Low frequency of septic arthritis after arthrocentesis and intra-articular glucocorticoid injection

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Category
Article

Running head
Septic arthritis after injection

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Abstract

Objectives:
The aim of this study was to evaluate the risk of septic arthritis (SA) in patients who received an intra-articular (IA) glucocorticoid (GC) injection and to describe the characteristics of these patients.
Methods:
All patients undergoing IA procedures at the orthopaedic and rheumatological departments on the Danish island of Funen from January 2006 to December 2013 were identified in the central database and included by register extraction. Patients who developed a clinically inflamed joint and positive synovial fluid culture within 14 days after IA GC injection were considered to have SA. Retrospectively, data on age, gender, affected joint location, bacterial agent, pre-existing inflammatory disorder and death within 30 days were extracted from the patient files. According to local recommendations, a non-touch sterile technique was used for IA procedures. Patients were informed about the risk of SA and advised to seek medical attention on suspicion of infection or lack of improvement.

Results:
A total of 22,370 IA procedures were performed. Among these, 14,118 GC injections and 8252 arthrocentesis were undertaken. Only 11 patients were diagnosed with SA (0.08%, confidence interval 95%) 0.03-0.12). In our data, risk factors for SA were male sex, age and pre-existing joint disease.

Conclusion:
In our study, we found a low frequency of SA subsequent to IA GC injections. Older patients with pre-existing joint disease are at higher risk of developing septic arthritis.

Introduction
Intra-articular (IA) joint puncture is used for both diagnostic and therapeutic purposes. The therapeutic benefit of IA glucocorticoid (GC) injection in patients with rheumatic diseases is well described(1). However, IA procedures are associated with a potentially increased risk of septic arthritis (SA). The prevalence of SA varies, but is estimated to be 4–10/100,000 in Western Europe (2). The most frequent form of SA is primary SA, haematogenic spread of pathogenic microorganisms from another infectious focus(3). The second most frequent is
secondarily SA, typically related to IA procedures(4). Although IA procedures are increasingly being performed, the incidence of secondary SA seems stable(5). However, iatrogenic SA is a well known and feared complication to IA procedures. Prompt diagnosis and treatment are crucial to minimise joint damage, sepsis and potentially fatal outcomes(2, 6). Some chronic diseases appear to be risk factors for SA. Furthermore, pre-existing joint damage or joint protheses tend to increase the risk(7).

**Objective**

The aim of this study was to evaluate the risk of SA in patients who received an IA GC injection, and to describe the characteristics of these patients. Furthermore, the frequencies of IA procedures in patient with rheumatoid arthritis (RA), psoriatic arthritis (PsA), gout, arthrosis and unspecified arthritis were registered.

**Methods**

*Study design and participants*

The Danish healthcare system provides care for all residents free of charge. All acutely ill patients are admitted to the nearest public hospital in their area of residence. Every hospital contact is registered according to a diagnosis code (ICD-10) and a procedure code (ICD-10) if a procedure is performed. Our primary data cover one geographically well-defined area (Funen) with 490,000 inhabitants served by the Department of Clinical Microbiology at Odense University Hospital, Odense, Denmark(8). All Danish residents have a unique personal identification number used for all health contacts, which permits unambiguous linkage between health administrative registries(9). All microbiological results from the Department of Clinical Microbiology, Odense University Hospital, are stored in an electronic laboratory database, the MADS system (10). All patients above the age of 18 years who had undergone a intra-articular GC injection and developed SA with positive synovial fluid within 14 days, in the study period from 2006 to 2013, were registered in this descriptive retrospective study. Data regarding IA procedures were extracted from the Department of Rheumatology Odense and Svendborg and the Orthopedic Department of Odense and Svendborg.
Data used to evaluate secondary outcomes were derived solely from the Rheumatology Department at Svendborg Hospital, Svendborg, Denmark, from January 2006 to December 2014 using internal registration databases.

Research committee approval

The Data Protection Agency of the Region of Southern Denmark (ID:18/4139) and the Danish Health and Medicines Authority (3-3013-461) authorised this study.

Clinical assessment

All medical journals were reviewed in patients registrered with SA, defined as a clinically inflamed joint and detection of bacteria in synovial fluid. Patients who developed SA more than 14 days after IA GC injection were excluded. SA patients were categorised according to age, gender, affected joint location, bacterial specimen, pre-existing risk factors for SA and death within 30 days.

Secondary outcomes were based on registry data. Five major diagnosis groups were chosen for evaluation: RA, PsA, gout, arthrosis and unspecified arthritis. Within every diagnosis group, frequencies of IA procedures, e.g. IA steroid injections and arthrocentesis, were identified and registered. IA steroid injections were registered according to localisation, i.e. upper or lower limbs. Arthrocenteses were registered according to the joint involved.

Statistics

Review and analysis of data were performed independently by three physicians. Descriptive statistical analysis was performed based on parametric testing.

