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ORIGINAL ARTICLE *Musculoskeletal*

Efficacy and safety of point-of-care ultrasound-guided intra-articular corticosteroid joint injections in patients with haemophilic arthropathy

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Introduction and Objectives: Intra-articular corticosteroid injections are standard of care for managing joint pain secondary to osteoarthritis or rheumatoid arthritis but are rarely used in haemophilic arthropathy. We have introduced and evaluated the efficacy and safety of ultrasound-guided corticosteroid injections for pain relief in patients with haemophilic arthropathy. **Patients and methods:** Ultrasound-guided intra-articular injections performed on haemophilia patients at UCSD between March 2012 and January 2016 were analysed. Needle placement and injection (40 mg triamcinolone; 3–5 mL lidocaine) were performed with musculoskeletal ultrasound and Power Doppler. Analysis included patient demographics, joint-specific parameters such as tissue hypervascularity and effusions, pain relief, and procedure-associated complications. **Results:** Forty-five injections (14 ankles, 13 elbows, 18 knees) were administered in 25 patients. Advanced arthropathy with hypervascularity and/or effusions was present in 91% and 61% of joints, respectively. Ninety-one per cent of injections resulted in pain relief which was significant in 84% (>30% reduction). Median pain score was reduced from 7 of 10 to 1 of 10 ($P < 0.001$), usually within 24 h. Median duration of pain relief was 8 weeks (range 1–16 weeks). Haemophilia B patients experienced longer periods of relief, and high Pettersson scores were associated with shorter duration of relief. There were no procedure-associated complications. Repeat ultrasound of eight joints within 4 weeks of injection demonstrated nearly complete resolution of hypervascularity. **Conclusions:** Point-of-care ultrasound enabled intra-articular corticosteroid injections that provided highly effective, safe, and relatively long-lasting pain relief in haemophilic arthropathy. This approach should be used to improve pain management in haemophilic arthropathy.

Keywords: arthropathy, corticosteroid injection, haemophilia, intra-articular, ultrasound

Introduction

Haemophilic arthropathy is a debilitating end-stage form of joint disease associated with physical disability, joint deformity, and impaired quality of life [1]. Arthropathic changes often result in pain syndromes and are a leading cause of morbidity in aging patients with haemophilia. Treatment options are limited and chiefly comprise conservative measures such as the administration of clotting factor concentrates, physical therapy, and oral analgesics or anti-inflammatory medications, which are often used to delay surgical interventions such as joint replacement at younger ages.

Intra-articular corticosteroid injections have been used to effectively treat joint pain and improve range of motion in patients with inflammatory or degenerative joint diseases since the 1950s [2–6]. While included in the American College of Rheumatology's treatment guidelines for rheumatoid arthritis (RA), osteoarthritis (OA) of the knee and hip, and juvenile idiopathic arthritis [7–9], intra-articular

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corticosteroids are not routinely used in the management of haemophilic arthropathy. Interestingly, methylprednisolone and dexamethasone intra-articular injections were pioneered for pain relief and reduction in synovitis in patients with haemophilia in the 1980s, demonstrating favourable outcomes such as reduced pain, warmth, and swelling as well as increased mobility and patient satisfaction [10–12]. Despite these promising early results, the use of corticosteroid injections in patients with haemophilia fell out of favour for unclear reasons. Plausible explanations at the time may have been providers' reservations regarding blind needle placement into complicated joints, prioritizing management of viral infections, or the increasing availability of safe clotting factor preparations that limited joint bleeding episodes and, perhaps, immediate inflammatory reactions. Controlling joint pain in haemophilic arthropathy continues to be an important focus in the management of patients with haemophilia. Therefore, we utilized point-of-care ultrasound to enable direct and accurate visualization of needle placement into haemophilic joints [13, 14], and evaluated the efficacy and safety of ultrasound-guided intra-articular corticosteroid injections for pain relief in patients with haemophilic arthropathy who had failed other conservative measures including clotting factor replacement.

