

Tofacitinib

Janus kinas inhibitor PO

2x/day reduced to 1x if
Potent CYP3A4 and CYP2c19 inhibitors (e.g. fluconazole)

Severe renal impairment

Mod liver impairment

Combined w/methotrexate or nonbio DMARD

DO NOT combine w/bio DMARD

Other DMARDs in Refractory RA

Azathioprine, Cyclophosphamide, Cyclosporine, Penicillamine

Last-line therapy in refractory disease

use is limited by higher rates of adverse effects

Anaesthetics SE

CNS effects

Reduction of vascular resistance

Increased intracranial pressure

Decrease BP

Entorane and Halothane decrease CO

Decreased blood flow to liver and kidneys

Decrease respiratory rate

Malignant hyperthermia (uncontrolled Ca release)

Treated with dantrolene

Local Anesthetics

Intermediate chain linking amino to aromatic ring

block Na⁺ channels in nerve

sympathetic → sharp/dull → touch/temp → motor paralysis

More effect on small C fibers and small A fibers

Amino Esters Surface: Benzocaine, cocaine

Short: Procaine

Long: Tetracaine

Amino Acids Medium: Lidocaine

Long: Bupivacaine, ropivacaine

Lidocaine Patch 12hr on/12 off

3 patch max

Lipid Lowering Drugs

HMG-CoA reductase inhibitors E.g. Atorvastatin, Rosuvastatin, red rice yeast

Primary agents

↓ LDL and TG, ↑ HDL, ↓ morbidity/mortality

antithrombotic effects, ↓ endothelial inflammation

SE: myopathy and hepatotox, elevated LFTs, CPK (muscle/jt pain, rhabdo), proximal muscle weakness

CYP450 (grapefruit, Cimetidine)

Memory loss, diabetes

Bile acid sequestrants (resins) E.g. Cholestyramine; ↓ LDL, ↑ HDL and TG; Unpleasant taste, GI effects, intxns; Other meds 1 hr before or 4 hr after

Fibrates E.g. Gemfibrozil, fenofibrate

↓ LDL and TG, ↑ HDL

Toxicity additive w/statins

Rhabdo, myopathy, LDL increase

Nicotinic Acid ↓ LDL and TG, ↑ HDL

Flushing, itching, HA, Hyperuricemia in gout, Hyperglycemia, Hepatotox

Chol absorption inhibitor E.g. Ezetimibe

Lipid Lowering Drugs (cont)

Decrease LDL, increase HDL

HA Diarrhea Upper resp infection

hepatotox + rhabdo with statins

Anti-Factor Xa Inhibitors

Fondaparinux SC treat/prevent DVT/PE

Avoid use in Crcl <30 ml/min

Monitor: Anti-Xa, sx of bleeding

Apixaban Inhibit factor X

adjust in Afib if 2/3 >80 yo, Scr >1.5, weight <60kg

Intxns: phenytoin, carbamazepine, fluconazole, rifampin

bleeding, compliance

Rivaroxaban inhibit factor X

Take w/evening meal

Intxns: phenytoin, carbamazepine, fluconazole, rifampin

Reversal of anticoagulation

Warfarin Vitamin K

Keparin Protamine

Enoxaparin Protamine (less reliable)

Dabigatran Idarucizumab

Apixaban zhzo Xa

Rivaroxaban zhzo Xa

Insulin

Lispro, Aspart Regular NPH Glargine, Detemir, Degludec (basal)

O:<15m O:.5-1 O:2-4 O:2-4

P:1-2 P:2-3 P:4-10 P:N/A

D: 3-4 D:3-6 D:10-16 D:24

Thiazolidinediones

E.g. Pioglitazone, Rosiglitazone (not used, ↑CVD)

