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ORIGINAL ARTICLE

POSTOPERATIVE COMPLICATIONS FOR PATIENTS WITH RHEUMATOID ARTHRITIS UNDERGOING ELECTIVE ORTHOPAEDIC PROCEDURES WITH AND WITHOUT METHOTREXATE

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ABSTRACT:
Background: This study was designed to determine whether continuing the treatment with methotrexate increases the risk of any postoperative infections or additional surgical complications in patients suffering from rheumatoid arthritis (RA) followed up for 6 months after elective orthopaedic surgery. **Methods:** 172 patients suffering from RA who were supposed to undergo elective orthopaedic surgery were selected. Patients receiving methotrexate were randomly allotted to groups that either continued methotrexate therapy (group A) or the ones who discontinued the use of methotrexate one month before and after surgery (group B). The rate of complications arising was compared with complications occurring in another group of 160 patients suffering from RA (group C) who did not receive methotrexate and underwent elective orthopaedic surgery. The main outcome measures recorded were signs of postoperative infection, including redness, amount of discharge, systemic infection, and frequency of wound dehiscence. **Results:** Surgical complications or infection frequency in group A was found to be significantly lesser than that in either group B ($p = 0.0045$) or group C ($p=0.038$). Analysis of the overall rate of complications showed that methotrexate, whether continued or discontinued before surgery, did not increase the incidence of complications in the patients with RA who underwent elective orthopaedic surgery. **Conclusion:** Methotrexate therapy was not found to increase the risk of infections or surgical complications occurring in patients with RA within 6 months of elective orthopaedic surgery.
Key words: Orthopaedic surgery; Rheumatoid Arthritis, Methotrexate; postoperative surgical complications.

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INTRODUCTION:

Rheumatoid arthritis (RA) is a disabling state frequently treated by the use of cytotoxic drug methotrexate[1]. After the associated inflammation is controlled, sudden withdrawal of the drug might propagate a flare of the rheumatoid disease, consequently making movement agonizing and eventually, rehabilitation and mobilisation more difficult. A previous study conducted on 53 patients with RA undergoing elective orthopaedic surgery found that in four of 19 procedures in which methotrexate treatment was continued before surgery, early postoperative complications developed; as compared with no complications in 34 procedures in patients who did not receive methotrexate treatment within four weeks of surgery.[2] The results of this study were widely suggestive of methotrexate being the agent increasing the risk of postoperative surgical complications in patients with RA who underwent orthopaedic surgery.

As previous publications[3-7] have reported relatively small numbers, this study was carried out to compare the risk of early postoperative surgical complications in patients with RA who underwent elective orthopaedic surgery in groups who either continue or discontinue methotrexate treatment immediately before surgery.

MATERIAL AND METHODS

Three groups of patients with RA who underwent elective orthopaedic surgery were studied. Group A: patients with RA who were receiving methotrexate for at least six weeks before surgery and in whom methotrexate

treatment was not discontinued. Group B: patients with RA who were receiving methotrexate matched with group A for type of surgery and in whom methotrexate treatment was stopped for one month before and after surgery. Group C: patients with RA who underwent elective orthopaedic surgery during the study phase but who had not received methotrexate treatment.

The incidence of early postoperative surgical complications occurring within 6 months of surgery in the different groups of patients was compared. Complications were enumerated as wound morbidity (reddening of wound, discharge from wound), systemic infection, or wound dehiscence.

The informed consent of all patients selected to be randomly allocated to either group A or group B was obtained. The study protocol was approved by the hospital's ethics committee. Surgical procedures were classified as shoulder replacements, elbow replacements, metacarpophalangeal joint replacement, wrist surgery, other hand surgery, hip surgery, knee replacements, ankle replacements, metatarsophalangeal joint surgery, or other foot surgery.

The influence of sex, rheumatoid disease duration, baseline disease activity as measured by the articular index[8], the influence of other drug treatments, including penicillamine, corticosteroids, and non-steroidal anti-inflammatory drugs, the presence of concurrent diseases such as diabetes, hypertension, osteoporosis, vasculitis, bronchiectasis, Felty's syndrome, asthma, ischaemic heart disease, and diverticulitis was assessed. Information about these disorders was obtained either from the patient's case notes or by interviewing the patient before surgery. The articular index was measured by the same observer[8] the day before surgery and at six weeks and six months after surgery. Presence of a rheumatoid disease flare was defined as the presence of both an increase in pain in two or more joints as noted by the patient after surgery and an increase in articular index[8] by at least 25% after surgery.

