

Research paper

Primary care attitudes to methotrexate monitoring

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ABSTRACT

Background Rheumatoid arthritis affects 1% of the UK population. First-line treatment is with the immunosuppressant, methotrexate (MTX). This is generally regarded as a safe and effective medication when taken at the right dose, with appropriate monitoring. Very occasionally it causes serious harm or death. In 2006, the National Patient Safety Agency issued a safety alert following increasing reports of prescribing errors and toxicity. Over the last decade, Northwick Park Hospital has seen two MTX-related deaths and other morbidity. Repeat prescriptions and monitoring are generally undertaken in primary care, although concerns have been raised about variation in local practice. Poor communication and inadequate monitoring are safety concerns. Duplication of monitoring has cost implications. Local (hospital Shared Care Guidelines (SCG)) and national guidelines, from the British Society of Rheumatology (BSR), on MTX monitoring are freely available and accessible.

Method We surveyed our local GP community to better understand their practice and establish where patient care could be improved.

Results We contacted 86 practices, of which 31 replied (a response rate of 36%). On average, there was one patient on MTX per 743 in the practice (0.13%), ranging from 0–0.5%. All GPs admitted they repeated MTX prescriptions, but only 77.4% monitored these. Of those who did monitor, 58.6% were aware of local guidelines and only 48.4% were aware of national guidelines. A total of 26.7% of GPs were monitoring and prescribing MTX but not aware of any guidelines. Among this number, 37.5% did not feel they needed further education.

Conclusion Serious safety concerns have been raised, including the poor response rate. Any doctor prescribing MTX should also be monitoring according to guidelines. Low numbers of patients on MTX per practice are surprising, possibly reflecting inadequate records or under-diagnosis. With these data, we have encouraged commissioners to fund a computer monitoring system accessible to primary and secondary care for improved patient safety, and to ultimately save costs by reducing duplication of work.

Keywords: drug monitoring, guidelines, methotrexate, patient safety

How this fits in with quality in primary care

What do we know?

MTX is a highly effective drug in reducing mortality and morbidity in rheumatoid disease. It is safe if prescribed and monitored appropriately (in line with the National Patient Safety Association guidance). Doctors who prescribe the drug do not always have access to the monitoring blood tests. Some patients are having monitoring tests duplicated in primary and secondary care, costing over £50 000 per year. More worryingly, some patients are 'slipping through the net' and having insufficient or no monitoring at all.

What does this paper add?

This paper highlights the safety concerns of MTX prescribing. This topic has been poorly addressed in the literature to date. We hope to bring this important matter to the attention of primary and secondary healthcare professionals who prescribe MTX.

Introduction

Methotrexate (MTX) was first used in the 1940s for the treatment of malignancy. In 1998, the Food and Drug Administration (FDA) approved its use in the treatment of rheumatoid arthritis, and it is now first-line therapy for patients with this condition. It is also used in psoriasis, psoriatic arthropathy and a number of other auto-immune diseases.

The majority of MTX prescriptions in the UK are for rheumatoid arthritis, which affects 1% of the UK population. Approximately 70% of patients in large cohorts of rheumatoid arthritis are prescribed MTX.¹ Although treatment is usually started in secondary care, general practitioners are commonly responsible for continuing prescriptions in the community. The prescriber is responsible for regularly monitoring and reviewing the medications.

The precise mechanism of MTX in inflammatory arthritis is unclear. It inhibits dihydrofolate reductase, which prevents *de novo* pyrimidine and purine synthesis, required for DNA and RNA synthesis. Consequently, there is inhibition of cellular proliferation of lymphocytes which are involved in the inflammatory process.² T-cell activation and apoptosis are inhibited and expression of T-cell cytokines and adhesion molecules is altered.³

MTX is given weekly for rheumatoid arthritis and connective tissue diseases. Doses usually range between 5 and 25 mg per week. Tablets are available in 2.5 mg and 10 mg strengths (although it is recommended only to use 2.5 mg tablets for rheumatoid arthritis, to minimise the risk of accidental overdose).⁴

Side effects of MTX include bone marrow suppression, hepatotoxicity and neutropaenia. Various drug interactions, including with trimethoprim, high-dose aspirin and isoniazid, may increase these risks.¹ Because of potential toxicities, MTX should be regularly monitored by blood tests and clinical review. National guidelines from the British Society of Rheumatology (BSR) recommend monitoring full blood count and liver function tests fortnightly, until six weeks after the last dose increase and, provided it is stable, monthly thereafter. Urea and electrolytes should be checked 6–12 monthly (unless there is a reason to suspect deteriorating renal function).⁵

