Welcome!

Initial Therapy:
Glucocorticoids and NSAIDs

March 28, 2022

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DISCLOSURES

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Disclosure Statement

Planners Jennifer Mandal, MD, Leslie Dexheimer Gleason, RN, and Tabitha Foraker, MPH have stated they have no relationships to disclose. Speaker Wendy Grant, MD has stated she has no relationships to disclose.

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NSAIDs: The Basics

NSAIDs - Key Points

- They are widely used in RA and are effective for treating inflammation and pain
- They do not reduce levels of acute phase reactants or prevent radiographic progression (ie, they are not DMARDs)
- All work by blocking production of prostaglandins via the cyclo-oxygenase enzyme
- COX-1: expressed under basal conditions
- COX-2: expressed during inflammation/stress

NSAIDs: The Basics

NSAIDs - Key Points

Most NSAIDs inhibit both COX-1 and COX-2, with variable relative potency for these targets

NSAIDs tend to accumulate in synovial fluid; anti-inflammatory effect may last longer than the ½ life suggests

Overall, their efficacy is about equal although individual responses may vary

Toxicities are largely related to COX-1 effects but also to bioavailabilty and T1/2

NSAIDs
The Basics

Major Structural Class	Subclass	Examples
Carboxylic Acids	Acetylated	ASA
	Acetic Acids	indomethacin, sulindac, diclofenac
	Propionic Acids	ibuprofen, naproxen
	Pyrollizine Derivatives	ketorolac
Enolic Acids	Oxicams	meloxicam
COX-2 Inhibitors		celecoxib

NSAIDs
The Basics

INHIBITION	Examples
COX-1 Specific	ASA (irreversibly binds/inhibits COX-1)
COX Nonselective	ibuprofen, naproxen, indomethacin
COX-2 Selective	meloxicam, diclofenac
COX-2 Highly Selective	celecoxib

NSAIDs
The Basics

NSAIDs: Complications

GI: dyspepsia, esophagitis, ulcers, erosions, strictures, colitis

Renal: Na retention, edema, HTN, ARF, RTA, AIN, accelerated CKD

CV: CHF, MI, stroke

Hepatic: transaminase elevations

CNS: confusion, seizures, aseptic meningitis

Allergic: ASA-exacerbated asthma; rash

Bone: delayed healing

NSAIDs
The Basics

NSAIDs: Mitigation Strategies

< 65 years, uncomplicated (no GI, renal or CV risk; no ASA or anticoag)

- traditional NSAID; short acting and lowest dose possible

> 65 years, intermediate risk

- Traditional NSAID + PPI or high dose H2 blocker
- If on ASA→ Celecoxib + PPI

NSAIDs
The Basics

NSAIDs: Mitigation Strategies

> 65 years, high risk
- intermittent, low-dose, short half-life if needed
- avoid chronic NSAIDs if possible
    if required:
        CV risk > GI risk: use naproxen + PPI
        GI risk > CV risk: use Celecoxib + PPI
- acetaminophen < 3 gm/day
- monitor blood pressure, renal function

NSAIDs
The Basics

NSAIDs in RA

- Avoid concomitant use with glucocorticoids
- MTX & NSAIDs: theoretically NSAIDs may increase MTX plasma concentrations. However, a 2012 Cochrane review concluded that NSAID + MTX was safe

Glucocorticoids: The Basics

GCs - Key Points

- both ACR and EULAR's guidelines advocate for using the lowest dose (10 mg or 7.5 mg) for the shortest time possible

- recommended to use with initiation of DMARD therapy with plan for taper off by 3 months (US) or 6 months (EU) and for flares

= clear data that GCs reduce disease activity in the short term

- medium and long term benefit? Some studies show decreased radiographic progression at 2 years in GC + MTX vs PBO + MTX

Glucocorticoids: The Basics

DURATION	GLUCOCORTICOID	POTENCY	MINERALOCORTICOID
Short Acting	Hydrocortisone	1	1
Intermediate Acting	Prednisone	4	0.25
	Prednisolone	4	0.25
	Methylprednisolone	5	+/-
Long Acting	Dexamethasone	40	+/-

Glucocorticoids: The Basics

GCs - RA

- Initial: 10 - 15mg QD, then taper to 5 mg while introducing DMARD therapy
- For flares:
  - Multiple options but if treating for 3-10 days, no need to taper
  - Consider IM methylpred at 80-120 mg; self-taper over 2 weeks
  - Unusual to require > 15 mg pred QD for a flare
- Chronic low-dose (5mg or less) used, rarely, as chronic therapy

Glucocorticoids: The Basics

Toxicities are generally related to dose and duration

Very low dose GC (3 mg/d) = no increased risk of toxicities at 7 years

- *Endocrine:* osteoporosis
- *Infectious:* any infection
- *GI*: gastritis/erosion/ulcers
- *Endo*: Risk of adrenal insufficiency at 3-5wks
- *Endo*: Risk of insulin resistance incr. at >10 pred/day
- *CV*: Fluid retention/hypertension; cardiovascular events
- *Integument:* skin fragility

Glucocorticoids: The Basics

Glucocorticoids: Mitigation Strategies

Lowest dose, shortest duration

Ca/Vit D supplementation

Screening/treatment for osteoporosis

GI protection

PJP prophylaxis for prednisone > 20 mg x 4 weeks

increased risk with baseline lymphopenia, pulse steroids, cyclophosphamide use

GCs and NSAIDs
The Basics

SUMMARY

- NSAIDs treat pain and inflammation - but are NOT effective DMARDs - in RA
- GCs at low dose may have some DMARD effects
- NSAID and GC treatment-related AEs are often manageable

Opioids and RA

Any benefit in treating RA pain?