Differences in the overall incidence of early infection or complication between the groups were analysed by Fisher's exact test. A logistic regression analysis was used to examine the risk of other clinical or therapeutic variables on the risk of early postoperative infections or surgical complications.

RESULTS

The incidence of infection/complications was lower in group A than in group B (Fisher's p = 0.0045) and also lower than in group C (p = 0.038). [Table 1]

A detailed analysis of the factors influencing the risk of infection or surgical complications was carried out by logistic regression analysis [Table 2]. The presence of any of the chronic diseases increased the risk of complications. Methotrexate in any dose and whether continued or discontinued before surgery did not increase the risk of surgical complications, but penicillamine, indometacin, cyclosporin, hydroxychloroquine, chloroquine, and prednisolone all did appear to increase the risk of complications.

Six weeks after surgery none of the patients who had continued methotrexate treatment has had a rheumatoid disease flare as compared with seven (8%) patients who stopped methotrexate and eight (5%) of those who had not received methotrexate treatment (p = 0.03). There were no statistically significant differences in the incidence of flares in the different groups at six months after surgery.

Table 1: Table showing the incidence of complications and comparison between the incidence among the three groups

Group	Redness	Discharge	Dehiscence	Systemic infection	Total	p - Value
A (82)	3	8	-	3	14 (16%)	
B (90)	6	5	1	4	16 (17%)	0.0045
C (160)	7	9	3	5	24 (15%)	0.038

p<0.05 is considered significant
fisher's exact test was used as test of significance
both groups B and C have been individually compared to Group A

Table 2: Result of logistic regression analysis of the associated conditions and medications

Condition	p-value	Odd's Ratio
Diabetes	0.004	4.37
Hypertension	0.021	2.44
Osteoporosis	0.001	5.91
Diverticulitis	0.016	6.24
Asthma	0.043	4.26
Heart condition	0.023	4.95
Medication	**p-value**	**Odd's Ratio**
Penicillamine	0.043	2.64
Indomethacin	0.032	2.72
Diclofenac	0.64	6.84
Prednisolone	0.043	5.73
Methotrexate	**0.36**	**4.86**
Flare up	0.26	0.53
Articular index	0.75	0.85

p<0.05 is considered significant.

DISCUSSION

The chief intent of this study was to ascertain whether continuing methotrexate treatment amplified the risk of early postoperative infection or complications in patients with RA who underwent elective orthopaedic surgery. It was seen clearly that in subjects continuing methotrexate treatment, no increase in the duration of early postoperative infection or complication was found. On the other hand, these problems were actually fewer than in those subjects who either stopped methotrexate treatment one month before surgery or who had not received methotrexate treatment previously.

From the logistic regression analysis certain other drugs, such as penicillamine, indomethacin, cyclosporin, antimalarial drugs, and prednisolone, materialize to augment the risk of postoperative infections or complications. As this association has been found as a part of a co-incidental analysis and not as a result of the main study design, the clinical significance is less certain. However, increased exposure to these drugs in groups B and C probably accounts for the apparently protective effect of methotrexate in group A [Table 2].

The presence of coincidental diseases, such as diabetes and psoriasis, increases the risk of sepsis after elective arthroplasty[9]. This effect was shown with all the chronic disorders here, including diabetes, emphasising that meticulous care needs to be taken to minimise the risk of infections in such patients. The reason for the association between increased risk of surgery and osteoporosis is unclear but surely reflects an association with inherited collagen variants which could both predispose to osteoporosis and to impaired wound healing.

Therefore, long term complication rates after elective orthopaedic surgery, in view of the results of infection or complications in the 6 months after surgery and the fact that flares are more frequent when the methotrexate treatment is stopped, we conclude that methotrexate treatment should not be stopped before elective orthopaedic surgery in patients with RA whose disease is controlled by the drug before surgery.

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