↓HDL, triglycerides; neutral LDL

Decrease fasting plasma glucose 35-40

Reduce A1C ~0.5-1%

6 weeks for max effect

SE: weight ↑, edema, hypoglycemia

Contraindicated liver problems or CHF

GLP-1 Agonist

E.g. Exenatide, Liraglutide

↑ insulin release

↓A1C ~0.7

SE: GI upset, weight loss

Maybe pancreatitis, gallbladder disease, thyroid cancer

Caution in renal disease

CV benefit

Acetaminophen

central COX inhibitor

Analgesic & Antipyretic

NOT anti-inflammatory or antithrombotic

SE: Hepatotoxicity

1st line for OA

Avoid alcohol

No Raye's syndrome

Similar to NSAIDs, better tolerated

2 wks before considering treatment failure

Opioids

Act on Mu, Kappa, Delta receptors

Phenanthr (natural) Codeine, Morphine enes

Phenanthr (semisynthetic) Hydrocodone, enes Hydromorphone, Oxycodone

Phenylpip Fentanyl, Meperidine (chills) eridines

Phenyleth Methadone, Propoxyphene ylamines

Extended Oxycodone, Morphine, Fentanyl

Opioids (cont)

Tramadol Mu receptor agonist, inhibit serotonin and NE reuptake

Mild to moderate pain

SE: ↓resp depression than other opioids, sedation, constipation, dry mouth, nausea, serotonin tox

Morphine Controlled or immediate

SE: potential accumulation, itch

Not indicated in pts w/renal

Oxycodone High oral bioavailability w/no food effect

No significant metabolites

minimally affected by age renal or liver

Methadone alpha 8-12, beta 24-36

NMDA receptor antagonist/ Serotonergic properties

SE: Toxicity, QTc prolongation

Meperidine Causes euphoria, most addictive, seizures

Agonists Oxycodone, Codeine, Hydrocodone

Mixed Buprenorphine

Antagonists Naltrexone, Naloxone

SE: CNS/resp depression (5-7 days), N/V (codeine), constipation, itch/rash

Capsaicin Cream

Inhibits release of substance P in peripheral

Max effect takes 2-4 wks application 4x/day

More role in OA than RA

Viscosupplementation

E.g. hyaluronic acid

lubricant during low-stress mvmt, anti inflam

Has more role in OA than RA, esp knee

3-5 wkly injections = 1 cycle

Max effect 8-12 wks, lasts 6-12 mo

Non-Bio DMARDs

RA w/in 3 mo, max 6-12 mo

LF, HCQ, MTX need blood count, liver, Cr every 2-4wk/3mo then every 8-12 wks

Methot 1st line, 2-8 wk onset PO/IM rexate immunosuppressant

SE: GI, liver tox, bone marrow, stomatitis, hair loss, pulm tox

Folic acid decrease sx

Lefluno Immunosuppressant effective as mide MTX

SE: GI, rash, hair loss, liver tox

Work w/in 1 mo, weaker

Hydrox Low tox, 2-6 mo onset, min monitor ychloro- quine

SE: GI, retinal, derm, HA

Sulfasa 2-3x/day PO anti-inflam lazine

SE: GI, leukopenia, anemia, photosensitive, skin, hepatitis, pneumonitis, agranulocytosis, hypersensitivity

>HCQ, <DMARDs

poor tolerate, lots of monitoring

Potentiate anticoagulants

IV Anesthetics

Etomidate Hypnotic

Rapid onset gen anesthesia

Min cardiopulm SE

Good for CV and pulm comorbid

Propofol Short acting hypnotic

Very rapid recovery

Thiopental Respiratory depressant, no sodium analgesia

Rapid safe induction

Barbiturate

Midazolam Benzodiazepine

IV Anesthetics (cont)

Amnesia

Potentially long half-life

Ketamine Dissociative analgesia

Local Anesthetics Additives

Vasodilation prevented by vasoconstrictor (e.g. epinephrine); prolong effect/decrease dose -- do not use in fingers/toes

Bicarbonate Decrease burning sensation during admin

Statin Monitoring

CK Baseline: only in pts at increased risk for musc injury

Routine: only in pts w/musc pain/weakness

ALT Routine: only if symptoms of hepatotox occur

FLP Routine: 4-12 wks after initiation, then Q3-12 months as indicated

Hgb Baseline: only if diabetes status
A1c unknown

Anticoagulants

Heparin Unfractionated heparin (UFH); IV/SC

monitor aPTT, platelets, hgb, hct, HIT

Low-molecular-weight heparin Enoxaparin, SC

Renal adjust Crcl <30

monitor less frqnt, Anti-Xa levels not aPTT

Anti-Factor Xa inhibitor Fondaparinux, SC

Apixaban, PO

Rivaroxaban, PO

Direct Thrombin Inhibitors Argatroban, IV

Dabigatran, PO

Vitamin K antag Warfarin, PO

Anticoagulants (cont)

