Ward MEDICATION MANAGEMENT

E- News

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From the Clinical Director

Rheumatoid arthritis (RA) is the second most common form of arthritis (after osteoarthritis), affecting nearly half a million Australians. RA is a major cause of disability and psychological distress, with many people affected requiring assistance with daily activities.

RA is an autoimmune disease that causes pain and inflammation of the joints. It is usually affects the smaller joints, such as those in the hands, feet and wrists, although larger joints such as the hips and knees can also be affected. Inflammation causes the joints to become painful, hot and swollen and movement to be restricted. Stiffness in the joints is common, especially in the morning. The inflammation caused by rheumatoid arthritis can result in damage to the joints, particularly if left untreated. RA affects women more frequently than men. The onset is usually between 35 and 60 years, however the majority of the disease burden in Australia is in people over 65 years.

The cause of rheumatoid arthritis remains unknown, although our understanding of the pathological processes has advanced greatly in the last 20 years. Some people may be more at risk of developing rheumatoid arthritis due to hereditary factors. Exactly what triggers the body's immune system to attack the joints is unknown.

Onset of rheumatoid arthritis is usually insidious, often beginning with systemic and joint symptoms. Systemic symptoms include early morning stiffness of affected joints, generalized afternoon fatigue and malaise, anorexia, generalized weakness, and occasionally low-grade fever. Joint symptoms include pain, swelling, and stiffness. Occasionally, the disease begins abruptly, mimicking an acute viral syndrome.

The disease progresses most rapidly during the first 6 years, particularly the first year. 80% of patients develop some permanent joint abnormalities within 10 years. The course is unpredictable in individual patients. Joint symptoms are characteristically symmetric. Typically, stiffness lasts > 60 min after rising in the morning but may occur after any prolonged inactivity (this sometimes referred to as "gelling"). Involved joints become tender, with erythema, warmth, swelling, and limitation of motion. The course and severity of rheumatoid arthritis varies from person to person and no two cases are the same. Symptoms may change from day to day and there may be times when the disease is active and 'flared' up, and at other times it may be inactive.

RA is a chronic autoimmune condition, in which the immune system targets the lining of the joints (the synovial membrane), causing inflammation and joint damage. The characteristic swelling happens when the joint produces too much lubricating (synovial) fluid in response to the inflammation. Sometimes other parts of the body such as the lungs and eyes may also be affected.

Rheumatoid arthritis is the 2nd most common form of arthritis, many affected require assistance with daily activities.

The cytokine environment in rheumatoid arthritis influences many physiological processes: these include promoting the influx of immune effector cells into the joint synovium, and activation of osteoclasts, chondrocytes and fibroblasts. There is a positive feedback loop that reinforces the inflammatory process. Unabated, this process results in joint pain and destruction, ultimately causing deformity and disability.

Chronic inflammation associated with RA may also contribute to an increased risk of myocardial infarction, stroke and death. In one Canadian population-based prospective cohort study researchers reported an absolute increase in rate difference cardiovascular events of 5.7 per 1000 person-years in patients with rheumatoid arthritis, compared to those without. The use of disease-modifying antirheumatic drugs (DMARDs) to attenuate the inflammatory process has been shown to prevent joint erosions and reduce pain, cardiovascular morbidity and mortality.

Remission is unlikely to occur in RA without intervention. Bone erosions are detectable in 25% of people within three months of onset and in 70% by three years. Delaying treatment beyond the three months causes more joint destruction and a higher chance of requiring persistent DMARDs to maintain remission. Early DMARD therapy during this 'window of opportunity' (that is within three months of onset) will more readily induce remission and delay progression. Many people with RA will usually require significant medication treatment, and it is for this reason that a medication review can be particularly helpful for preventing medication-related harm arising from adverse drug reactions and potential drug interactions.

Dr Chris Alderman, Director of Clinical Excellence, Ward MM.

Feature Article:

Focus on Rheumatoid Arthritis

Optimal care of patients with rheumatoid arthritis (RA) requires an integrated approach that includes both pharmacological and non-pharmacologic therapies. Many non-drug treatments are available and include exercise, massage and physiotherapy. Splinting can reduce local inflammation and may relieve severe symptoms of pain or compressive neuropathies. Cold packs can be used to reduce joint pain and swelling. Occupational therapy and self-help devices enable many patients with debilitating symptoms to perform activities of daily living.

What is known is that RA is fundamentally an inflammatory condition affecting synovial joints. Without treatment, the underlying inflammatory process leads to joint destruction, pain, deformity, disability and accelerated cardiovascular disease. Therefore, treatment is provided to reduce inflammation so as to prevent erosions, progressive deformity, and loss of joint function.

