Pharmacy Friday

Brief pearls related to acute care pharmacology and evidence-based medicine
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Management of Acute Gout in the ED

Introduction

1. Acute gout is common inflammatory arthritis in the adult US population.
2. Gout results from inflammation caused by precipitation of uric acid crystals from supersaturated extracellular fluid.
3. The ACR guidelines recognize NSAIDs, corticosteroids, and colchicine as first-line monotherapy for the treatment of gout.

Pharmacology				
Properties	**Naproxen**	**Prednisone**	**Triamcinolone**	**Colchicine**
Dose	**750 mg orally followed by 250-500 mg every 8 hours until the attack has subsided**	**40 mg/day for 3 to 5 days, with or without a taper)**	**20-40 mg for the knee and 5 to 10 mg for smaller joints**	**1.2 mg PO x 1 followed by 0.6 mg an hour later***
Administration	Oral	Oral	Intra-articular	Oral
PK/PD	**Onset: 0.5- 1 hr** Duration: up to 12 hrs Renal Excretion: 95 %	**Onset: 1-2 hr** Elimination ½ life 2-3 hr Renal Excretion: >95%	**Onset: 12-24 hr** Duration: up to 30 days Renal Excretion: 75%	**Onset: 0.5-2 hr** Elimination ½ life 27-31 hr Renal Excretion: 45-65%
Adverse Effects	Edema, GI discomfort, headache, dizziness, renal dysfunction	Hypertension, fluid retention, hyperglycemia, disturbance in mood	Headache, injection site pain, influenza-like illness, pharyngitis	GI discomfort, diarrhea, nausea, neuromyopathy, and vomiting
Drug Interactions and warnings	Consider against in patients with high bleeding risk, **peptic ulcer disease, heart failure, dehydration, and renal impairment**.	Warning with oral contraceptives, CVD, diabetes, GI problems, psychiatric disorders, and live vaccines	Warning if **considering joint sepsis**, and in patients with diabetes, CVD, GI problems or psychiatric disorders	Drug interaction with CYP3A4 or P-glycoprotein inhibitors. Warning in patients with hematologic, renal, and hepatic insufficiency
Location in GHS	Zone 1,2, 3 + Trauma	Zone 1,2, 3 + Trauma	Main Inpatient Pharmacy	Zone 1,2, 3 + Trauma
Comments	It is critical that therapy is initiated within 24 hours of acute gout attack onset		ACR guidelines recommend intraarticular or oral corticosteroids If only one or two joints are involved	ACR guideline recommends drug started within 36 hours of attack onset

*renal and hepatic dose adjustments

Alternative Agents in Acute Gout			
NSAIDS	**Corticosteroids**	**Interleukin-1 inhibitors**	**Other Therapies**
Ibuprofen PO 400-800 mg three to four times daily	Prednisone PO 0.5 mg/kg equivalent daily for 5-10 days followed by discontinuation Oral methylprednisolone dose pack may be considered	Anakinra (Kineret) 100 mg SC daily for 3 days	ACTH 40 units IM or SC every 72 hours
Indomethacin PO 50 mg three times daily	Triamcinolone acetonide 60 mg IM once followed by oral prednisone or prednisolone	Canakinumab (Ilaris) Single dose 150 mg SC	Local ice application is the most effective non-pharmacologic therapy
Celecoxib PO 800 mg followed by 400 mg on day one then 400 mg twice daily for 1 week	Methylprednisolone 100 mg IM once followed by oral prednisone or prednisolone		Local or regional anesthetic blocks are a potential adjunctive therapy

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Monotherapy	Combination Therapy	Elderly ± Multiple Comorbidities	Renal insufficiency	NPO
•NSAID •Systemic Corticosteroid •Colchicine	•Colchine + NSAID •Colchicine+ Oral Corticosteroid •Intraarticular steroid +oral colchicine, NSAID, or corticosteroid	•Corticosteroids > NSAIDS (particlarly indomethacin) or Colchicine	•Intraarticular, oral, or parenteral glucocorticoids	•ACTH

Overview of Evidence

Author, year	Design/ sample size	Intervention & Comparison	Outcome
Zhang, 2014	Observation al, n=60	IM betamethasone 7 mg x 1 vs diclofenac 75 mg BID x 7 days	**Betamethasone > diclofenac pain reduction at day 3** Betamethasone = diclofenac pain reduction at day 7 Betamethasone< diclofenac adverse effects
Daoussis, 2013	Observation al, n=181	IM ACTH 100 units	**78% of patients improved after one day after a dose** Minimal impact on blood pressure and serum potassium Elevation in fasting blood sugar for 24 hours
Terkeltaub, 2010	RCT, n=184	colchicine 1.8 mg total over 1 hour vs colchicine 4.8 mg total over 6 hours vs Placebo	**Low-dose colchicine and high dose colchicine = comparable efficacy** Low-dose colchicine safety profile = same as placebo
Man, 2007	RCT, n=90	**prednisolone 30 mg**/APAP 1g vs **indomethacin 50 mg**/APAP 1 g	Prednisolone/APAP is **as effective as oral** indomethacin/acetaminophen in relieving pain but ↓ adverse effects.
Siegel, 1994	RCT, n=31	IM adrenocorticotropic hormone 40 IU vs IM triamcinolone acetonide 60 mg	Resolution of **all symptoms occurred** at an **average of 8 days for both groups.** No adverse reactions were noted in either group 11 reinjections in the ACTH group vs 5 reinjections in the triamcinolone acetonide group
Alloway, 1993	RCT, n=27	Indomethacin 50 mg TID Vs IM triamcinolone acetonide 60 mg	Resolution of **all symptoms occurred at 8 days for a patient taking indomethacin vs 7** days with triamcinolone
Maccagno ,1991	RCT, n=61	etodolac 300 mg BID x 7 days vs naproxen 500 mg BID x 7 days	**Significant in both treatment groups at each time intervals** 93-97% of patients report improved condition treated with either agent

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