WEBINAR

Rheumatoid arthritis:
getting the facts straight about methotrexate

Thursday, 12 April 2018

7.00 – 8.00 pm AEST

Australian Rheumatology Association

Arthritis AUSTRALIA

NPS MEDICINEWISE

CELEBRATING 20 YEARS 1998–2018

Rheumatoid arthritis: getting the facts straight about methotrexate

The interdisciplinary discussion will focus on:

- early diagnosis and timely initiation of methotrexate
- clarity on health professional roles and interdisciplinary care for prescribing and monitoring of methotrexate
- counselling on use of, and persistence with, methotrexate.

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MEET ANTHONY

VISIT 1

- 51 year old; house painter
- Presents with 4 week history of pain and swelling affecting the hands, wrists, ankles and feet
- Migratory pattern, sometimes unable to hold a brush or lift a cup
- Morning stiffness until lunchtime
- Had an episode of knee pain and swelling lasting a few weeks last year. Treated with NSAIDs and settled.

PATIENT HISTORY

MEDICAL HISTORY
hypertension
coronary artery disease with 2 x stents (2 years ago)
no rash, recent travel or viral illness

SOCIAL HISTORY
works as a house painter
ex smoker
drinks 3 stubbies of beer daily

Current medicines list

MEDICINE	DOSE
rosuvastatin	10 mg daily
candersartan	16 mg daily
metoprolol	50 mg daily
aspirin	100 mg daily
citalopram	20 mg daily

EXAMINATION
swollen and tender small joints of the hands and feet as well as wrists
blood pressure 140 / 80 mm Hg

HISTORY AND CLINICAL EXAMINATION

Features suggestive of rheumatoid arthritis[1]

FEATURES
family history of inflammatory arthritis
early morning stiffness (> 1 hr)
swelling in five or more joints
symmetry of the areas affected
bilateral compression tenderness of metatarsophalangeal joints
symptoms present for longer than 6 weeks
presence of rheumatoid nodules

The diagnosis of RA is made on the basis of clinical presentation, in association with autoantibodies and evidence of systemic inflammation.[1]

1. Rheumatology Therapeutic Guidelines

FOLLOW UP INVESTIGATIONS

INVESTIGATIONS	FEATURES SUGGESTIVE OF RHEUMATOID ARTHRITIS[+]
inflammatory markers (ESR*, CRP*)	raised inflammatory markers in the absence of infection
autoantibodies (RF*, anti-CCP*)	RF positivity, anti-CCP positivity
FBC*, renal function*, LFTs*, fasting lipids, glucose, urinalysis*	
X-rays chest, hands and feet – rarely needed in early disease	bony erosion evident on X-rays of wrist, hands or feet (uncommon in early disease)
other tests as clinically indicated – ANA*, urate, synovial fluid	

* minimum testing panel in EULAR recommendations for management of early arthritis
[+] features suggestive of rheumatoid arthritis

ANTHONY'S RESULTS

INVESTIGATIONS	RESULTS
inflammatory markers (ESR*, CRP*)	CRP= 98+ (< 10 mg/L)
autoantibodies (RF*, anti-CCP*)	RF = 55+ (<16 IU/mL) anti-CCP = 546+ (< 5 U/mL)
FBC*, renal function*, LFTs*, fasting lipids, glucose, urinalysis*	FBC (Hb = 150 g/L, WCC = 7.3 x 10^9/L, Pt = 175x 10^9/L) LFTs and renal function normal;
X-rays chest, hands and feet – rarely needed in early disease	X-rays hands normal; small erosion at 5th MTP right foot+
other tests as clinically indicated – ANA*, urate, synovial fluid	ANA negative uric acid = 0.40 (0.2 – 0.5 mmol/L) Hep B surface antigen, surface antibody and core antibody negative Hep C antibody negative

*Minimum testing panel in EULAR recommendations for management of early arthritis
+ Features suggestive of rheumatoid arthritis

KEY INDICATORS OF POOR PROGNOSTIC FACTORS[1]

POOR PROGNOSTIC FACTORS	ANTHONY
high RF titre and/or positive anti-CCP antibody test	strongly positive anti-CCP
sustained raised inflammatory markers (CRP or ESR)	significantly raised CRP
swelling in more than 20 joints	
impaired function in early disease	sometimes unable to hold a brush or cup
bony erosion evident on X-rays early in disease	bony erosion on 5th MTP on right foot
smoking	previous smoker

1. Rheumatology Therapeutic Guidelines

WHAT IS IN A HELPFUL REFERRAL LETTER?

