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BRIEF REPORT

Safety of joint and soft tissue injections in patients on warfarin anticoagulation

Richard Conway · Finbar D. O'Shea · Gaye Cunnane · Michele F. Doran

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Abstract Performance of joint and soft tissue injections in patients receiving anticoagulation is subject to different protocols, some of which suggest continuing treatment within the therapeutic range, while others recommend stopping the treatment prior to procedures. The aim of this study was to evaluate the safety of two approaches to the management of patients prescribed warfarin requiring joint or soft tissue injection. A systematic literature review on this subject was undertaken. Our departmental protocol was changed from one where anticoagulation treatment was temporarily stopped prior to joint/soft tissue injection to one where treatment was continued in the context of a therapeutic international normalised ratio (INR) level within 24 h of the procedure. In patients in whom warfarin was withheld, 32 procedures were performed in 18 patients (13 rheumatoid arthritis, 11 osteoarthritis, 5 spondyloarthritis and 1 each of adhesive capsulitis, rotator cuff tendinopathy and trochanteric bursitis). Of these, 30 were joint injections and 2 were soft tissue injections. In patients who continued warfarin, 32 procedures were performed in 21 patients (11 rheumatoid arthritis, 7 osteoarthritis, 6 crystal arthritis, 4 rotator cuff tendinopathy, 2 spondyloarthritis and 1 each of adhesive capsulitis and carpal tunnel syndrome). Of these, 27 were joint injections and 5 were soft tissue injections. There were no clinical hemarthroses or complications in either group. Joint and soft tissue injections appear to be safe in patients receiving warfarin anticoagulation with an INR <3. Continuation of anticoagulants reduces staff workload and patient inconvenience with no evidence of increased risk of complications.

R. Conway (✉) · F. D. O'Shea · G. Cunnane · M. F. Doran
Department of Rheumatology, St. James Hospital, James's Street, Dublin, Ireland
e-mail: drrichardconway@gmail.com

G. Cunnane
Department of Clinical Medicine, Trinity College Dublin, Dublin, Ireland

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Introduction

A paucity of literature exists on the appropriate management of patients on anticoagulants who require joint or soft tissue aspiration or injection. A recent large retrospective chart review of arthrocentesis and joint injections performed in therapeutically anticoagulated patients revealed an incidence of 0.2 % for clinically significant bleeding [1]. A small number of published case series also support the safety of the procedures in patients on anticoagulants who are in the therapeutic range [2–4].

Despite this evidence, many authorities recommend reversal of anticoagulation in patients receiving warfarin who require these procedures [5, 6]. The temporary cessation of anticoagulation has the potential to cause rare but serious adverse events such as thromboembolic stroke, consumes staff time and causes patients inconvenience. The aim of this study was to evaluate the safety of two approaches to the management of patients prescribed warfarin requiring joint or soft tissue injection.

Methods

This project was carried out in the rheumatology department of a large university teaching hospital (St James's Hospital, Dublin). The protocol in our department prior to September 2011 was to withhold warfarin for 5 days prior to an elective joint or soft tissue injection. During this time, the warfarin was replaced with low molecular weight heparin which was not given on the day of the procedure. Aspirin and/or clopidogrel were continued if prescribed. Warfarin was recommenced the

day after the procedure with low molecular weight heparin continued until a therapeutic international normalised ratio (INR) was achieved. Patients were contacted by phone prior to their appointment for the procedure by a clinical nurse specialist to be informed of this protocol. All patients were provided with a helpline phone number to contact in case of procedural complications.

A systematic literature review supported the concept of performing these procedures in patients on warfarin with an INR <3 [1–4]. A retrospective chart review was then initiated on all patients attending the joint injection clinic of the rheumatology service in the preceding 6 months to assess the safety of the existing protocol. Demographic details, site of injection, indication for injection, INR at time of injection and information on co-prescription of antiplatelets and non-steroidal antiinflammatory drugs (NSAIDs) were collected on all patients. Review of the medical record and the logbook of calls to the patient helpline number took place to assess for any procedural complications within 4 weeks of the procedure.

A new protocol was introduced, whereby warfarin was continued with an INR check within 1 day of the planned procedure. A nurse contacted all patients to inform them of this protocol prior to their appointment. The procedure was performed if the INR was <3. Aspirin and/or clopidogrel were continued if prescribed. All patients were provided with a helpline phone number to contact in case of complications associated with the injections.