Onset: slow, anticoagulation occurs 48-72 h after the first dose once factors are depleted

Monitor INR (goal 2-3), Hgb/hct, bleeding

Intxn: Food: green leafy vegetables Meds: cipro, bactrim, flagyl, fluconazole, rifampin

Preferred in renal dysfunction

Direct Thrombin Inhibitors

Do not require antithrombin

Monitor aPTT, platelets, hgb, het, bleeding

Continuous infusions

Used in HIT mgmt

Short duration

Argatroban Falsely elevate INR

No monitoring or reversal agent

ADE: upset stomach, bleed

Intxns: avoid rifampin

Store in original container and use within 30 days of opening

Anticoagulant Dosing

DVT pp: enoxaparin 40mg q24 or 30mg q12 or heparin 5k units bid-tid.

PE/DVT tx: Enoxaparin 1.5mg/kg q24 hrs and 1mg/kg q12 hrs; heparin drip 18 units/kg/hr

Biguanides

e.g. metformin

↓ glucose product, ↑ glucose uptake

↓ A1C 1-1.5

Low risk hypoglycemia

SE: Diarrhea/GI, ↓ B12, l. acidosis, weight ↓

Contraindicated GFR <30

Meglitinides

e.g. Repaglinide, Nateglinide

Stimulate insulin secretion

Shorter acting, best taken after eating

↓ A1C ~1

SE: Hypoglycemia, weight ↑

Safe w/greater renal insufficiency than SU

SGLT2 Inhibitors

E.g. Canagliflozin, Empagliflozin

↑ glucose excretion

↓ A1C 0.7-1

Empagliflozin: avoid if GFR <45

SE: Genital fungal infxn, UTI, AKI, dizzy, hypotension, hyperkalemia, hypoglycemia, fractures, ↓ BMD, CV benefits

Non-Opioid Analgesics

NSAIDs, Prostaglandin inhibitors
ASA, salicylates

Inhibit COX-1 and COX-2

GI side effects

ASA = antiplatelet primarily used to prevent heart disease and stroke

Thromboxanes involved in platelet aggregation and thrombus formation

Selective COX-2 inhibitor e.g. Celecoxib

↑ MI and stroke

Rofecoxib and Valdecoxib taken off market

Celecoxib ↓ GI SE in pt not on ASA

Do not cause tolerance, not addictive

All have ceiling effect to analgesia



Opioid Withdrawal

Body aches, weakness, fatigue
Diarrhea, stomach cramping
Insomnia
Irritability
Loss of appetite
Nausea/vomiting
Increased BP/HR
Runny nose, sneezing, yawning
Chilliness and "goose bumps"

Patient Controlled Analgesia

e.g. Morphine, hydromorphone
Monitor HR, BP, RR, Pain, usage, O2

Glucosamine/Chondroitin

Glucosamine cartilage building block
Chondroitin Increase protein synthesis
OTC, not 1st line, may improve OA knee pain
Weeks to months for effect
SE: GI upset

Corticosteroids

E.g. Dexamethasone, Hydrocortisone, Methylprednisolone
Intraarticular 1-6 wk relief for OA/RA knee
3-4/yr limit
Lidocaine sometimes added
Systemic RA, not OA
Acute SE: Hyperglycemia, HTN, euphoria/psychosis, weight↑/edema, GI bleed
Chronic SE: Cushing's appearance, cataracts, hyperlipidemia, muscle/tendon, OP/fractures, infection, HPA suppression

Bio DMARDs

Non-TNF Abatacept SE: Pulmonary infection, allergic rxn, HA/dizzy
Anakinra SE: inj site rxn, infection, allergic rxn

Bio DMARDs (cont)

Rituximab SE: rash, infection, neuro, infusion rxn, Tumor Lysis, multifocal leukoencephalopathy
TNF inhibitor Adalimumab: SC every 2 wk, mild-mod inject rxn
Etanercept: SC 1-2/wk, mild-mod inject rxn
Infliximab: IV at 0,2,6,8 wk; infusion rxn
Increased malignancy risk
SE: hypersensitivity, Lupus-like, hepatotox, pancytopenia, aplastic anemia, heart failure
MTX combo or solo
Mod-severe RA
Possibly reactivates TB, no live vaccine