Disease-modifying antirheumatic drugs will attenuate the inflammation. Their benefits are seen at all stages of the disease, however the best outcomes are achieved when they are used shortly after the onset. Disease-modifying antirheumatic drugs are often used in combination, but it is important to note that these drugs can have serious adverse effects. Their safe use requires careful ongoing monitoring to identify potential adverse events.

Other drug classes, including biologic agents, also have the capacity to slow the progression of RA. NSAIDs are of some help for the pain of RA but do not prevent erosions or disease progression and thus should be used only as adjunctive therapy. Low-dose systemic corticosteroids (prednisone < 10 mg once/day) may be added to control severe polyarticular symptoms, usually with the long term objective being to replace the steroid in the regimen with a DMARD. Intra-articular depot corticosteroids can control severe monarticular or even oligoarticular symptoms but may have adverse metabolic effects, even in low doses.

One of the most common DMARDs used for RA treatment is methotrexate. Methotrexate is a folate antagonist with immunosuppressive effects at high dose. It is anti-inflammatory at doses used in RA. It is very effective and has a relatively rapid onset (clinical benefit often within 3 to 4 weeks). Methotrexate should be used with caution in patients with hepatic dysfunction or renal failure. Alcohol should be avoided and folic acid supplementation is recommended, as this reduces the likelihood of adverse effects during treatment.

Non-steroidal anti-inflammatory drugs (NSAIDs) are of some help for the pain of RA but do not prevent erosions or disease progression and thus should be used only as adjunctive therapy. Due to their side effect profile, including issues such as an increased the gastrointestinal ulcers and mucosal damage, renal impairment and cardiovascular disease, NSAIDs not always be suitable to be used in the elderly, who are especially more susceptible to the adverse effects of these medications. Drug interactions may also impact upon the appropriateness of incorporating NSAIDs into the management approach. For example, older people with Atrial Fibrillation may require anticoagulation to reduce the risk of embolic stroke, but concurrent use of NSAIDs for these people may increase the risk of gastrointestinal bleeding considerably. Older people may also be treated with Angiotensin Converting Enzyme inhibitors (ACE inhibitors) or Angiotensin II Receptor Antagonsists, either for hypertension or for the management of Congestive Cardiac Failure (CCF) – if NSAIDs are used for these people there will be a markedly increased risk of impaired renal function.

Intra-articular injections of depot corticosteroids may temporarily help control pain and swelling in particularly painful joints. If these injections are administered too often (more than 3 to 4 times a year to a single joint) they may accelerate joint destruction, and thus this approach must be used with caution. Surgery may be considered if drug therapy is unsuccessful.

Despite widespread use of complementary medicines for management of RA, there remains a lack of evidence of their benefit. No complementary medicines have demonstrated convincing disease-modifying effects. Meta-analyses of published data do suggest that omega-3 polyunsaturated fatty acids are effective at improving pain and reducing NSAID use. It is important to remember that complementary medicines may also be associated with adverse effects and drug interactions, and for these reasons ongoing caution and monitoring is needed.

Na Lim, Clinical Pharmacist, Ward MM

Quick Tip

Methotrexate treatment for Rheumatoid Arthritis

- The goal of immunomodulatory therapy in inflammatory rheumatological diseases is sustained remission; cure is usually not possible and patients generally require ongoing immunomodulatory therapy. The immunomodulatory drugs used in rheumatology are systemic corticosteroids, conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), biological disease-modifying antirheumatic drugs (bDMARDs) and targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs).

- When csDMARD therapy such as methotrexate is started, disease activity is regularly monitored and therapy adjusted to achieve clinical remission. A response to csDMARDs should be apparent within 12 weeks. If remission is not achieved despite an adequate dose of csDMARD, adjustment of the csDMARD regimen is considered (eg switching to a different combination regimen, addition of a second or third csDMARD to an existing regimen).

- Methotrexate is given 10 – 25 mg orally/SC weekly rather than daily, and serious toxicity can occur if the drug is administered more frequently than this. The clinician and patient should agree on which day of the week the patient will take their methotrexate and this should be specified on the prescription.

- Folic acid supplementation decreases the risk of adverse effects, including gastrointestinal adverse effects, liver transaminitis and mouth ulcers. It should not be taken on the same day as the weekly methotrexate dose.

- Adverse effects can be limited by administering the methotrexate dose at night, splitting the weekly dose over 2 consecutive days (usually 12 hours apart) or administering the dose subcutaneously.

- At the doses typically used in rheumatology, there is no risk of toxicity to close contacts of patients taking methotrexate, and special precautions in handling bodily fluids are not required. Methotrexate is usually packed separately from other medications and should not be handled by pregnant staff.

Michael Morcos, Clinical Pharmacist, Ward MM

Latest News

Ward MM Publish Article on Medication Complexity

Ward MM staff recently played a key role in new research addressing medication regimen complexity and potentially inappropriate prescribing after hospitalisation. Given the relative lack of information about this subject, both in Australia and elsewhere, this South Australian study was of importance.