Over the last 10 years, our hospital has seen two deaths, together with other morbidity, directly related to MTX use. In July 2004, the National Patient Safety Agency (NPSA) recorded 137 safety incidents relating to MTX over a 10-year period in England, including 25 deaths and 26 cases of serious harm.⁶ Two-thirds were due to errors of prescribing oral MTX, particularly incorrect frequency of administration. In 2006, there was a patient safety alert after a further 165 cases involving oral MTX.⁴ The recommendations included

that in organisations with shared care guidelines (SCG), the following issues should be addressed:

- clarity of prescribing and monitoring responsibilities
- how often blood tests will be conducted and in which location
- which clinician will be responsible for receipt and review of the results
- who will communicate any necessary dosage changes to the patient and GP
- who will record test results in the patient-held monitoring booklet.

If there are no SCGs, there must be similar appropriate arrangements. It suggests that '*the BSR guidelines are a useful source of information*'.⁴

Despite these recommendations being published over five years ago, there are still concerns about MTX monitoring in our local area. Communication between primary and secondary care is often poor and it appears that many of our patients are not being monitored according to the guidelines. This may result in under-monitoring, a patient safety issue, or duplicate monitoring (i.e. by both the hospital and GP), a potential money-saving area.

In our trust, each set of monitoring blood tests costs £28. Last year we requested around 13 000 tests costing approximately £364 000. We estimate that two-thirds of stable uncomplicated patients could be monitored in the community. A recent audit of our department showed that 12% of patients had excess or duplicate monitoring costing around £53 000 per year.

Therefore, the aim of this study was to further understand MTX prescribing and monitoring habits of GP practices in our local Primary Care Trust (PCT) to improve current service and patient safety.

Methods

A questionnaire was designed and sent to each GP surgery in the Brent PCT in North London (see Box 1). The 70 GP surgeries (178.25 WTE GPS) in this area provide cover for approximately 330 000 patients, the majority aged between 25 and 45 years.⁷ The survey was designed to capture data including size of practice, number of patients on MTX, whether repeat MTX prescriptions were issued and whether blood tests were monitored by anyone in the surgery. Additional questions asked whether the people monitoring were aware of the hospital's SCG or the BSR guidelines and whether there was phlebotomy on site. We enquired who felt they needed further education on this topic.

GP surgeries were emailed the questionnaire. Non-responders were contacted again after approximately

Box 1 Questionnaire sent to GP surgeries**Methotrexate monitoring and prescribing in primary care**

Thank you for taking the time to complete this questionnaire. We are trying to establish the monitoring and prescribing habits in our local primary care trusts.

Name and address of Practice

How many patients do you have in your Practice?

How many patients in your Practice are taking Methotrexate? _

Does the Practice prescribe the Methotrexate? (please circle) YES NO

If "NO" is it because of:

Lack of resources

Lack of funding

Lack of experience with Methotrexate

Other (please specify)

Does the Practice monitor blood tests for Methotrexate? YES NO

If "NO" is it because of:

Lack of resources

Lack of funding

Lack of experience with Methotrexate

Other (please specify)

If "YES" who monitors the blood results?

GP

Nurse

Please circle – practice nurse/district nurse/community matron/other

Other (please specify)

Are you aware of/have access to the hospital's shared care guideline document? YES NO

Are you aware of/have access to BSR guidelines regarding DMARD monitoring? YES NO

Is there a phlebotomy service on site at your Practice? YES NO

Do you think the practice would benefit from an educational session regarding Methotrexate monitoring? YES NO

1 month. After this, all non-responders were sent a postal copy of the questionnaire, which they were asked to return.

Results

Of the 86 practices that were contacted, 31 replied (a response rate of 36%), despite being sent the questionnaires on three occasions by post and electronically. The size of practice varied from 2300 to 14 280 patients. The number of patients reported as being on MTX varied greatly, ranging from no patients to 0.5% per practice. The average was one per 743 patients (0.13%).

All general practitioners (GPs) were happy to issue repeat prescriptions of MTX. However, only 77.4% had a member of staff (nurse 0%, GP and/or nurse 12% or GP 88%) in the practice who monitored the blood tests. Only 6.4% (two) of the GPs admitted that

patients were monitored by both the GP and hospital, and 16.1% presumed the hospital were monitoring.

Of those practices who monitored MTX, 58% had phlebotomy services on site. Of the 31 participating surgeries, 18 had phlebotomy on site, with only 12 undertaking monitoring (66.7%).

