional protocol
- Consider endocrine consultation if patient is symptomatic/hyperglycemia cannot be controlled

Moderate or worse hyperglycemia (Likely New-Onset Type 1 Diabetes); No DKA
- Continue pembrolizumab, nivolumab, or ipilimumab
- Consider endocrinology management for Type 1 DM
- Monitor serial blood glucose at each dose
- Institute diet/lifestyle modification
- Provide antidiabetes medication per institutional protocol

Moderate or worse hyperglycemia (Likely New Onset Type 1 Diabetes); DKA
- Hold pembrolizumab, nivolumab, or ipilimumab
- Obtain endocrinology consultation
- Provide inpatient care
- Insulin to be provided as directed by inpatient team and/or endocrinologist
- DKA to be managed per institutional guidelines (e.g., intravenous fluids, potassium supplementation, intravenous insulin, hourly glucose, serum ketones, blood pH, and anion gap)
- Consider resuming immune checkpoint inhibitor therapy once DKA has been corrected and glucose level has been stabilized

Implementation:
- For patients with new-onset Type 1 diabetes, discuss that it will most likely be permanent
- Review signs and symptoms of hyper/hypoglycemia
- Follow patients closely with checks on blood glucose levels, signs of DKA (fruity breath, confusion, nausea, etc), and other symptoms (e.g., increased infections)
- Provide insulin education (or refer)
- Discuss possibility of other immune-related AEs, including others of endocrine origin
- Discuss dietary modification

*Administering Corticosteroids:

<u>Steroid taper instructions/calendar as a guide but not an absolute</u>
- Taper should consider patient's current symptom profile
- Close follow-up in person or by phone, based on individual need & symptomatology
- Steroids cause indigestion; provide antacid therapy daily as gastric ulcer prevention while on steroids (e.g., proton pump inhibitor or H2 blocker if prednisone dosage is >20 mg/day)
- Review steroid medication side effects: mood changes (angry, reactive, hyperaware, euphoric, manic), increased appetite, interrupted sleep, oral thrush, fluid retention
- Be alert to recurring symptoms as steroids taper down & report them (taper may need to be adjusted)

<u>Long-term high-dose steroids</u>:
- Consider antimicrobial prophylaxis (sulfamethoxazole/trimethoprim double dose M/W/F; single dose if used daily) or alternative if sulfa-allergic (e.g., atovaquone [Mepron®] 1500 mg po daily)
- Consider additional antiviral and antifungal coverage
- Avoid alcohol/acetaminophen or other hepatoxins
- If extended steroid use, risk for osteoporosis; initiate calcium and vitamin D supplements

DKA = diabetic ketoacidosis; DM = diabetes mellitus; GAD = glutamic acid decarboxylase; po = by mouth; ULN = upper limit of normal