Obesity and Incretin Therapeutics

shm EDUCATION
Rapid Clinical Updates

Obesity Medicine Essentials for the Hospitalist

Practice Gap

Context: Obesity is a chronic metabolic disease with complex pathophysiology

Current: Avoid thinking about obesity as a disorder of excessive intake and under-activity

There are many etiologies of weight gain, including medications, stress, and sleep disorders.

Guidelines recommend using weight-neutral medications when possible.

Cost and coverage are barriers to initiation and continuation of incretin therapies. There are several FDA-approved and off-label affordable options for weight loss.

Medication class	Proposed weight gain mechanism	Alternatives
Antihistamines	Increased appetite	Leukotriene inhibitors, Loratadine, Flonase
Atypical antipsychotics	Increased appetite and binge eating	Ziprasidone, Aripiprazole
Beta-blockers (esp selective β1)	Reduced REE & thermogenesis; Fatigue; Reduced exercise tolerance; Increased insulin resistance	ACE inhibitors, ARBs, CCBs
Corticosteroids	Impaired glucose tolerance; Increased truncal fat	NSAIDs (if appropriate)
Insulin	Anabolic effects; Increased appetite; Fluid retention	Biguanides, GLP-1 receptor agonists, GLP-1/GIP dual agonist, SGLT2 inhibitors
SSRIs	Increased appetite; Increased food cravings	Bupropion
Sulfonylureas	Anabolic effects; Increased appetite; Fluid retention	Same as insulin
TCAs	Increased appetite	Bupropion
TZDs	Increased adipogenesis; Fluid retention; Increased appetite	Same as insulin
Antiepileptics	Increased appetite; Insulin resistance; Fluid retention	Felbamate, topiramate, zonisamide

Cutting Edge: Be aware of lipedema, an adipose tissue disorder commonly misdiagnosed as lymphedema or obesity.

Weight loss with certain incretin therapies is approaching and that seen with metabolic surgery

GLP-1 has a myriad of effects in the body other than in gastric emptying, and studies are underway

GLP-1 and Cardiometabolic Disease

Context: GLP-1RAs should be prescribed to reduce CV death irrespective of A1C[1,2]

Current: Diabetes is considered a major CV risk factor, not just A1C reduction. GLP-1 used to reduce cardiovascular risk in those with obesity and without T2DM

Cutting Edge: Well-designed RCT now show GLP-1 and GLP-1/GIP inhibitors are now demonstrating cardiovascular risk reduction in those with CKD, MASH/MASLD, HFpEF, OSA, and CKD due to T2DM

There are multiple benefits of GLP-1 in metabolic disease beyond T2DM/glucose lowering and weight loss

Upcoming large RCT pending for HFrEF, MASH and cirrhosis

Peri-procedure Considerations

Current: Risks of aspiration are not known, studies are showing retained gastric contents > 7d but no increased rates of aspiration

Current: Use shared decision making: If no symptoms unclear, benefit if stopping for just 1 half-life → more studies pending[2]

If a recent dose increase or symptoms→ may need to reduce

Solids: longer fasting times, use liquid diet 24h prior; rapid sequence intubation (full stomach precautions) for urgent procedures

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References:

1. ElSayed N et al. *Diabetes Care* 1 January 2023; 46 (Supplement_1): S140–S157.
2. Michos E et al. J Am Heart Assoc. 2023 Jun 6;12(11):e029282
3. Kindel TL, et al. Surg Obes Relat Dis. 2024