Materials and methods

Patient population and data extracted

The study population included all patients with haemophilia A or B who presented to the Haemophilia and Thrombosis Treatment Center at the University of California, San Diego (UCSD) and received intra-articular steroid injection for chronic joint pain. Indications for injection were unresponsiveness, inability, unwillingness, or contraindications to alternative treatment strategies such as physical therapy, oral pain medications, and oral anti-inflammatory agents. Patient data were collected retrospectively between March 2012 and January 2015 ($n = 25$ intra-articular injections) and prospectively between March 2015 and January 2016 ($n = 20$ intra-articular injections). Data collection included: patient age, gender, haemophilia type, haemophilia severity (with severe, moderate and mild defined as factor levels <1%, 1–4%, and 5–40% of normal, respectively), inhibitor status, Haemophilia Joint Health Score (HJHS), radiographically derived Pettersson score, patient-reported joint pain (Visual Analogue Scale of 0–10) before and after corticosteroid joint injection, time from injection to onset of pain relief, duration of pain relief, and procedure-associated complications. Clinically significant pain relief was defined as >30% reduction in pain score [15]. Per clinic protocol, patients were contacted the day after joint injection and were monitored at regular intervals (every 2–4 weeks for up to 24 weeks) for response assessments by telephone interview or in-person clinic visits.

Patient confidentiality and data acquisition methods were reviewed and approved by the University of California, San Diego, Human Research Protection Program.

Ultrasound evaluation

Point-of-care high-resolution musculoskeletal ultrasound with Power Doppler (MSKUS/PD) was performed and interpreted prior to each joint injection by one of three physicians [A.v.D, $n = 22$; A.C., $n = 16$; S.T.B. (see Acknowledgement), $n = 2$] formally trained in MSKUS examination. MSKUS was performed with either the GE Loqiq e BT11 or GE Logiq S8 US-module (General Electrics, Fairfield, CT, USA) using a high-frequency 8–13 MHz linear transducer for sonographic evaluation. PD and grey scale examinations were performed according to standardized imaging protocols for each joint area as previously described [16, 17]. Sonopalpation was used to evaluate compressibility and displacement of intra-articular material. Dynamic joint evaluations were performed when appropriate.

Presence of soft tissue hypervascularity was diagnosed when PD signal in soft tissue was present in any of the applied transducer positions [18], as normal microvascular blood flow in joints is not detectable by PD [19]. The tissue area with the highest signal was re-scanned in seven patients (eight intra-articular injections) during return visits at 1–4 weeks post injection. PD images were analysed using ImageJ. Colour threshold settings were adjusted to select the signals corresponding to vascular flow within the regions of interest. The same settings were used for each image.

Intra-articular corticosteroid injections

Patients received a dose of at least 30 U kg^{-1} FVIII or 60 U kg^{-1} FIX within 24 h prior to intra-articular injection of 40 mg Triamcinolone Acetonide (Kenalog®; Bristol Meyers Sqibb, New York, NY, USA) admixed with 3–5 mL Lidocaine 1% as recommended by the American Academy of Family Physicians [20]. Intra-articular injections were performed under usual sterile conditions, with sterile ultrasound gel and sterile transducer surface. Prior to each injection, the risks, benefits, and alternatives of the procedure were discussed with the patient and informed consent was obtained. Appropriate factor replacement prior to joint injection was confirmed verbally with patients self-infusing at home. Patients unable to self-infuse received a dose of clotting factor in clinic. Patients

received either single or, if pain recurred, repeated intra-articular injections into the same joint. Repeat joint injections were at least 3 months apart.

Statistical analysis

Differences between pre- and post-injection pain scores were evaluated by the matched-pairs signed-rank test. Associations between the outcome variables (onset of pain relief, degree of pain relief, and duration of pain relief) and potential predictor variables (joint type, age, HJHS, Pettersson score, presence/absence of effusion, injection provider) were examined with Wilcoxon tests or Fisher's exact tests as appropriate. We used the Spearman rank correlation coefficient when examination of graphs suggested linear associations. Plots of duration of pain relief on Pettersson score and degree of pain relief on Pettersson score each indicated a curvilinear relationship, with separation of points according to haemophilia type. Generalized additive models (GAM) were fitted, with duration or degree of relief as the outcome, a spline function for Pettersson score, and haemophilia type as a covariate. Statistical analysis for the quantification of Ppixel areas representing vascularity on PD images was performed using a paired Student's *t*-test ($n = 8$).