A prospective study of 6-months duration was initiated to coincide with the introduction of the new protocol. Demographic details, site of injection, reason for injection, INR at time of injection and information on co-prescription of antiplatelets was collected on all patients referred from the out-patient rheumatology service for injection. Any procedural complications identified through contact with the telephone helpline or with a medical practitioner within 4 weeks of the procedure were recorded.

All procedures were performed in accordance with standard departmental protocol by experienced operators. All injections were performed using the landmark method. Needle size used was 21, 23 or 25G as deemed appropriate for the procedure by the operator. Local anaesthetic was not used pre-procedure. Solutions injected consisted of a mix of methylprednisolone (10–80 mg) and lidocaine (0–1 cc of 2 % solution) as deemed appropriate for the clinical condition by the operator. Procedural complications were defined as any adverse event occurring in the 4 weeks following the procedure that was significant enough for the patient to contact the helpline phone number or a medical practitioner, and deemed to be related to the procedure by the investigator. A pre-specified protocol existed that in the event of persistent worsening symptoms >48 h post-procedure, arthrocentesis would be performed to determine the cause.

Statistical analysis was carried out using Microsoft® Excel (Microsoft, Redmond, WA) and GraphPad InStat version 3.10 (GraphPad Software, San Diego, California, USA). Descriptive statistics were used, including as appropriate, means/standard deviations, medians/inter-quartile ranges or numbers/percentages, with P values for between-group differences calculated using t test for continuous variables and Fisher's exact test for categorical variables. The study was approved and conducted in accordance with the audit guidelines of St James's Hospital.

Results

In the initial cohort of patients, in whom warfarin was temporarily withheld, 32 procedures were performed in 18 patients. Thirty of these procedures were joint injections comprising of 24 knee joint, 5 glenohumeral joint and 1 elbow joint. There were two soft tissue injections performed, one each of trochanteric bursa and subacromial bursa. Ten of the patients who had knee joint injections performed had the joint aspirated immediately beforehand. Joint injections were performed for a variety of indications including 13 for rheumatoid arthritis, 11 for osteoarthritis, 5 for spondyloarthritis and 1 for adhesive capsulitis. Soft tissue injections were performed for one case each of rotator cuff tendinopathy and trochanteric bursitis. There were no clinical hemarthroses or other complications in this group of patients.

In the cohort of patients who continued warfarin, 32 procedures were performed in 21 patients. Twenty-seven of these procedures were joint injections comprising of 24 knee joint, 1 glenohumeral joint, 1 elbow joint and 1 metatarsophalangeal joint. Five soft tissue injections were performed comprising of four subacromial bursa injections and one carpal tunnel injection. Twelve of the patients who received knee joint injections and the patient who received the metatarsophalangeal joint injection had joint aspiration performed immediately beforehand. Joint injections were prescribed for a variety of diagnoses including 11 for rheumatoid arthritis, 7 for osteoarthritis, 6 for crystal arthritis, 2 for spondyloarthritis and 1 for adhesive capsulitis. Four soft tissue injections were performed for subacromial bursitis and one for carpal tunnel syndrome. There were no clinical hemarthroses or other complications in this group of patients.

The baseline characteristics and outcomes of the study population are illustrated in Table 1 and are comparable between the two groups. Among the 39 patients included in the study, the indication for warfarin was atrial fibrillation in 29 patients (2 of whom also had deep venous thrombosis, one of whom had a pulmonary embolus and one who had a mitral valve replacement), deep venous thrombosis in 6 patients (2 of whom also had pulmonary emboli), aortic thrombus in 2

patients and 1 patient each with dilated cardiomyopathy and left atrial thrombus. One of the patients with atrial fibrillation and deep venous thrombosis had developed his deep venous thrombosis when his warfarin was previously held for a joint injection.

Discussion

Our study provides evidence that joint and soft tissue aspirations/injections are safe in patients prescribed warfarin with a therapeutic INR. There were no bleeding or thrombotic events in either group during our study. One patient had a history of deep venous thrombosis, which occurred when warfarin was previously held for a joint injection. The potential adverse events occurring as a result of temporary cessation of warfarin, such as stroke and pulmonary embolus, are severe but rare and would need a much larger study group to identify [4, 7]. In addition, the savings in staff and patient time and convenience gained by continuing warfarin were substantial.