Results

Patients with septic arthritis and intra-articular procedures

Our study population was defined as shown in the flowchart (Figure 1). A total of 22,370 IA procedures were registrered, 14,118 as IA GC injections and 8252 as arthrocenteses. Eleven patients with SA within 14 days of IA GC administration were identified (Figure 2). The risk of SA subsequent to IA GC injection in our data was 0.08% (95% CI 0.03-0.12).
Subgroup analysis showed that only two patients developed SA subsequent to IA GC injection at our local department. This correspond to a risk of 0.05%.

**Characteristics of patients with septic arthritis**

The majority of patients were males (64%). The mean age was 67.4 years (range 50–83). The most frequent bacteria detected were *Staphylococcus aureus* (n=6) followed by streptococcus species and gram-negative rod-shape bacteria (e.g. *Escherichia coli* and *E. faecalis*). The majority of SA patients had pre-existing risk factors for SA prior to IA GC injection. Pre-existing joint disease was a dominat factor. Only large joints were affected, primarily in the lower limbs. One patient died within 30 days of diagnosis of SA. Despite intravenous antibiotics and operational synovectomies, severe sepsis developed with septic polyarthritis and endocarditis that led to cardiopulmonary failure. The mortality rate in this study was 9% among patients with SA. Patient characteristics are shown in Table 1.

**Intra-articular procedures and distribution: a subgroup analysis of patients from our own department**

A total of 5307 IA procedures were registrered. In all, 3947 IA GCs were performed and 1360 athrocenteses. Fifty-four percent of the IA GCs (n=2129) were performed in the upper limb versus 46% (n=1818) in the lower limb. Most of the IA procedures were carried out in patients with RA, 48% of those in the lower limb and 35% in the upper limb. Patients with gout or arthritis primarily received IA GC injections in a lower limb (Figure 3). Injections in patients with arthrosis and PsA were evenly distributed between upper and lower limbs (12% vs. 9% and 12% vs. 14%). Athrocentesis was primarily performed in the lower limb, the knee being punctured most frequently (Figure 4).

**Discussion**

Only 11(0.08%) patients were diagnosed with SA subsequent to IA GC injection within the 8-year study period. Our study was restricted to adults with confirmed bacterial SA. Our patients’ mean age was 67 years, similar to that reported in other studies (7, 11). A reason for the higher incidence of SA in older patients could be the presence of comorbidities. In a previous study, twice as many men (64%) were diagnosed with SA(12). Seven of 11 SA
patients had pre-existing joint disease in the affected joint (three RA, two gout, two arthrosis). Two patients also had pre-existing type 2 diabetes. Inflammatory joint disease and diabetes are generally considered risk factors for secondarily SA (7, 12). In our study, SA affected large joints, primarily knees and shoulders. The lower limb was more frequently affected. These results have been found in other studies as well (7, 12). Clinically, it is easier to perform IA procedures in large joints, and this could be the explanation for these findings. The difficulty of joint aspiration in small joints may have led to an underestimation of SA due to the definition used in our study, and this could be considered a limitation. The most frequent bacterial agent was S. aureus followed by streptococcus species and gram-negative rod-shape bacteria. These bacteria are the most common in SA in Europe (7, 13). S. aureus has a high degree of selectivity for synovial fluid, and can be difficult to eradicate due to virulence factors such as biofilm (7). In Southern Denmark Region, intravenous dicloxacillin is recommended for treating SA. In the case of penicillin allergy, cefuroxim is used. A previous study showed that empirical use of benzylpenicillin in addition to dicloxacillin will probably not improve the treatment of SA (14) because dicloxacillin covers a microbiological spectrum that includes the most common bacteria causing SA. Some less common bacteria are not sensitive to penicillinase stable penicillin. However, these bacteria are less aggressive and are not known to cause irreversible joint damage. Therefore clinicians may wait for gram staining, bacterial culture and antibiotic sensitivity testing before deciding on antibiotic treatment. One patient died within 30 days of SA diagnosis. This underlines the severity of SA and the need for prompt, correct diagnosis as well as treatment. The mortality rate in this study is comparable with previous studies (5, 7).

Our definition of SA may lead to an underestimation of its incidence. Prior studies anticipate the proportion of positive cultures after joint aspiration range from 60-80% (5, 15). An explanation could be that antibiotics had been administered before joint puncture. Also, surgeons treating severe SA with surgical decontamination may not send synovial fluid to microbiological examination. Regardless of the severity the SA, we recommend that blood cultures should always be done, if possible before initiating antibiotic treatment. Another possible variable leading to underestimation could be the presence of SA in patients with ongoing sepsis. In these cases, patients are treated with wide spectrum antibiotics and despite a clinical suspicion of SA, joint puncture is not performed. The existence of such cases is regarded as a limitation in our study. We chose a time limit for evolving SA subsequent to IA
GC injection. The purpose was to reduce the possibility of other external factors causing SA. Coagulase negative staphyloccus species are considered low virulent and it is likely that some of these bacteria could lead to SA after our time limitation. Compared to the microbiological distribution in SA we consider this as a potential exclusion of a few patients.