Good referral letter assists in effective triaging[1,2] and includes:

- demographic details
- brief clinical history and examination
- findings
- co-morbidities
- ALL current drug therapy
- treatments tried for the condition to date, outcome
- any relevant investigations and results
- your provisional diagnosis- “?new-onset RA”
- reason for referral- what do you want to get out of it?

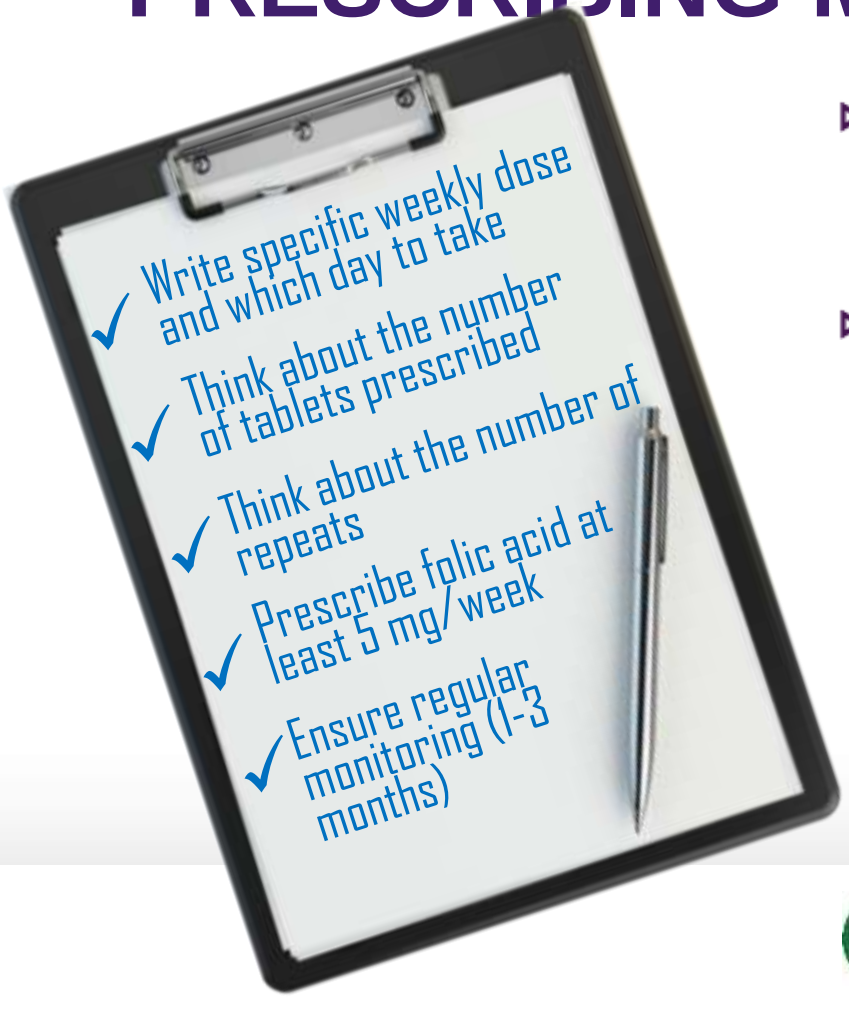
1. Tay et al, Clin Rheumatol (2014); 33: 409 -13.
2. Ong et al, Aust Fam Physician (2006); 35:920-2.

ROLE OF METHOTREXATE

- Methotrexate is recommended first choice for monotherapy due to demonstrated long-term benefits, cost, acceptable safety profile and synergy with other DMARDs.[1,2]
- Methotrexate is the drug of choice for most people and forms the backbone of the regimen when combination therapy is required.[3]
- Methotrexate monotherapy:
  - reduces radiographic progression and improves quality of life;[4]
  - around 40% of patients respond (symptom relief, normalisation of inflammatory markers and the absence of joint swelling).[5]
- Most significant avoidable toxicity is a result of dosage errors
- Regular monitoring (FBC, LFTs, urinalysis) helps minimises adverse side-effects and promotes safe use

1. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological DMARDs (2016)
2. American College of Rheumatology guideline for the treatment of rheumatoid arthritis (2015)
3. Rheumatology Therapeutic Guidelines
4. Lopez-Olivia et al, Cochrane Database Syst Rev (2014); 6:CD000957
5. Hazlewood et al, BMJ (2016): 353:i777