- Trials are of short duration
- Benefit is modest in these trials
- Most evidence does not support the use of opioids in chronic non-cancer pain

Opioids and RA

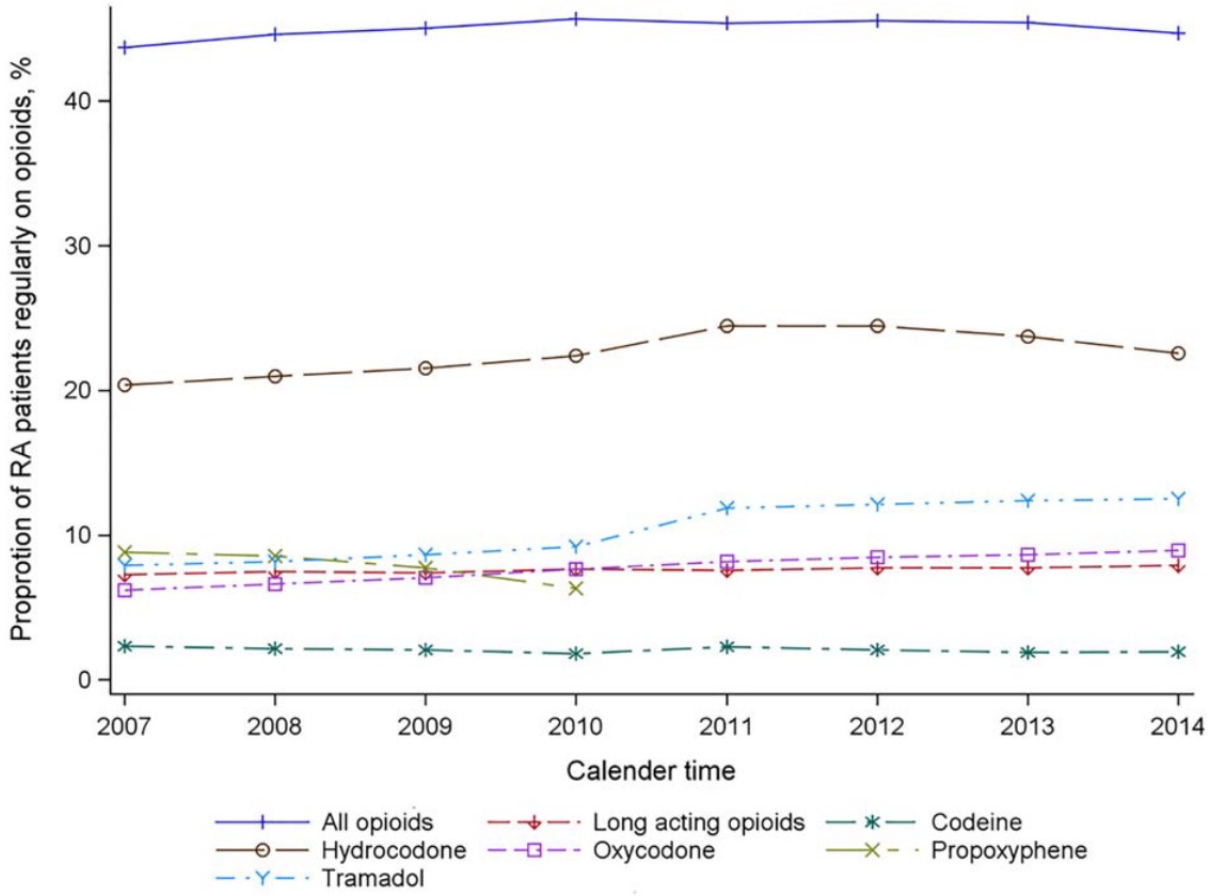

Figure 1. Trends in regular opioid receipt (defined as ≥3 filled prescriptions or at least 90 days of cumulative use in each 12-month calendar interval) in patients with rheumatoid arthritis (RA).

Curtis et al. Arthriis and Rheumatology. Vol 69, No 9, Sept 2017; 1733-1740

Opioids and RA

Regular opioid use was associated with

- female sex
- fibromyalgia
- depression/anxiety
- back pain
- use of durable medical equipment

In a separate study, 25% of regular opioid use among RA patients was associated with obesity

Curtis et al. Arthritis and Rheumatology. Vol 69, No 9, Sept 2017; 1733-1740

What about diet?

Altered microbiome postulated as possible etiology in pathogenesis of RA

Most trials are small (15-30 patients)

Short term benefits found in:

- Subtotal fasting → vegan diet
- Vegan diet

What about diet?

Short term benefits found in:

- Subtotal fasting → vegan diet
- Vegan diet
- Mediterranean diet
- ITIS diet (Mediterranean plus)

References

Crofford, LJ. Use of NSAIDs in treating patients with rheumatoid arthritis. Arth Res Ther, 2013; 15 (Suppl 3)

Colebatch AN. Safety of NSAIDs in people receiving methotrexate for inflammatory arthritis. J Rheum Suppl 2012; 15: 62-73

Hua C. Glucocorticoids in rheumatoid arthritis: current status and future studies. RMD Open 2020; 6:e000536

Corras R. RA Improvement after exposure to ITIS diet. ACR 2020 Abstract

Khanna S. Managing Rheumatoid Arthritis with Dietary Interventions. Front Nutr 2017; 4: 52

Case Presentation

Dr. Daniel Mays

CME Credit Link