Results

Patient and joint characteristics

A total of 45 intra-articular corticosteroid injections (14 ankles, 18 knees, and 13 elbows) were administered. Nine (36%) patients received two or more injections into the same joint and six (24%) patients received two or more injections into different joints. Haemophilia type and severity, presence or absence of inhibitor, and patient age at time of injection are detailed in Table 1.

Table 1. Patient characteristics.

Number of patients	25
Median age in years (IQR)*	38.7 (32.4–54.1)
Haemophilia type	
A	20 (80%)
B	5 (20%)
Haemophilia severity	
Mild	6 (24%)
Moderate	2 (8%)
Severe	17 (68%)
Inhibitor	
Present	1 (4%)
Absent	24 (96%)
Number of patients with ≥2 injections into same joint†	9 (36%)
Number of patients with ≥2 injections into different joints	6 (24%)

*IQR, interquartile range.
†Injections into the same joint were performed at least 3 months apart except in two patients who requested repeat injection after 1 and 2 months respectively.

Thirty-four (76%) joint injections were administered to patients with haemophilia A and 11 (24%) to patients with haemophilia B. Thirty-four (76%) injections were administered to patients with severe haemophilia; 3 (7%) to patients with moderate haemophilia, and 8 (18%) to patients with mild haemophilia.

HJHS and Pettersson scores were available for 43 and 34 of the injected joints, respectively. The median single joint HJHS was 7.0 (IQR 3–10) and the median single joint Pettersson score was 9.5 (IQR 7–11), indicating advanced arthropathy in most patients (Table 2).

Joint pain assessment before and after intra-articular corticosteroid injection

Any degree of pain relief was reported following 41 (91%) of the 45 injections. Overall, there was a significant reduction in median pain score from 7 out of 10 on the Visual Analogue Scale to 1 out of 10 following injection ($P < 0.001$) (Fig. 1a). Clinically significant pain relief (>30% reduction in pain score) was observed following 38 (84%) of the joint injections (Fig. 1b). These patients also reported that the injection resulted in meaningful clinical benefit. There were no reports of increased pain or procedure-associated complications.

The onset of pain relief occurred immediately following 10 (24%) of the injections and within 48 h following 24 (59%) of the injections. Pain relief lasted for a median of 8 weeks (Fig. 2), with a large majority of patients experiencing relief for 4 or more weeks.

Table 2. Characteristics of injected joints.

Number of joints injected	45
Type of joint	
Ankle*	14 (31%)
Knee	18 (40%)
Elbow	13 (29%)
Pettersson score, single joint†	
Median (IQR)	9.5 (7.0–11.0)
Hemophilia Joint Health Score (HJHS), single joint‡	
Median (IQR)	7.0 (3.0–10.0)
Power Doppler signal on MSKUS§	
Present	40 (91%)
Absent	4 (9%)
Joint effusion on MSKUS	
Present	27 (61%)
Simple	1 (2%)
Complex	26 (59%)
Absent	17 (39%)

*Including one injection into retro-Achilles bursa.
†Maximum Pettersson score of 13 per joint, Pettersson score for six patients not available.
‡Maximum HJHS of 21 per joint, HJHS for one patient not available.
§Musculoskeletal ultrasound, MSKUS data for one patient not available.
IQR, interquartile range.