There have been a small number of previous studies examining this question. Thumboo and O'Duffy showed no increased risk of joint or soft tissue haemorrhage in a prospective study of 15 joint aspirations and 17 soft tissue injections in 25 patients receiving warfarin [2]. A prospective study of 15 Italian patients where arthrocentesis was performed at all levels of INR reported 2 cases of hemarthrosis, both in patients with an INR >3 [3]. In a retrospective review of 640 procedures in 514 patients on warfarin, Ahmed and Gertner showed no statistically significant difference in bleeding complications between those with an INR ≥2 and those with an INR <2. In addition, their study demonstrated no clinically significant bleeding events in 103 procedures performed in patients with an INR >3 [1]. Studies in other specialities provide further support to the safety of continuing anticoagulation in patients undergoing minor procedures [8, 9].

Our study evaluated real world clinical practice with a wide range of indications and co-morbidities in our subjects. The numbers in our study are small but of a similar size to previous prospective studies. It is possible that a small increased risk of hemarthrosis in those receiving warfarin would have been revealed by a larger study. The study by Ahmed and Gertner is, however, reassuring in this regard [1]. Our study followed local procedural protocol, and the results cannot be extrapolated to larger gauge needles or different techniques. The use of ultrasound-guided joint injection is not a routine practice in our institution and was not assessed; given that no procedural complications occurred in our study, it is unlikely to have had an impact in this setting. The occurrence of hemarthrosis in our study was evaluated by symptom reporting. While repeat arthrocentesis to assess for hemarthrosis would have been more accurate, its performance in asymptomatic individuals was deemed to be unethical. In addition, the primary endpoint was the occurrence of clinically significant hemarthrosis. For the same reason, post-procedure ultrasound assessment to evaluate for subclinical hemarthroses was not performed. Our study focused on warfarin anticoagulation, and the results cannot be extrapolated to the use of other forms of anticoagulation. Our study was not designed to assess the impact of antiplatelet agents, NSAIDs or other agents on bleeding risk either alone or in combination with warfarin, and applying the results to such patients should be done with caution, given the small numbers included in our study. This is consistent with the local clinical practice; there are relatively few indications for the simultaneous use of antiplatelet agents and warfarin, and if possible, we avoid the use of NSAIDs in this high-risk patient group. Finally, our study did not assess the performance of arthrocentesis in patients with higher INR levels, such as those with prosthetic heart valves, in whom anticoagulation cannot easily be reduced to <3; this is an area which requires additional studies.

In conclusion, our study adds to the evidence that joint and soft tissue injections are safe in patients receiving warfarin with a therapeutic INR.

Table 1 Comparison of procedures performed with warfarin withheld or continued

	Warfarin held	Warfarin continued	*P* value[a]
Patients, n	18	21	–
Procedures, n	32	32	–
Joint injections, n (%)	30 (94 %)	27 (84 %)	*P*=0.24
-Knee	24 (75 %)	24 (75 %)	
-Glenohumeral	5 (16 %)	1 (3 %)	
-Elbow	1 (3 %)	1 (3 %)	
-Metatarsophalangeal	0 (0 %)	1 (3 %)	
Soft tissue injections, n (%)	2 (6 %)	5 (16 %)	*P*=0.42
-Subacromial bursa	1 (3 %)	4 (12 %)	
-Trochanteric bursa	1 (3 %)	0 (0 %)	
-Carpal tunnel	0 (0 %)	1 (3 %)	
Male, n (%)	14 (44)	14 (44)	*P*=1.00
Age, mean (SD)	77 (+−8.1)	74 (+−9)	*P*=0.15
INR, median (IQR)	1.2 (1.1–1.5)	2.4 (2.1–2.6)	*P*<0.001
Aspirin, n (%)	3 (9 %)	1 (3 %)	*P*=0.61
Clopidogrel, n (%)	0 (0 %)	0 (0 %)	–
NSAIDs, n (%)	2 (6 %)	1 (3 %)	*P*=1.00
Complications, n	0	0	–
Clinical hemarthroses, n	0	0	–

[a] *P* values shown from *t* test (continuous variables) and Fisher's exact test (categorical variables)

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Disclosures None.

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