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Periarticular Magnesium Injection Therapy Provides Pain Relief and Enables Steroid Avoidance in Sickle Cell Arthropathy Patients

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Abstract

Background: Sickle cell disease (SCD) is associated with arthropathy. Arthropathy pain may require periarticular injection therapy. However, steroid injections may be unsuitable for SCD patients. Alternatively, magnesium injection may provide analgesia and avoid steroid requirement. This is a study of the impact of periarticular injection therapy on pain, sleep, and walking function improvement in SCD. It studied periarticular magnesium injection versus periarticular dexamethasone injection in SCD and matched non-SCD patients.

Methods: This is an observational study of twenty adults with severe arthropathy. Data collected included patients' pain score, walking function score, sleep score, and periarticular injection therapy outcomes. Walking ability was assessed using the arthritis self-efficacy scale of 10-100. Pain was measured using the 10-point numeric scale. Sleep was assessed using the 10-point Likert scale.

Results: Ten consecutive SCD patients were matched with ten non-SCD patients with similar clinical characteristics. Eleven patients had knee arthropathy, and nine patients had hip arthropathy. Twelve patients used codeine analgesic, and eight patients used tramadol analgesic regularly. The patients' pre-treatment numeric pain scores were 7-9, Likert sleep scores were 2-4, and walking function scores were 20-30. Periarticular magnesium or dexamethasone injections produced similar improvements in the walking function, pain, and sleep scores of the SCD and non-SCD patients. One SCD patient developed a sickle cell crisis after a dexamethasone injection. One non-SCD patient experienced insomnia after dexamethasone injection. Magnesium injection was not associated with any complications.

Conclusion: SCD arthropathy pain is severe. Periarticular magnesium injection provides safe and effective analgesia for SCD arthropathy. Periarticular dexamethasone injection may be employed in SCD patients with no hypothermia, infection, or immunocompromise. Magnesium injection is a better and safer alternative in clinical situations that require steroid avoidance. Periarticular magnesium injection therapy promotes value-based healthcare for SCD arthropathy patients.

Keywords: *Magnesium injection, Chronic arthropathy pain, Sickle cell disease, Steroid avoidance, Value-based healthcare*

Introduction

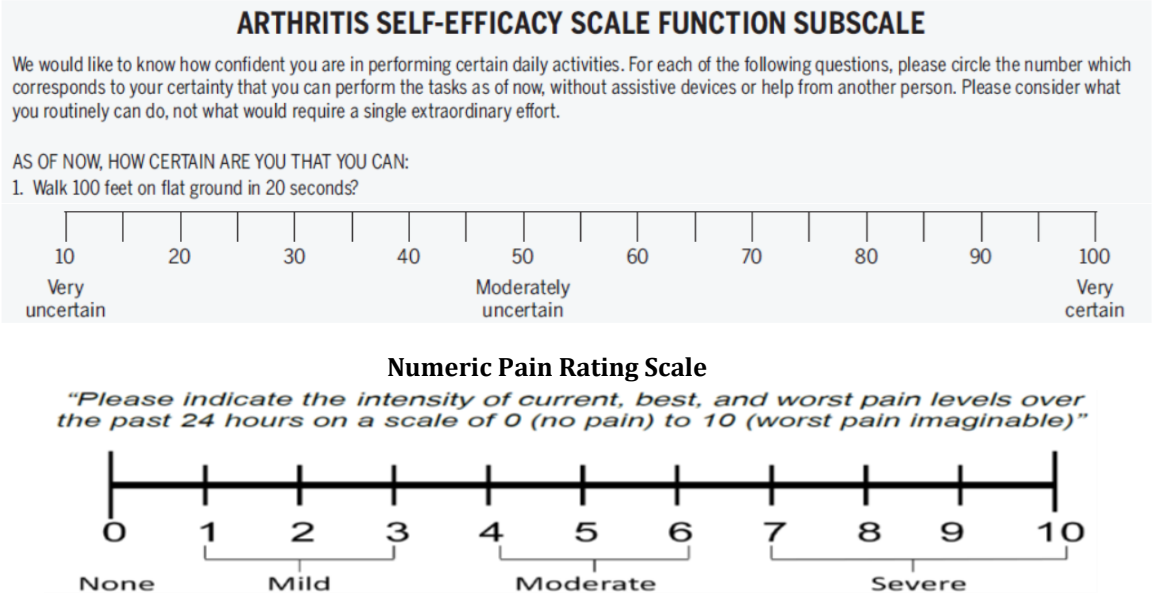
Sickle cell disease (SCD) is an inherited autosomal recessive haemoglobinopathy in people of African, Persian, South Asian, Middle Eastern, and Mediterranean ancestry [1]. SCD is complicated by haematological, splenic, cardiovascular, skeletal, arthropathy, respiratory, neurologic, and renal disorders. SCD arthropathy is chronic, progressive, debilitating, and distressing [2]. The management of arthropathy pain is challenging and may require opioid, multimodal, or interventional therapy [3,4]. Interventional treatment usually involves periarticular steroid injection with dexamethasone, methylprednisone, or triamcinolone.

