DRUGS AFFECTING BODY WEIGHT AND FAT DISTRIBUTION

Drug class	Examples	Average weight gain (per year)	Notes
WEIGHT GAIN EFFECT			
Antidiabetics			
Insulin	insulin aspart, insulin lispro, insulin regular		More pronounced in rapid-acting regimens
Sulfonylureas	glimepiride, glipizide, glyburide	~4kg	More pronounced in the 1st months, then reaches a plateau
Thiazolidinediones	pioglitazone, rosiglitazone	1.5–4kg	
Antihypertensives			
Beta-blockers	atenolol, metoprolol, propranolol	~1.2kg	• Ranges from no significant change to an increase of ≥4kg among the class • More pronounced in the 1st few months, then no further weight gain • Select vasodilating beta-blockers (eg, nebivolol, labetalol, carvedilol) in patients with high risk for metabolic effects
Psychotropics[1]			
Anticonvulsants	lamotrigine, levetiracetam, tiagabine, oxcarbazepine	<1kg	• Most prominent with valproate and carbamazepine • Valproate induces weight gain in 71% of patients, with most weight gain observed within 1st year. Females, post-puberal adolescents, and those overweight at baseline are the most susceptible. Weight gain is not dose- or serum level-related. • Carbamazepine induces weight gain in 43% of patients
	gabapentin, pregabalin	1–5kg	
	valproate, carbamazepine	>5kg	
Antipsychotics (atypical)[2,3]	aripiprazole, ziprasidone, lurasidone, paliperidone, iloperidone, asenapine	<1kg	• More pronounced in patients with normal baseline body weight and in females • More significant weight gain in drug-naïve patients vs previously exposed (more in children vs adults) • Weight gain from long-term treatment is time- and dose-dependent
	quetiapine, risperidone	1–5kg	
	clozapine, olanzapine	>5kg	
Antipsychotics (typical)[2]	haloperidol, perphenazine	1–5kg	
MAOIs	phenelzine	1–5kg	
Mood stabilizers	lithium	>5kg	• Significant weight gain (>5% of initial body weight) occurs in as high as 60% of patients • Risk factors: females, high baseline weight, younger age, concomitant antidepressants
SNRIs	duloxetine, venlafaxine	<1kg	Weight gain with chronic therapy
SSRIs	escitalopram	<1kg	• Weight gain with chronic therapy • Greatest long-term weight gain with paroxetine
	paroxetine, citalopram, fluoxetine, sertraline	1–5kg	
Tricyclic antidepressants (TCAs)	amitriptyline, nortriptyline, imipramine, desipramine, doxepine, clomipramine	1–5kg	Greatest with amitriptyline and nortriptyline
Other antidepressants	trazodone, nefazodone	<1kg	
	mirtazapine, maprotiline	1–5kg	
WEIGHT GAIN AND LIPODYSTROPHY EFFECT			
Antiretrovirals[4]			
Integrase inhibitors	raltegravir, dolutegravir		• Associated with lipohypertrophy (central/truncal fat accumulation) or weight gain • A switch from NRTI, NNRTI or PIs to integrase inhibitors may cause even greater weight gain
NRTIs	didanosine, lamivudine, stavudine, zidovudine		• Lipoatrophy (loss of subcutaneous fat) greatest with NRTIs stavudine and zidovudine • Lipoatrophy risk factors: males, older age, lower baseline weight, lower CD4 count, higher baseline viral load, hepatitis C co-infection • Lipohypertrophy is not antiretroviral-specific; does not reverse on switching antiretrovirals • Lipohypertrophy risk factors: females, older age, baseline weight, diet, longer treatment duration • PIs are more associated with lipo-accumulation and metabolic effects • Older PIs (eg, indinavir, lopinavir, ritonavir) are associated with threefold increase in diabetes risk • A switch from NRTI and NNRTI to PIs showed no changes in weight
NNRTIs	delavirdine, efavirenz, etrivirine, nevirapine, rilpivirine		
Protease inhibitors (PIs)	amprenavir, atazanavir, darunavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir, tipranavir, fosamprenavir		
Glucocorticoids			
Corticosteroids (oral and IV)	prednisone, dexamethasone, methylprednisolone	>10kg in ~20% of patients	• Weight gain significantly increases with doses >5mg/day prednisone or equivalent • Inhaled corticosteroids and single epidural steroid inj do not affect body weight • Lipodystrophy greater in females, younger patients, and higher baseline BMI
Hypolipidemics			
Anti-sense apo-B oligonucleotide	mipomersen		Associated with approx. 4 times higher risk for hepatic steatosis[5]
Microsomal triglyceride transfer protein (MTP) inhibitor	lomitapide		Induces intrahepatic fat accumulation with up to six-fold increase in hepatic fat content and more severe increase in transaminases

NOTES

Key: **BMI** = body mass index; **MAOIs** = monoamine oxidase inhibitors; **NRTIs** = nucleoside/nucleotide reverse transcriptase inhibitors; **NNRTIs** = non-nucleoside reverse transcriptase inhibitors; **SNRI** = serotonin and norepinephrine reuptake inhibitors; **SSRI** = selective serotonin reuptake inhibitors

[1] Monitor weight before and shortly after initiation of psychotropic drugs. Reconsider therapeutic options or initiate weight-controlling strategies if a 5% increase above baseline weight occurs after the first month of treatment.

[2] Up to 80% of patients on antipsychotics experience weight gain that exceeds their ideal body weight by ≥20%.

[3] The American Diabetes Association and American Psychiatric Association (ADA/APA) Consensus Development Conference recommends close monitoring of weight and metabolic and cardiovascular risk factors in all patients taking atypical antipsychotics. Switch to other antipsychotic with less potential for weight and cardiometabolic effects if >5% weight gain or worsening of lipid or glycemia parameters.

[4] Patients on HAART have greater cardiometabolic risk due to weight gain compared to non-HIV patients. Monitor changes in body composition using BMI, waist circumference, waist-to-hip ratio, and screen regularly for clinical lipodystrophy in all HIV patients at diagnosis, prior to HAART initiation, and annually thereafter.

[5] Not associated with increased inflammation or fibrosis unlike in NAFLD.

REFERENCES

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