However the study size and multicentre organisation illustrate the normal clinical setup, and how SA is handled routinely in the hospital setting. Our use of the laboratory register ensured that all positive synovial cultures analysed in the study population were identified. The ICD-10 procedure coding system have variable ways to code IA procedures. We chose per protocol therapeutic steroid injection in joint on upper-or lower limb (BLHN00, BLHN01) before evaluation of data. Further it is required by the clinician to add a procedure code in order to registrate. According to our dataset about 75 IA GC injections were performed per hospital per month which seems plausible. However the number seems low and could lead to underestimation.

Only two patients in our rheumatology department were diagnosed with SA, a rate of 0.05%. At our department, patients are routinely informed of the risk of joint infection. They are urged to contact us if there is any suspicion of infection, e.g. persisting or progressing signs of inflammation or lack of improvement. Furthermore, an aseptic non-touch technique was used for intra-articular procedures.

Our calculated risk of SA secondarily to IA GC injection is low. It is likely underestimated. We might have found more case patients if we included data from primary care or exceeded the time limit after IA GC injection. Further we presume, that the use of antibiotic may have lead to negative synovial culture and even some patient treated with sepsis without joint aspiration. Even if our calculated frequency is underestimated the risk of SA is still considered low. The clinical benefit of IA GC injection is proven and we argue that the risk of SA should not retain the clinician from performing IA GC injections.
Conclusions

This study demonstrates that IA procedures can be performed with little risk of SA. The risk factors identified, e.g. older patients with inflammatory joint diseases, among others, are consistent with those described in the literature.

We consider the use of a proper joint puncture technique and provision of patient information to be essential when doing IA procedures. However, if SA occurs it is potentially fatal, and therefore GC injection should be performed only by physicians with experience treating joint diseases.

References

Figure 1: Flowchart for the inclusion/exclusion of patients

All intraarticular procedures in Funen from 2006 to 2013 (n= 22,370)

Excluded (n=14,118)
- Arthrocentesis

Intraarticular glucocorticoid injections (n=8,252)

Excluded (n=8,241)
- Synovial fluid without bacteria

Septic arthritis within 14 days of intraarticular glucocorticoid injection (n=11)
Figure 2: Frequency of intra-articular procedures and septic arthritis.

- Intraarticular steroid injections: 14118
- Arthrocentesis: 8252
- Septic arthritis: 11
Figure 3: IA GC injection frequency and location based on diagnosis.

Frequency table GC injection, location

RA: rheumatoid arthritis; PsA: psoriasis arthritis
Figure 4: Arthrocentesis distribution based on diagnosis.

RA: rheumatoid arthritis; PsA: psoriasis arthritis
<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Joint</th>
<th>Bacterial agent</th>
<th>Risk factors</th>
<th>Death, 30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>83</td>
<td>Shoulder</td>
<td><em>Grp. A streptococcus</em></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>M</td>
<td>53</td>
<td>Elbow</td>
<td><em>S. aureus</em></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>M</td>
<td>55</td>
<td>Ankle</td>
<td><em>S. aureus</em></td>
<td>Gout</td>
<td>-</td>
</tr>
<tr>
<td>M</td>
<td>67</td>
<td>Knee</td>
<td><em>Grp. A streptococcus</em></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>F</td>
<td>83</td>
<td>Knee</td>
<td><em>E. faecalis</em></td>
<td>Arthrosis in the affected joint</td>
<td>-</td>
</tr>
<tr>
<td>M</td>
<td>58</td>
<td>Knee</td>
<td><em>S. aureus</em></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>M</td>
<td>73</td>
<td>Knee</td>
<td><em>S. aureus</em></td>
<td>Gout</td>
<td>-</td>
</tr>
<tr>
<td>F</td>
<td>50</td>
<td>Shoulder</td>
<td><em>Grp. A streptococcus</em></td>
<td>RA, type 2 DM</td>
<td>-</td>
</tr>
<tr>
<td>F</td>
<td>66</td>
<td>Knee</td>
<td><em>S. aureus</em></td>
<td>Arthrosis in the affected joint, type 2 DM</td>
<td>-</td>
</tr>
<tr>
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<td><em>S. aureus</em></td>
<td>RA</td>
<td>-</td>
</tr>
<tr>
<td>M</td>
<td>73</td>
<td>Elbow</td>
<td><em>E. coli</em></td>
<td>RA</td>
<td>-</td>
</tr>
</tbody>
</table>

*RA*: rheumatoid arthritis; *DM*: diabetes mellitus; *Arthrosis*: pre-existing arthrosis in affected joint