Despite normal basal cortisol levels, SCD patients may have adrenal insufficiency [1]. Steroid injection is used to treat vaso-occlusive crisis, acute chest syndrome, allergy, asthma, arthritis, pain, and autoimmune disorders in SCD [5]. However, there is controversy about the suitability of steroid therapy in SCD. Additionally, there is inadequate information about the safety of steroid injections in SCD during the COVID-19 pandemic. The pandemic presented challenges to patients and healthcare staff [6,7]. Magnesium injection is an alternative but underutilized modality for pain therapy [4,8]. Magnesium injection avoids steroids and associated complications. This study analyzed SCD arthropathy patients who received periarticular injection therapy. It examined periarticular injection treatment outcomes on sleep, pain, and walking function. It compared the efficacy, safety, and outcomes of periarticular magnesium injection versus periarticular dexamethasone injection in SCD and matched non-SCD patients.

Methods

This prospective observational study was registered on the Clinical Trials PRS website, with the PRS number NCT05983055. It studied 20 adult patients, comprising 10 SCD and 10 matched non-SCD patients. The healthcare organization approved it, confirming that it is a quality assurance study and does not require research ethics review. All the patients provided informed consent. Data collected included age, gender, body mass index (BMI), race, smoking history, alcohol intake, regular analgesics, pain score, sleep quality, ability to walk 100 feet in 20 seconds, periarticular injection outcomes, the limb joint that was injected, post-injection analgesia duration, and complications. Patients were educated about the validated tools for collecting data (Figure 1). The ability to walk 100 feet was assessed using the arthritis self-efficacy scale function subscale (ASESFS), ranging from 10 to 100, with a change of 20 points considered significant. The 10-point numeric pain rating scale (NPRS) was used to measure and categorize pain severity as mild (score 1-3), moderate (score 4-6), or severe (score 7-10), with a change of 2 points considered significant [9]. The 10-point Likert sleep scale was used to assess the quality of night sleep, with a change of 2 points considered significant [9].

Figure 1. Validated measurement scales to collect data from severe arthropathy patients, January 2018 to December 2023.



Likert Sleep Scale

Please rate the current quality of your sleep at night, on a scale of 0 (very poor) to 10 (excellent)