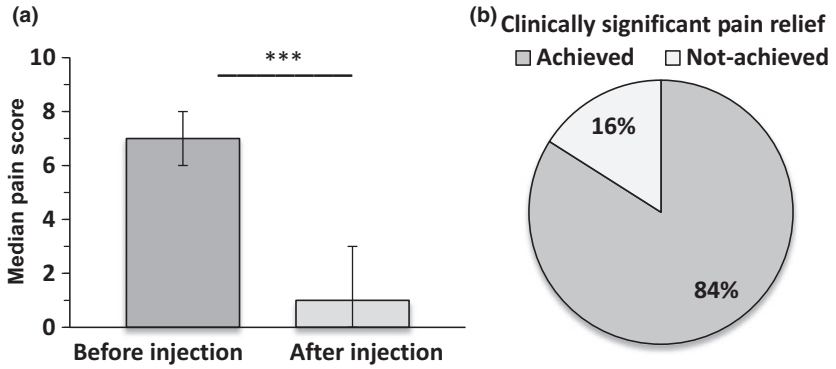

Fig. 1. Efficacy of pain relief with intra-articular corticosteroid injection. (a) Decrease in patient-reported joint pain (Visual Analogue Scale 0–10) following corticosteroid injection (n = 45) expressed as reduction in median pain score. Statistical significance was determined by matched-pairs signed-rank test. Error bars represent interquartile ranges. (b) Percent of corticosteroid injections associated with clinically significant pain relief (n = 45). Clinically significant pain was defined as reduction in pain of 30% or greater. Error bars represent interquartile range and ***denotes statistical significance at $P \leq 0.001$.

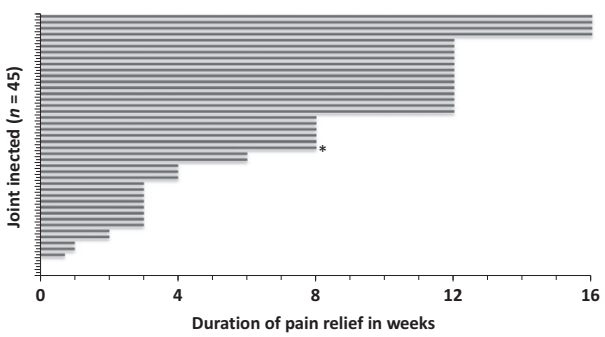

Fig. 2. Duration of pain relief following intra-articular corticosteroid injection. Waterfall plot depicting the duration of pain relief for each single joint. Patients were monitored in regular intervals (every 2–4 weeks) for 24 weeks for response assessments after intra-articular corticosteroid injection by telephone interview or in-person clinic visits. There were four reports of no pain relief following injection. *Patient deceased from pulmonary haemorrhage prior to final assessment.

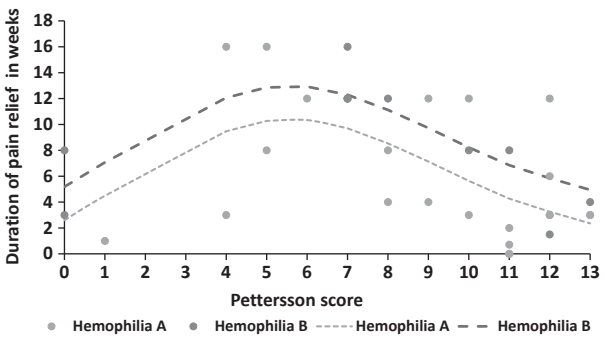

Fig. 3. Effect of Pettersson score and haemophilia type on duration of pain relief. Marked curvilinear relationship between duration of pain relief and Pettersson score, illustrated by fitting a generalized additive model (GAM) with duration of pain relief as the outcome, a spline curve for Pettersson score ($P < 0.011$), and haemophilia type as a covariate ($P = 0.089$). The broken lines are the curves fitted by the GAM for each haemophilia type.

Variables associated with corticosteroid -associated pain relief

The following variables were examined for prediction of absolute pain relief (defined as the difference in pre- and post-injection pain scores) or duration of pain relief: age, joint type, haemophilia type, haemophilia severity, joint HJHS, joint Pettersson score, injection provider, and presence of effusion. Only Pettersson score and haemophilia type showed associations.

The GAM shows a marked ($P < 0.001$) curvilinear relationship between duration of pain relief and Pettersson score (Fig. 3). Patients with Pettersson scores between 4 and 8 experienced the longest periods of pain relief, with decreased duration of relief associated with higher Pettersson scores. This association was seen for both patients with haemophilia A and haemophilia B; however, patients with haemophilia B reported 2.6 (95% CI = −0.4, 5.6, $P = 0.089$) weeks longer pain relief compared to patients with haemophilia A after adjustment for Pettersson score. There was also a curvilinear relationship between pain relief and Pettersson score ($P = 0.011$) (Fig. 4). Again, there was a difference in pain relief between haemophilia types A and B ($P = 0.044$), with a strong interaction term ($P = 0.052$) illustrated by the curves that cross in Fig. 4.