The study, recently published in the International Journal of Clinical Pharmacy examined medication regimens of people aged older than 65 years, before and after admission to hospital. Medication complexity was measured by using the Medication Regimen Complexity Index (MRCI). Mean MRCI scores increased from 29 at the time of admission to 32 at the time of discharge ($p < 0.05$). Factors such as baseline medication regimen complexity (pre-admission MRCI) and length of stay in the hospitals appear to influence the change in medication complexity. However, the proportion of patients prescribed at least one potentially inappropriate medicine (PIM) decreased significantly, from 52% pre-hospitalization to 42% at discharge ($p = 0.04$). The study provided important insights into the patterns of medicines usage in the community and the effects of a hospital stay upon this.

If you would like to read the full article, please contact us at info@wardmm.com.au.

Your Questions Answered

Notes from facilities serviced by Ward MM

It is quite common for us to receive similar enquiries from more than one facility in our network. In this section we summarise questions with a common basis – as a part of our "connect – network – share" ethos, we share the information with all of our facilities.

Q. "There is a lot of talk about biological therapies for rheumatoid arthritis – what are these?"

A. Advances in RA therapy over the last 20 years have significantly changed the way the disease is managed, thereby leading to improved patient outcomes. Such advances include the development of targeted monoclonal antibodies and small-molecule kinase inhibitors which are commonly referred to as "biological agents" or "biologics". Pro-inflammatory cytokines, such as interleukin-1 and -6 (IL-1, IL-6) and TNF alpha are involved in the pathogenesis of RA. The use of disease-modifying antirheumatic drugs (DMARDs) to attenuate these inflammatory cytokines has been shown to prevent joint erosions and reduce pain. Biological DMARDs tend to have a rapid onset of action compared with older antirheumatic agents and are used when other antirheumatics, including methotrexate, are inadequate. They are generally used in combination with conventional agents such as methotrexate.

Some examples of the more frequently used biological DMARDs include those that bind to TNF alpha and inhibit its activity such as: adalimumab (Humira), certolizumab (Cimzia), etanercept (Enbrel), golimumab (Simponi), and infliximab (Remicade). The other predominantly used group of biological DMARDs comprises of those agents which bind to interleukin-1 and -6 receptors and neutralise its inflammatory activity. Examples include: anakinra (Kineret), and tocilizumab (Actemra).

Biological DMARDs are typically administered by SC injection, or IV infusion (diluted in sodium chloride 0.9%, given over 30 minutes). Due to the risk of adverse effects, caution needs to be exercised when administering these medications including the use of basic protective measures such as wearing gloves and a mask.

Adverse effects of these agents include a markedly increased risk of serious infections. This risk is highest in the first six months of therapy. These infections are of concern, particularly the reactivation of tuberculosis and herpes zoster. Other adverse effects include injection site reactions, allergic reactions, headache, dizziness, neutropenia, and liver transaminase elevation.

Biological DMARDs are normally reserved for cases of established severe active RA which has failed to respond to conventional therapy combinations. Such cases are characterised by persistent symptoms of poorly controlled and active disease. Rheumatologists define poorly controlled and active disease as affecting 6 or more swollen and tender joints, or 4 non-hand joints.

Kamran Zia, Clinical Pharmacist, Ward MM

Meet your Ward MM Team Member

Kamran Zia joined Ward MM in the capacity of a Clinical Pharmacist in April. He was looking for a new challenge which allowed him to better utilise his clinical skills and extensive experience in aged care to make a direct impact on patient health outcomes. Having a young family, he was also keen to have a job which offered more flexibility to share the special moments of childhood development.

Most meaningful moments… in 2011 my wife and I travelled to Cuba as part of a volunteer project into how health care is delivered in a country with the highest number of per capita medical practitioners, yet one of the poorest in terms of per capita GDP. Due to crippling trade sanctions leading to a lack of medical equipment and pharmaceuticals, Cuban doctors are forced to rely much more on physical examinations, clinical signs and symptoms. Without access to medical equipment, the main focus is on preventative health care and in this way the country has achieved a level of health care that is comparable to that of developed nations. This experience made me appreciate how grateful we should be at home, and reminded me of the importance of preventative health care. Furthermore, it also allowed me to reflect on many of the wasteful practices (e.g. unused medicines that are thrown out, and unnecessary pathology tests) which are rampant throughout the health care systems of developed nations, including our own.

My biggest challenge… getting ready for work on time in the morning, especially in the winter when all I want to do is catch up on sleep!

I'd be lost without… my GPS. For a guy, I must admit that I have a terrible sense of direction, which would have been a big problem given that my current job requires me to travel to a different site every day – but thank goodness for my trusty GPS!