Outpatient Glycemic Control Algorithm for Adults with Type 2 Diabetes

Healthy eating, weight control, increased physical activity, education

(1) Initial Drug therapy: Metformin

- Efficacy ($\downarrow$ HbA$_{1c}$): ...
- Hypoglycemia...
- Weight...
- Side effects...
- Costs...

(2) If HbA$_{1c}$ target not reached after 3 mo. proceed to two-drug combination:

<table>
<thead>
<tr>
<th>Metformin +</th>
<th>Metformin +</th>
<th>Metformin +</th>
<th>Metformin +</th>
<th>Metformin +</th>
<th>Metformin +</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylureas: Glipizide or glyburide</td>
<td>DPP4i: Sitagliptin or Linagliptin</td>
<td>SGLT2 inhibitor: Dapagliflozin</td>
<td>GLP1-RA: exenatide or liraglutide</td>
<td>Basal insulin: detemir or glargine</td>
<td></td>
</tr>
<tr>
<td>...High</td>
<td>...Intermediate</td>
<td>...Intermediate</td>
<td>...High</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...Moderate risk</td>
<td>...Low risk</td>
<td>...Low risk</td>
<td>...Highest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...Low risk</td>
<td>...Neutral</td>
<td>...Neutral</td>
<td>...High</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...Gain</td>
<td>...Rare</td>
<td>...Rare</td>
<td>...Gain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...Edema, HF, Fx</td>
<td>...High</td>
<td>...Loss</td>
<td>...Gain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...Low</td>
<td>...High</td>
<td>...GU, dehydration</td>
<td>...Hypoglycemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>...Low</td>
<td>...Neutral</td>
<td>...High</td>
<td>...Variable</td>
<td></td>
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</tr>
</tbody>
</table>

(3) If HbA$_{1c}$ target not reached after 3 mo. proceed to three-drug combination:

| Metformin + SU + TZD or DPP4i or SGLT2i or GLP1-RA or Insulin | Metformin + TZD + SU or DPP4i or SGLT2i or GLP1-RA or Insulin | Metformin + DPP4i + SU or TZD or SGLT2i or GLP1-RA or Insulin | Metformin + SGLT2i + SU or TZD or DPP4i or Insulin | Metformin + GLP1-RA + SU or TZD or Insulin | Metformin + Insulin + TZD or DPP4i or SGLT2i or GLP1-RA |

(4) If combination therapy that includes basal insulin did not achieve HbA$_{1c}$ target after 3-6 mo., proceed to a more complex insulin strategy usually in combination with one or two non-insulin agents:

Combination Injectable therapy

Key:
- GI: gastrointestinal
- TZD: thiazolidinedione
- DPP4i: dipeptidyl peptidase 4 inhibitors
- SGLT2i: sodium-glucose cotransporter 2 inhibitors
- GLP1-RA: glucagon-like peptide 1 receptor agonist
- SU: sulfonylureas
- HF: heart failure
- Fx: bone fractures
- GU: genitourinary infections

Reference: Diabetes Care January 2015 vol. 38 no. 1: 140-149

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Criteria for Use:
Choice of agent must also take into consideration efficacy, side effects, and cost.

(1) Initial Drug Therapy:
Metformin is preferred initial drug therapy

Avoid use: metabolic acidosis, SCr >1.5mg/dl (men) or 1.4 mg/dl (women), or abnormal CrCl from any cause (i.e. shock, myocardial infarction, septicemia)

Consider alternative monotherapy agent for patients unable to tolerate or with contraindications (CI) to metformin:
- SU: avoid use in diabetic ketoacidosis
- TZD: consider use in patients unable to tolerate or with CI to SU; avoid use in NYHA Class III/IV heart failure
- DPP4i – consider use in patients unable to tolerate or with CI to TZD; avoid use in patients with serious hypersensitivity reaction
- GLP1-RA – consider use in patients unable to tolerate or with CI to above agents; avoid use in patients with personal or family history of medullary thyroid carcinoma or with Multiple Endocrine Neoplasia syndrome type 2

(2) Two-drug Combination Therapy
Consider starting with combination therapy when HbA1c ≥ 9%

- Metformin plus [SU, TZD or DPP4i] should be considered for initial oral combination therapy
- SGLT2i: consider use in patients unable to tolerate or with CI to metformin plus [SU, TZD, or DPP4i]
  
  Avoid use: estimated GFR < 60mL/min/1.72m², dialysis, active bladder cancer
- GLP1-RA: consider use in patients unable to tolerate or with CI to oral combination therapy
- Basal insulin: consider use in patients unlikely to achieve HbA1c target on oral combination therapy

(3) Three-drug Combination Therapy – choice of therapy should be made in stepwise approach listed above

(4) Combination Injectable Therapy – consider starting at this step when HbA1c ≥ 10-12%

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