MSKUS/PD findings

MSKUS/PD was performed on all joints prior to intra-articular corticosteroid injection with documented findings for 44 of the 45 injections. Soft tissue hypervascularity was present in 40 (92%) and mild effusions were present in 27 (61%) of MSKUS/PD examinations (Table 2). Repeat MSKUS/PD for eight joints in patients who volunteered to return to clinic within 1–4 weeks after the initial injection demonstrated resolution of hypervascularity (Fig. 5). The PD positive signal area decreased from an average of

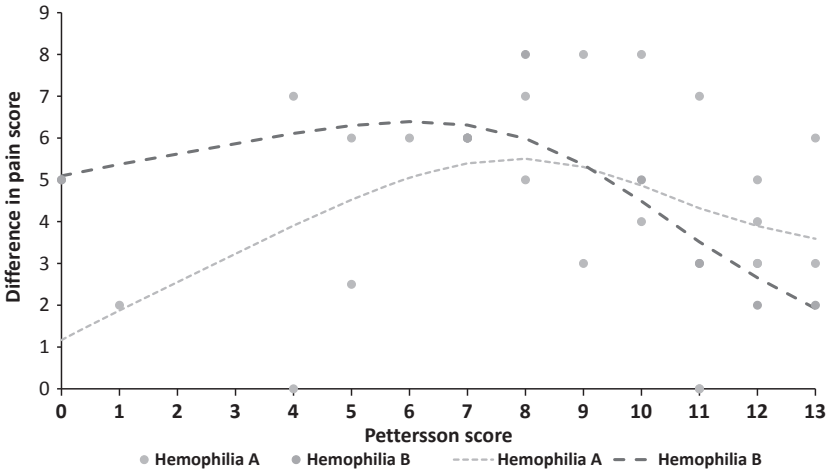

Fig. 4. Effect of Pettersson score and haemophilia type on pain relief. A curvilinear association between Pettesson Score and haemophilia type on pain relief was illustrated by fitting a generalized additive model (GAM) with pain relief as the outcome, a spline curve for Pettersson score, and haemophilia type as a covariate ($P = 0.044$). The broken lines are the curves fitted by the GAM for each haemophilia type. The interaction for Pettersson score by haemophilia type ($P = 0.052$) shows how the curves cross.

1817.5 pixel^2 (SEM 277.5) pre-injection to 143.8 pixel^2 (SEM 41.5) post injection ($P \leq 0.001$).

Discussion

Haemophilic arthropathy contributes significantly to disability in aging patients with haemophilia, especially in those patients who did not have regular access to clotting factor concentrates earlier in life [21]. Even in the modern era of prophylactic clotting factor replacement therapy, haemophilic arthropathy is not entirely preventable [21–24]. Therefore, there is a growing need for effective management strategies to address chronic pain and joint dysfunction [25].

Here, we show that ultrasound-guided intra-articular corticosteroid injections are both safe and effective in alleviating chronic joint pain in patients with haemophilic arthropathy. Pain relief was clinically meaningful and also statistically significant. Although duration of pain relief ranged from 1 week to 4 months, most patients experienced pain relief for 4 or more weeks. Moreover, the vast majority of patients felt that the injection resulted in a personal benefit, irrespective of intensity or length of duration of pain relief. Those beneficial effects went beyond pain relief and included the ability to be more physically active, to feel less limited in particular movements, to sense a higher degree of mobility and to enjoy increased confidence and independence.

Several corticosteroid preparations (including betamethasone, triamcinolone, methylprednisolone, dexamethasone and hydrocortisone) have proven effective at alleviating joint pain after intra-articular administration in RA and OA, with a paucity of clinical trials comparing efficacy and toxicity among different corticosteroid preparations [26]. Triamcinolone (acetonide or hexacetonide) is preferred by many physicians due to its decreased solubility and thus longer intra-articular duration of action [27, 28]. It has been common practice since the 1970s to inject corticosteroid admixed with lidocaine for several reasons. First, lidocaine elicits immediate analgesic effects, which in turn aid in confirmation of correct injection site when ultrasound guidance is not available. Second, lidocaine reduces the risk of 'post-injection flare' caused by precipitating corticosteroid crystals as well as corticosteroid-associated soft tissue atrophy [29].