NM Blocking Agents

Non-Depolarizing Competitive Ach antag
Pancuronium O: 4-6 min D: 120-180 min
Rocuronium O: 1-2 min D: 30-60 min
Depolarizing Overstimulate receptor
Succinylcholine O: 1-1.5 min D: 5-8 min

Anaesthetics Pharmacokinetics

highly lipid soluble
When discontinued, drugs will continue to enter systemic circulation
Lethargy, confusion

Lidocaine Patch

12 hr on/12 hr off
3 at a time max

monoclonal antibodies/PCSK9 inhibit

SC
Reduce LDL by additional 60% with statin
E.g. evolocumab, alirocumab
Advantages: injected once or twice/month
SE: common cold, itching, flu, injxn site rxns, allergic rxns

Antiplatelets

Aspirin
ADP receptor inhibitors e.g. Clopidogrel, Prasugrel, Ticagrelor
PO

Thrombolytics

Alteplase (IV)
Dissolve clots acutely/clear IV line
Relative contraindication: HTN
Absolute contraindication: recent head trauma
ADR: bleeding, hemorrhage
C

Heparin Induced Thrombocytopenia

Type 1 10-20%
Onset: 2-3 d
Platelet <50% decrease, nadir >100k
Type 2 1-3%
Onset: 5-10 d
Platelet >50% decrease, nadir 10-20k
Antibody mediated
Thromboembolic sequelae 30-80%
D/c all heparin products, initiate direct thrombin inhibitor/coumadin

ADP Receptor Inhibitors

Clopidogrel Indications: ASA + Clopidogrel in pts receiving stents
Prasugrel More potent, less variable platelet response than Clopidogrel

ADP Receptor Inhibitors (cont)

reduction of thrombotic CV events (including stent thrombosis) in pts w/ACS who are to be managed w/PCI

Risks may exceed benefits in pts w/ >75 yo Previous history of TIA or stroke <60kg

Likely to undergo CABG = bleed risk

Hold for 7 days before surgery

Ticagrelor SE: bleeding, dyspnea, bradycardia

2x/day

Avoid in pts w/hx of hemorrhagic stroke

Avoid aspirin >100 mg CYP 3a4 inducers (rifampin, carbamazepine, phenytoin) CYP 3A4 inhibitors (ketoconazole, ritonavir) Monitor digoxin levels

Sulfonylurea

e.g. Glyburide, Glimepiride, Glipizide

↑ endogenous insulin secretion

↓A1C 1-2

SE: hypoglycemia, ↑ weight, photosensitive

Least expensive

Caution in renal, elderly

Often discontinued once insulin started

DPP-4 inhibitors

e.g. Sitagliptin, Saxagliptin

↑ incretin, insulin release

↓A1C ~0.7

Well tolerated, no weight gain, no hypoglycemia

Maybe pancreatitis, jt pain, heart failure

Dose modification in renal impairment

CYP3a4 interactions

Other Antidiabetics

Alpha-glucosidase inhibitors e.g. Acarbose

block enzymes that digest starches in small intestine

GI upset, flatulence, bloating

Amylin analogs e.g. Pramlintide

Injectable

Bile acid sequestrants e.g. Colesevelam

GI side effects

NSAIDs

1st line in RA, 2nd in OA

Aspirin Most widely used, analgesic, antiinflammatory, antipyretic, antiplatelet

Diclofenac more potent than other NSAIDs, ADRs occur in 20%

Ibuprofen fever, GI side effects ~5-15%

Indomethacin Dose related side effects (i.e. confusion); 35-50% pts

Ketorolac Orally or IM, IV doses provide postoperative analgesia equivalent to opioids

not used >5 days due to ADR

Naproxen Similar to ibuprofen, less frequent dosing 2x/day

SE: GI, acute renal failure, BP, hypersensitivity

GI SE: Celecoxib < Diclofenac < Ibuprofen & Naproxen < ketorolac

Take ibuprofen at least 2 hours after ASA -- makes aspirin ineffective

GI ulcers/bleed prophylaxis: Misoprostol, Proton pump inhibitors (pantoprazole), H2RAs (ranitidine)

Use with caution on pt on anticoagulants

Need to take continuously for antiinflam

2-4 wk trial needed