Overall Quality of Sleep

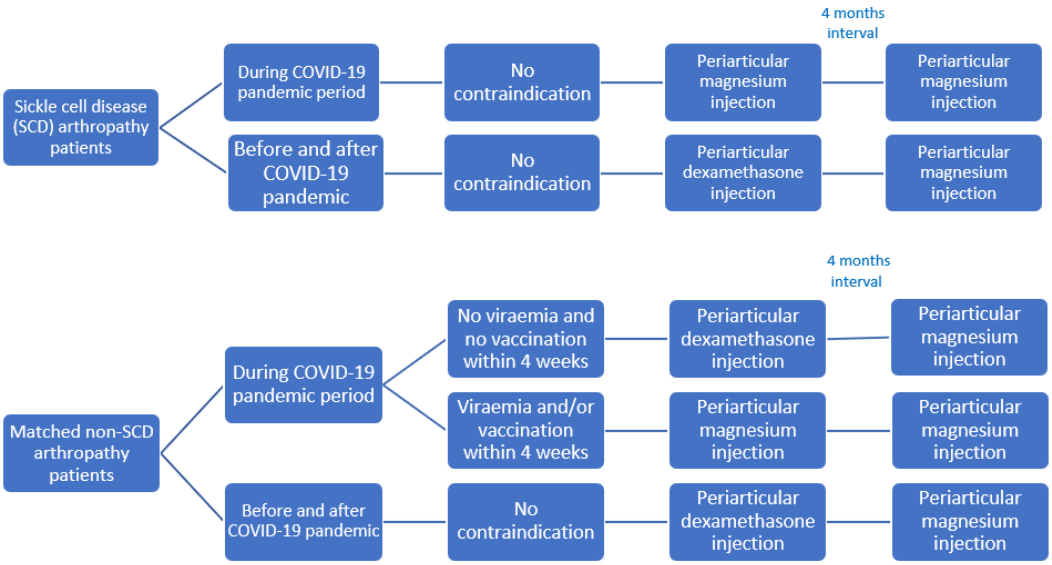
	0	1	2	3	4	5	6	7	8	9	10
Overall Quality of Sleep											
	Very Poor										Excellent
Score	0	1	2	3	4	5	6	7	8	9	10

Multiple measurements were collected and analyzed with IBM® SPSS® Statistics 28 (IBM Corp, Armonk, NY). P-value <0.05 was considered significant. We used the Chi-square test to compare SCD and non-SCD patients. To compare the walking function, pain, and sleep scores between SCD and non-SCD patients, we used the T-test. To compare the pre-treatment and post-treatment walking function, pain, and sleep scores within each group, we used the T-test. To compare the pre-treatment and post-treatment walking function, pain, and sleep scores between SCD and non-SCD patients, we used the paired T-test. The end-points of walking function, pain, and sleep scores measured treatment efficacy. We used the ANOVA and the T-test to compare the effectiveness of magnesium injection versus dexamethasone injection within each group. We used the ANOVA and paired T-test to compare the efficacy of magnesium injection versus dexamethasone injection between SCD and non-SCD patients. We used regression analysis to compare treatment outcomes and complications between SCD and non-SCD patients.

Case Presentation

We studied consecutive SCD patients who underwent pain management from January 2018 to December 2023. The SCD patients were matched with non-SCD patients with similar arthropathy severity and treatments during the same period. The patients underwent ultrasound-guided periarticular injections for hip or knee arthropathy pain management at an interventional pain clinic in Canada. During January 2018-March 2020 and May-December 2023, patients received dexamethasone 10mg injection or magnesium 1000mg injection at alternate treatment sessions, and treatment sessions occurred at 4-month intervals. The study was commenced in January 2018, before the COVID-19 pandemic. The COVID-19 pandemic occurred from March 2020 to April 2023 [7,10]. During the pandemic, dexamethasone injection was avoided to minimize steroid-related immunosuppression. During the pandemic, SCD patients were treated with magnesium injections only. During the pandemic, non-SCD patients were treated with magnesium injections if symptomatic of viraemia or within 4 weeks of vaccination. The treatment decision flowchart is shown in Figure 2.

Figure 2. Treatment decision flowchart for patients with severe arthropathy pain, January 2018 to December 2023.



Results

Ten adult male SCD patients were matched with ten non-SCD patients, as shown in Table 1. The patients were male, aged 42-60 years, non-obese, and non-smokers. Twelve patients used oral codeine+acetaminophen analgesic daily, and eight used oral tramadol+acetaminophen analgesic daily. Eleven patients were treated for knee arthritis, and nine for hip arthritis.

The patients' pre-treatment pain score range was 7-9. The pre-treatment sleep score range was 2-4. The pre-treatment 100-feet walking function range was 20-30. Of the 10 SCD patients, 7 were black African, 1 was Persian, 1 was Arab, and 1 had Mediterranean ancestry.