Pertaining to accuracy, efficacy, and safety of intra-articular injections, the American College of Rheumatology Task Force endorses ultrasound-guided procedures because accuracy of blind injections is suboptimal. Comparisons of the accuracy of ultrasound-guided injections with blind injections consistently demonstrated superiority with ultrasound, which in turn is associated with higher efficacy and avoidance of unintended deposits into cartilage, tendons, and ligaments [30]. However, while ultrasound guidance is the preferred modality for intra-articular drug delivery, procedures do not need to be deferred if ultrasound equipment is not available.

The pathophysiology of haemophilic arthropathy is not yet fully characterized and appears to share at least some similarities with both RA and OA. Some degree of local inflammation and especially vascularity changes are important features of most arthritic conditions [1, 33, 34] and are targeted by intra-articular corticosteroids [35–37]. Corticosteroids inhibit expression of inflammatory cytokines in synovium and synovial fluid that include Interleukin (IL)-1 and IL-6 [38, 39], which are considered important mediators of perpetuated chronic synovitis, cartilage degradation, and joint destruction in haemophilic [31, 40, 41] and other arthritic conditions [42, 43]. Corticosteroids also have anti-angiogenic effects [44–46], that are exploited in other clinical conditions [47]. Therefore, corticosteroids hold significant potential to also decrease inflammation and synovial vascularization in haemophilic arthropathy. Abnormal angiogenesis in haemophilic arthropathy is distinguished by an additional layer of complexity since, unlike in RA or OA, it is associated with vascular