PRESCRIBING METHOTREXATE

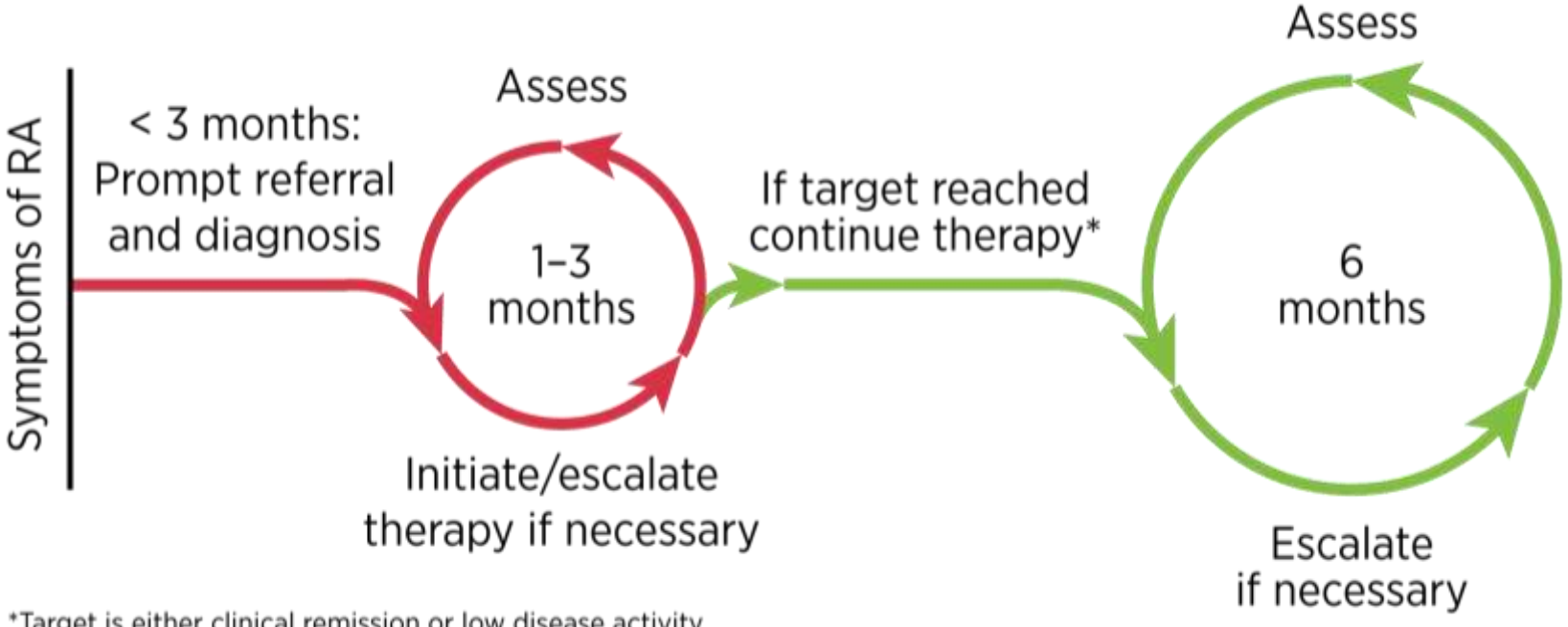


- Subcutaneous methotrexate is characterised by higher bioavailability, greater clinical efficacy and a better tolerability profile than oral methotrexate.[1]
- **Co-prescribe folic acid 5 – 10mg orally per week,[2]** preferably not on the same day methotrexate is taken. It reduces GI side-effects, mucositis and hepatic dysfunction.[3]

Many different ways to prescribe folic acid

1. Bianchi et al, Adv Ther (2016); 33:369-78
2. Rheumatology Therapeutic Guidelines
3. Shea et al Cochrane Database Syst Rev (2013), CD00951

TREAT TO TARGET



*Target is either clinical remission or low disease activity

BACK TO ANTHONY

- Originally prescribed prednisone 10mg daily until diagnosis of RA
- Patient required significant counselling and support- worried about future life and work
- GP asked to ensure all vaccinations including HepB up to date
- Commenced methotrexate 20mg once weekly*, in the evening+
- Commenced folic acid 10mg the day after methotrexate dose
- Commenced hydroxychloroquine 200mg daily+
- Prednisone reduced to 7.5mg daily
- Review 4-6 weeks, with a view to adding a third DMARD if necessary and further reducing/ceasing prednisone

* methotrexate prescribed 10 mg once weekly for two weeks, then 20 mg once weekly;
+ commenced on combination DMARD therapy due to active disease and significantly impaired function and other indicators of poor prognosis.

IMPORTANT ISSUES TO CONSIDER FOR ANTHONY

- Poor prognostic features in this patient- strongly positive anti-CCP, erosions
- Alcohol and methotrexate
- Hypertension and coronary artery disease and NSAIDs
- Screening for viral hepatitis
- Vaccinations
- Corticosteroid side-effects
- Monitoring for methotrexate and hydroxychloroquine