Table 2 shows the parameters of the SCD patients after periarticular injections. Table 3 shows the parameters of the non-SCD patients after injections. After injection therapy, all the patients reported 75% pain reduction in the treated joint (p=0.001); 50% sleep quality improvement (p=0.011); and 75% ambulation improvement (p=0.001). The clinical effects were similar in the SCD and non-SCD patients (p=0.511). The clinical parameters were similar after periarticular magnesium or dexamethasone injections (p=0.441).

One SCD patient developed a sickle cell crisis 24 hours after a dexamethasone injection, and this event occurred during the cold winter season. The patient was treated for 12 hours in the emergency department with intravenous fluids and morphine. It happened after the first treatment when he had bilateral hip joint injections. Subsequent treatments were uneventful, as he had only one joint injected. No other SCD patient developed complications.

One non-SCD patient experienced insomnia for the initial 24 hours after dexamethasone injection. The incident occurred after the first and second treatment sessions. Subsequent treatment sessions were uneventful. No other non-SCD patient developed complications.

Table 1. Characteristics of SCD and matched non-SCD patients with severe arthropathy pain, who underwent periarticular injection therapy during January 2018 to December 2023, total number=20 patients.

ID	SCD	Age	Race	BMI	Smoke regularly	Alcohol weekly	Analgesic daily	Arthritis joint	Pre-therapy pain score	Pre-therapy sleep score	Pre-therapy ASESFS 100-feet walk in 20secs
A	Yes	60	Black African	27	No	No	Codeine+acetaminophen	Hip	8	3	30
B	No	57	Caucasian	30	No	No	Codeine+acetaminophen	Hip	7	4	30
C	Yes	49	Persian	28	No	No	Tramadol+acetaminophen	Knees	9	2	30
D	No	50	South Asian	29	No	No	Codeine+acetaminophen	Knee	9	2	30
E	Yes	51	Black African	23	No	No	Codeine+acetaminophen	Knee	9	3	20
F	No	55	Caucasian	28	No	No	Codeine+acetaminophen	Knee	9	3	30
G	Yes	50	Black African	24	No	No	Codeine+acetaminophen	Hips	8	3	30
H	No	54	Caucasian	29	No	No	Codeine+acetaminophen	Hip	7	4	30
I	Yes	48	Black African	28	No	No	Tramadol+acetaminophen	Hip	9	3	20
J	No	53	Caucasian	30	No	No	Tramadol+acetaminophen	Knee	8	3	30
K	Yes	44	Black African	26	No	No	Tramadol+acetaminophen	Knee	9	2	20

Table 1 Continued…

L	No	47	Arab	30	No	No	Tramadol+acetaminophen	Knee	9	3	20
M	Yes	42	Black African	24	No	No	Codeine+acetaminophen	Hip	8	2	30
N	No	48	North Asian	29	No	No	Codeine+acetaminophen	Hip	8	2	20
O	Yes	43	Mediterranean	27	No	No	Tramadol+acetaminophen	Knee	9	2	20
P	No	52	Caucasian	30	No	No	Codeine+acetaminophen	Knee	8	3	20
Q	Yes	46	Arab	28	No	No	Codeine+acetaminophen	Knee	9	2	30
R	No	50	South Asian	30	No	No	Codeine+acetaminophen	Knee	9	2	30
S	Yes	54	Black African	26	No	No	Tramadol+acetaminophen	Hip	9	3	20
T	No	59	Caucasian	30	No	No	Tramadol+acetaminophen	Hip	8	3	30

ID= participant reference, SCD= sickle cell disease, BMI= body mass index, ASESFS= arthritis self-efficacy scale function subscale

Table 2. Clinical outcomes of the SCD patients with severe arthropathy pain, who underwent periarticular injection therapy during January 2018 to December 2023, total number=10 patients.