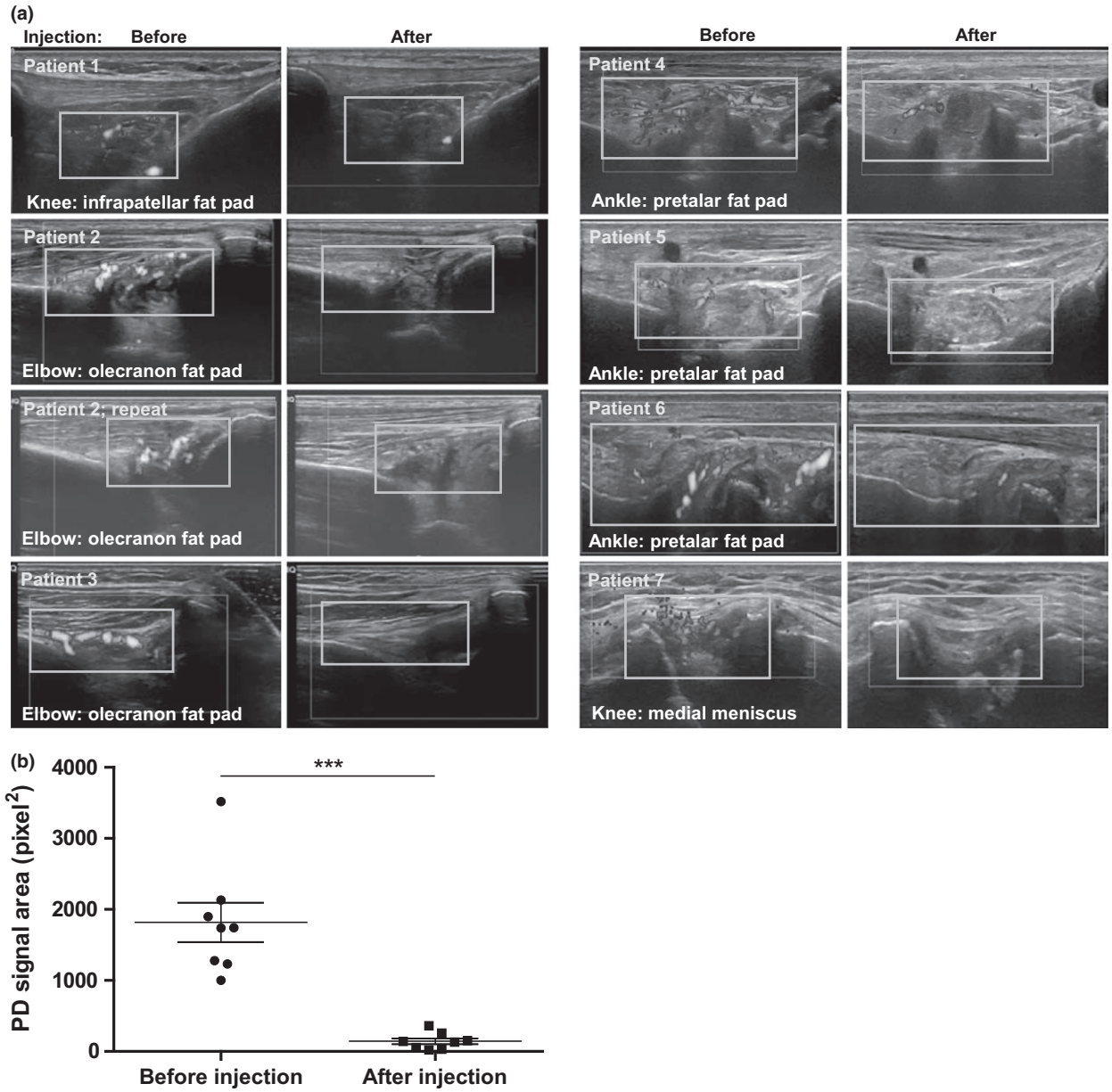

Fig. 5. Reduction in vascularity in response to intra-articular corticosteroid injection. Seven patients who underwent intra-articular injection with triamcinolone acetonid (Kenalog® 1 mL; 40 mg) and Lidocaine 1% (3–5 mL) returned for re-evaluation 1–4 weeks after injection. Joints were examined by high-resolution musculoskeletal ultrasound with power Doppler. To assess vascularity changes, power Doppler signals were recorded at the time of injection and during re-examination. Patient #2 received a repeat injection 3 months after the first injection, when pain re-occurred. (a) Depiction of joint areas with the most pronounced vascular changes. (b) Quantification of vascularity before and after joint injection using imageJ to determine signal area corresponding to vascular flow. Following all eight injections vascularity decreased remarkably in response to the intra-articular treatment. Notably, the relapse in pain in patient #2 was associated with re-appearance of vascular structures. Error bars represent standard error of the mean, and *** denotes statistical significance at $P \leq 0.001$.

remodeling, characterized by abnormal dynamic vascular architecture changes and strong expression of angiogenic factors such as VEGF-A [21] and α-Smooth Muscle Cell Actin (α-SMA) [49]. These vascular changes contribute to vascular fragility and re-bleeding tendencies [49, 50] and may therefore also play a key role in fueling persistent joint pains. Towards that end, corticosteroid-mediated reduction in vascularity in intra-and peri-articular haemophilic tissues may be particularly important since reduced vascularity has the potential to interrupt the cycle of perpetuated bleeding and neoangiogensis. Although such effects will need to be explored in future studies, it is noteworthy that, in this study, intra-articular corticosteroid injections resulted in interval resolution of hypervascularity in all seven patients (corresponding to eight joints) who

volunteered to undergo repeat joint examination with MSKUS/PD at 1–4 weeks post injection, results that are similar to those previously reported in RA. The resolution of hypervascularity was associated with pain relief in all instances. Notably, the relapse of pain in the elbow joint of one patient who was followed serially was associated with recurrence of hypervascularity and fluctuating hemarthosis despite intense clotting factor prophylaxis [50]. In this patient, vascularity, pain, and hemarthrosis responded to repeated intra-articular corticosteroid injections. Altogether these observations suggest that the anti-inflammatory properties of corticosteroid injections not only contribute to pain resolution in patients with haemophilic arthropathy, but may also portend anti-angiogenic effects that may add benefit in patients with subclinical or perpetuated bleeding. In this context, it is conceivable that corticosteroids not only decrease neovascularization, but may also mitigate vascular permeability through vascular wall stabilization. Our observations also suggest that, as in RA, the modulation of PD signals appears to be a useful biomarker to gauge effectiveness of local or systemic anti-inflammatory treatments in haemophilic arthropathy [51].

