Drugs in Rheumatology Practice

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Various drugs are mainstay in the treatment of rheumatic diseases. There is good evidence that they modify disease severity and progression. Most of the rheumatological diseases are chronic and hence, drugs must be taken continuously unless otherwise advised. The situation is akin to diabetes, blood pressure and heart diseases. Number of drugs are initially prescribed in diseases such as rheumatoid arthritis and systemic lupus erythematosus. Some of these drugs are slowly withdrawn in 6-12 months after a satisfactory disease control is achieved. Some drugs may have to be taken for life time.

These drugs have excellent risk-benefit profile and adverse events due to drugs are well documented. Adverse events must be monitored by blood and other examinations at regular intervals. Adverse events are like road accidents. No one stops traveling on roads for fear of an accident. Drug induced adverse events are usually mild and easily treatable. Most of them can be anticipated by careful monitoring and will subside on withdrawal of offending agent. Alternate drugs for achieving disease control can then be used in such situations.

Dosages and common adverse effects of routinely prescribed disease modifying anti-rheumatic drugs (DMARDs) are given in the adjoining table (Table 1). Doses may vary according to body weight. Lower doses are advocated in children and elderly.

Table 1 Common DMARDs

Drug	Dose	Common adverse effects	Monitoring
Chloroquin Hydroxychloroquin	250-500 mg/d oral 200-400 mg/d oral Dose at night	Skin pigmentation, visual disturbances	Eye check up at baseline and every 6-12 months
Sulphasalazine	1.5 - 3.0 gm/d Supplement with folic acid	Rashes, dyspepsia, myelosuppression, hepatotoxicity	Regular blood check
Methotrexate	10 -25 mg once a week with folic acid At least 24 hrs apart Oral/injecteble*	Oral ulcers, myelosuppression, hepatotoxicity, lung disease	Regular blood check
Leflunomide	10 -20 mg/d oral	Diarrhea, rash, alopecia, weight loss, hypertension, myelosuppression, hepatotoxicity	Regular blood check and BP monitoring
Azathioprine	100-150 mg/d	Rashes, dyspepsia, myelosuppression, hepatotoxicity	Regular blood check
Mycophenolate	100-200 mg/d	Diarrhoea, myelosuppression, hepatotoxicity	Regular blood check

***Methotrexate Injection:**

Subcutaneous injection of methotrexate is stomach-friendly and faster acting due to higher bio-availability of the drug. This is a simple and almost painless injection which patients can take themselves. The procedure is similar to insulin injection prescribed in diabetes.

Subcutaneous injection procedure:

1. Fill insulin syringe with prescribed dose. (Methotrexate 25 mg/ml = 40 units/ml in Insulin syringe i.e. 2.5 mg = 4 units)
2. Clean area over thigh or abdomen with spirit or iodine.
3. Pinch skin and insert needle from side parallel to skin surface.
4. Pull back piston. No blood should be seen in syringe.

5. Inject the drug.

6. Remove syringe and press for a while. Do not rub.

Drugs during pregnancy and lactation

Any drug should be taken in lowest possible dose and for shortest period of time (Table 2). Use short acting drugs e.g. paracetamol, ibuprofen or diclofenac for pain relief. Inadvertent exposure of drug is not an indication for termination of pregnancy. Decision regarding termination must be based on potential risk to the fetus as determined by ultrasound examination (for structural abnormalities) and amniocentesis (for chromosomal abnormalities).

Nonsteroidal anti-inflammatory drugs (NSAIDs): Adverse effects are possible in mother as well as fetus although these drugs do not cross placenta. These drugs are categorized B in first part of pregnancy. It is advisable to stop NSAIDs after 32 weeks of gestation in view of increased risk of premature closure of ductus arteriosus. Edema, raised blood pressure and masking of infection related symptoms are possible.

Glucocorticoids: Hydrocortisone, cortisone and prednisone have minimal or no effect on fetus. Betamethasone and dexamethasone cross placenta and are used for fetal abnormalities. Use lowest possible dose (prednisone < 20 mg/day). Avoid abrupt discontinuation. Common side effects include edema, infection, muscle weakness, osteoporosis, osteonecrosis and hyperglycemia. High doses can cause cleft palate (during first trimester), adrenal suppression and growth retardation in fetus. Most complications are dose related.

Table A2.2 DMARDs in Pregnancy and Lactation

Drug	Category	Pregnancy	Lactation
Paracetamol	A	Safe	Safe. Dose shortly after feeding.
NSAIDs	B	Use lowest dose up to 32 weeks. Monitor fetus with ultrasound examination.	Safe. Dose shortly after feeding.
Glucocorticoids (Prednisolone)	C	Use prednisone in lowest effective dose.	Safe. Feed after 2 hours following oral dose.
Hydroxychloroquin Chloroquin	C	Safe. Risk of eye and ear toxicity higher with chloroquin.	Safe. Peak milk level for 2-9 hours after ingestion
Sulphasalazine	B	No increased risk. Only one report of birth defects.	Compatible. Be watchful.
Methotrexate*	X	Discontinue 2-3 months before attempting conception.	Peak levels at 9 hours after ingestion. Avoid feeding around this time. Potential but unproven risk.
Leflunomide	X	Stop 2 years before attempting conception or undergo cholestyramine washout. No adverse outcome in 85 human pregnancies.	Not known whether excreted in breast milk. Not recommended during lactation.
Azathioprine*	D	Safe. No fetal abnormalities reported.	Peak milk levels at 2-8 hours. No adverse effects in babies.
Mycophenolate	D	Unsafe. Stop 6 months before attempting conception.	No data in humans. Use if benefits outweigh risks. Excreted in rat milk but not in human milk.

**Check blood of baby for hematologic, hepatic and renal abnormalities at regular intervals. Breast feeding may be stopped at an early date.*

Drug categories :

A. Safe. No risk to fetus.

B. No controlled studies in humans. Safe in animals. Risks observed in animals unproven in humans. Use with caution.

C. Unsafe in animals. No studies in humans. Use only if benefits outweigh risks. Risk cannot be ruled out.

D. Evidence of risk in humans. Benefits may be acceptable with due risk.

X. Fetal abnormalities observed. Drug is contraindicated in pregnancy.

Fatherhood

Sulphasalazine reduces sperm count in up to 70% patients. Sperm count returns to normal 3 months after stopping this drug. Cyclophosphamide therapy, too, reduces sperm counts in a dose and duration dependant manner. Testosterone injection appears to normalize sperm counts in such cases. A recent report of 40 men taking methotrexate at the time of conception did not appear to cause any congenital malformations.

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