

Supplementary Table 1. Some Medications Associated with Constipation

Class	Examples
5-HT ₃ -receptor antagonists	ondansetron
Analgesics	
Opiates ¹	morphine
Nonsteroidal anti-inflammatory agents [†]	ibuprofen
Anticholinergic agents	librax, belladonna
Tricyclic antidepressants ¹	amitriptyline > nortriptyline
Antiparkinsonian drugs	benzotropine
Antipsychotics	chlorpromazine
Antispasmodics ¹	dicyclomine
Antihistamines ¹	diphenhydramine
Anticonvulsants ¹	carbamazepine
Antihypertensives	
Calcium channel blockers	verapamil, nifedipine
Diuretics ^{1,2}	furosemide
Centrally acting	clonidine
Antiarrhythmics	amiodarone
Beta-adrenoceptor antagonist	atenolol
Bile acid sequestrants	cholestyramine, colestipol
Cation-containing agents	
Aluminum ¹	antacids, sucralfate
Calcium	antacids, supplements
Bismuth	
Iron supplements	ferrous sulfate
Lithium	
Chemotherapy agents	
Vinca alkaloids	vincristine
Alkylating agents	cyclophosphamide
Miscellaneous compounds	barium sulfate, oral contraceptives, polystyrene resins
Endocrine medications	pamidronate and alendronic acid
Other antidepressants	monoamine oxidase inhibitors
Other antipsychotics	clozapine, haloperidol, risperidone
Other antiparkinsonian drugs	dopamine agonists
Other antispasmodics	mebeverine, peppermint oil
Sympathomimetics	ephedrine, terbutaline

¹ Drugs associated with constipation in community-based studies ^{1,2}

² Perhaps related to electrolyte disturbances

5-HT, 5-hydroxytryptamine

Supplementary Table 2. Medical Conditions Associated With Constipation

Drug effects

See Supplementary Table 1

Mechanical obstruction

Colon cancer
External compression from malignant lesion
Strictures: diverticular or postischemic
Rectocele (some)

Metabolic conditions

Diabetes mellitus
Hypothyroidism (severe)
Hypercalcemia(severe)
Hypokalemia
Hypomagnesemia

Heavy metal poisoning

Myopathies

Amyloidosis
Scleroderma

Neuropathies

Parkinson's disease
Spinal cord injury or tumor
Cerebrovascular disease
Multiple sclerosis

Other Conditions

Depression
Autonomic neuropathy
Cognitive impairment
Immobility

Conditions that are frequently encountered in clinical practice and associated with constipation are identified in italics.

Adapted from *Gastroenterology*,³ with permission.

Supplementary Table 3. Treatments for Opioid-Induced Constipation

Drug	Receptor antagonism			Permeable to blood brain barrier	Dose	NNT (95% CI)	Wholesale cost/month*
	M	K	δ				
Methyl-naltrexone	+++	++	++	No	12 mg EOD (oral); 8-12 mg QOD (SC)	3.4 (3 – 6) ¹²¹	\$1807.35
Naloxegol	+++	-	-	No	25 mg QD	7 (4 - 26) ¹²¹	\$ 324.30
Naldemedine	+++	-	-	No	0.2 mg QD	5 (4 – 8) ¹²¹	\$ 280.50
Lubiprostone	NA	NA	NA	NA	24 mcg bid	15 (9 - 51) ¹²¹	\$ 445.32

*Courtesy of Dr Michael Hirsch, Department of Pharmacy, University of Wisconsin Hospitals, Madison.

References:

1. Talley NJ, Fleming KC, Evans JM, et al. Constipation in an elderly community: a study of prevalence and potential risk factors. *Am J Gastroenterol.* 1996;91:19-25.
2. Talley NJ, Jones M, Nuyts G, et al. Risk factors for chronic constipation based on a general practice sample. *Am J Gastroenterol.* 2003;98:1107-1111.
3. Locke GR III, Pemberton JH, Phillips SF. AGA Technical Review on Constipation. *Gastroenterology.* 2000;119(6):1766-1778.