As reported for intra-articular corticosteroid injections in other arthritic conditions, the extent and duration of clinical response in our haemophilia patient population varied substantially, with inter-individual differences [52]. Results from a recent meta-analysis seeking to determine predictors of response to intra-articular corticosteroid injections in OA suggested that effusion status, severity of disease, synovial inflammation, and corticosteroid delivery under ultrasound guidance all play a role; but the findings were inconsistent across studies [52]. Therefore, we also evaluated variables such as age, joint type, haemophilia type, haemophilia severity, joint HJHS, joint Pettersson score, injection provider or presence of effusion in search of predictors, of clinical response in our study. We found a curvilinear relationship between duration and extent of pain relief and Pettersson score. Specifically, patients with joint Pettersson scores between 4 and 8 (best score = 0; worst score = 13, i.e. joints with moderately severe haemophilic arthropathy), experienced the best and longest duration of pain relief, whereas joints with mild or very severe arthropathy benefitted less. This pattern was seen for patients with either haemophilia A or haemophilia B. While these observations are currently unexplained, one might speculate that the aetiology of pain is different in various stages of arthropathy and, therefore, more or less amenable to corticosteroid treatment. For instance, corticosteroid-treatable inflammatory and angiopoietic changes may be less pronounced in very early or late stage arthropathy, where other reasons for chronic pain may prevail, such as joint malalignment in early, or scarred tissues in late, stage arthropathy respectively. Interestingly, patients with haemophilia B had a longer duration of pain relief than patients with haemophilia A. While this finding remains unexplained, it is consistent with previous studies suggesting that some features of haemophilic arthropathy differ between haemophilia A and B. For instance, patients with haemophilia A were described to have more frequent bleeding events, more severe manifestations of arthropathy, and more frequent joint replacements than patients with haemophilia B with a similar degree of clotting factor deficiency [53–55].

Questions pertaining to long- and short-term side effects of intra-articular corticosteroid injections arise frequently in practice and require discussion with the patient prior to the intervention. In our experience most patient questions centred on negative effects on overall joint health, permissible frequency of injections, and systemic effects due to local absorption. While there has been concern that frequent administration of intra-articular corticosteroid injections may promote joint destruction [28], multiple studies have failed to show evidence of long-term joint damage due to corticosteroid injections [6, 27, 56]. There is no formal consensus on the optimal frequency of repeat injections, but it is general practice to wait 3 months before re-injecting corticosteroids into the same joint [57]. Three-month intervals seem to be reasonable given that median duration of pain relief was 8 weeks in our experience. Systemic absorption of intra-articular corticosteroids may occur, however, the locally delivered dose of triamcinolone acetonide of 40 mg is low, corresponding to the equivalent of 50 mg of oral prednisone. Considering that systemic absorption is only a fraction of the local dose and that some physicians administer short courses of systemic high-dose corticosteroids ranging from 20 to 80 mg daily for several days in the setting of haemophilic arthopathic flares, the gradual absorption of locally administered triamcinolone acetonide (which has been shown to occur over roughly 14 days [58]) is likely to have limited clinical significance.

Conclusion

In summary, our results demonstrate that ultrasound-guided corticosteroid injections for painful haemophilic joints are safe and clinically efficacious, increasing the armamentarium of options for point-of-care pain management in clinic. Next steps would be to determine predictors of durable response, considering clinical and imaging findings that include vascularity changes in association with bleeding states. In the long term, however, new knowledge about the pathobiology of progressive haemophilic arthropathy is paramount to enable the discovery of novel molecular therapeutic targets to advance alternative and intra-articular treatment strategies for this disabling complication of haemophilia.

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Author contributions

E.J.M. contributed to data collection, analysis, interpretation and manuscript drafting. E.J.C. performed analysis of Power Doppler signals, and contributed to data interpretation and manuscript drafting. A.C. provided concept of intervention, performed ultrasound-guided joint steroid injections and contributed to ultrasound interpretation. R.F.B. performed statistical analyses and contributed to data interpretation and manuscript drafting. C.M.M. performed Hemophilia Joint Health Scores and assisted with ultrasound examinations. S.H. assisted with ultrasound-guided intra-articular injections. T.H.H. performed Pettersson Scores. R.E.M. assisted with joint injection techniques and ultrasound interpretation. A.v.D. provided study concept and oversight, performed ultrasound-guided joint injections and interpretations of ultrasound, contributed to data collection, analysis, interpretation and manuscript drafting.

Disclosures

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