In total, 61.5% were aware of the hospital's SCG and 42.3% of the BSR guidelines. Only 38.4% knew of both and 34.6% were unaware of either guideline.

Of the 31 participating practices, 64.5% of practices felt they needed further education on monitoring, while 6.5% were unsure. Of those who were not aware of any guidelines, all were practices that monitored, yet only 22.2% did not feel they needed further education.

Questionnaires were also annotated with comments. These included positive comments such as 'the practice would very much like to improve our service to this small group of patients' and 'always happy to have more education'. However, there were also less positive comments, including a practice that

did monitor 'only because hospital does not follow joint protocol and organise any blood tests' and 'depends on whether the hospital will follow the joint protocol'.

Discussion

Our findings raise serious safety concerns about monitoring habits of MTX. The poor response rate of 36% was disappointing. Organisation and culture within a primary care practice are important, as clinical care and responsibility for generating, checking and signing prescriptions is usually shared. It has been shown that practices with an individual prescriber(s) responsible for the 'high-risk prescriptions' may put more emphasis on patient safety.⁸

Of the practices that did reply, it was surprising that there were such small numbers of patients reported to be on MTX per practice. We presume this may be due to under-reporting from inadequate records, or possibly due to under-diagnosis of rheumatoid arthritis. One study from an ambulatory care outpatient service showed that infrequently prescribed medications were less likely to have the recommended monitoring.⁹ It is known that physicians are more familiar with prescribing and monitoring habits of drugs that they regularly prescribe, than those they do not.¹⁰

Although all practices admit they will prescribe MTX, only three-quarters had a healthcare professional within the practice monitoring the drug. This leaves a large margin for error if the prescriber is not aware of problems that may have arisen with monitoring.

Those who are being monitored by both hospital and GP are not making efficient use of services and this has cost implications. Only 16.1% of GPs presumed the hospital was monitoring MTX. It is not clear how that assumption was made, as at present we do not have written agreements with primary care physicians about monitoring. There is a possibility that these patients may fall into a void of no monitoring at all, especially if the GP continues to prescribe the MTX.

We found that having a phlebotomy service on site did not correlate with the practice monitoring MTX. This was surprising, as we assumed that lack of monitoring may be due to lack of access to blood tests in the surgery.

There was a large variation between the size of practice, number of patients being prescribed MTX and whether phlebotomy was on site. None of these seemed to correlate with the variation of monitoring.

There was also a proportion of doctors monitoring MTX without being aware of any guidelines. It would be interesting to know how the monitoring was being carried out, if there were no standards or guidelines to

measure results against. This is a potential danger for patients, as the recommendations guide how often and what to monitor, as well as how to manage abnormal results. Alarming, 6% of the GPs unaware of either of the guidelines did not feel that they needed further education on this subject.

There needs to be a change in attitude about monitoring both by hospitals and general practitioners. Both primary and secondary care physicians should be working together to deliver improved and safe patient care. With the current climate of revalidation and evidence of continuing medical education, it is no longer acceptable for doctors to practise without following written guidelines.

Patients and their families should also be educated, where appropriate, to remind physicians and ensure they are having regular monitoring. At the start of treatment, each patient should be issued with a NPSA MTX treatment booklet explaining when to have blood tests and also explaining who looks at the results. All pharmacists issuing MTX should ensure that blood monitoring tests have been done (and checked) before dispensing the tablets.

As MTX has potentially life-threatening side-effects, it should only be prescribed by a physician who has access to the results of blood monitoring tests. These should be interpreted in terms of the local and/or national guidelines. It would be beneficial to have a written agreement between the primary and secondary care physicians as to whom has the main responsibility for prescribing and monitoring MTX.

To facilitate monitoring between primary and secondary care in our area, we have encouraged commissioners to fund a computer monitoring system, with results and prescription data available to both primary and secondary care. This will alert doctors when blood tests have not been done, or when there are abnormal results, and will improve communication between the hospital and general practitioner to improve patient care. Streamlining services will also aim to save costs by reducing duplication. We have negotiated to launch a system costing approximately £3,000 plus £120 per practice. This has been budgeted at £6,000 to set up and subsequently £3,600 per year in running costs. This is significantly cheaper for both primary and secondary care than duplicate monitoring, which has been shown to cost around £53,000 per year. Such a system would also aid communication between primary and secondary care and thus be safer for all of our patients.

Through work, including this survey, we have influenced commissioners responsible for services of patients with rheumatoid arthritis. We have introduced a unified monitoring service with clear lines of responsibility and accessibility from primary and secondary care.

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