ID	Arthritis joint injected	Pre-therapy pain score	Pain after magnesium injection	Pain after dexamethasone injection	Pre-therapy sleep score	Sleep after magnesium injection	Sleep after dexamethasone injection	Pre-therapy ASESFS 100-feet walk in 20secs	100-feet walk after magnesium injection	100-feet walk after dexamethasone injection	Complication
A	Hip	8	2	2	3	8	7	30	90	90	No
C	Knees	9	1	2	2	9	8	30	90	90	No
E	Knee	9	1	2	3	9	7	20	90	90	No
G	Hips	8	2	2	3	8	8	30	90	90	Sickling crisis after dexamethasone 24hrs
I	Hip	9	2	2	3	9	8	20	90	90	No
K	Knee	9	1	1	2	9	8	20	90	90	No
M	Hip	8	1	2	2	9	7	30	90	90	No
O	Knee	9	1	1	2	9	8	20	90	90	No
Q	Knee	9	1	1	2	9	8	30	90	90	No
S	Hip	9	1	2	3	9	7	20	90	90	No

ID= participant reference, ASESFS= arthritis self-efficacy scale function subscale

Table 3. Clinical outcomes of the matched non-SCD patients with severe arthropathy pain, who underwent periarticular injection therapy at during January 2018 to December 2023, total number=10 patients.

ID	Arthritis joint injected	Pre-therapy pain score	Pain after magnesium injection	Pain after dexamethasone injection	Pre-therapy sleep score	Sleep after magnesium injection	Sleep after dexamethasone injection	Pre-therapy ASESFS 100-feet walk in 20secs	100-feet walk after magnesium injection	100-feet walk after dexamethasone injection	Complication
B	Hip	7	1	2	4	8	8	30	90	80	No
D	Knee	9	1	1	2	9	7	30	90	90	No
F	Knee	9	1	1	3	9	8	30	90	90	No
H	Hip	7	1	2	4	8	8	30	90	80	No
J	Knee	8	1	1	3	9	8	30	90	90	No
L	Knee	9	1	1	3	9	8	20	90	90	No
N	Hip	8	2	2	2	8	7	20	90	80	No
P	Knee	8	1	1	3	9	7	20	90	90	No
R	Knee	9	1	1	2	9	8	30	90	90	No
T	Hip	8	2	2	3	8	8	30	90	80	Insomnia after dexamethasone 24hrs

ID= participant reference, ASESFS= arthritis self-efficacy scale function subscale

Discussion

Our study involved adult males who regularly used oral codeine or tramadol analgesics, and these low-potency opioids are similarly effective for managing moderate pain. Our data shows that hip or knee arthropathy is associated with significant pain, corroborating previous studies [2,11]. Despite regular opioid analgesics, the patients' pain was compounded by insomnia. Insomnia is a complication of chronic pain [9]. The pain also limited the walking ability of most patients since it affected the major lower limb joints.

Most SCD patients in our study are black African, corroborating many publications [1,2,5]. Other SCD patients are of Persian, Arab, and Mediterranean ancestry. Adrenocortical insufficiency worsens arthropathy pain, and pain acts as a further stressor in SCD, perpetuating the cycle of inflammation and pain. Therefore, periarticular steroid injections benefit SCD arthropathy pain. Periarticular dexamethasone injection significantly improved the sleep, analgesia, and ambulation of our SCD patients. Most of the SCD patients (90%) did not have complications after repeated dexamethasone injections. This indicates that periarticular dexamethasone injection provides safe, reliable, and effective analgesia for SCD arthropathy.

One SCD patient had a sickle cell crisis after bilateral hip joint dexamethasone injections. The crisis was possibly precipitated by the multiple joint injections and relatively higher steroid dose. The patient recovered from the crisis, and subsequent dexamethasone injections into a single joint were uneventful. These findings indicate that periarticular steroid injection in SCD should be limited to a single joint, and the injectate dose limited to dexamethasone 10mg. The post-injection crisis occurred during the winter influenza season. The crisis was possibly triggered by hypothermia and/or viraemia. Hypothermia may precipitate illness and hospitalisation [12]. This finding suggests that periarticular steroid injection should be avoided in SCD during vulnerable situations such as hypothermia or infection.

Our study revealed similar outcomes after periarticular magnesium or dexamethasone injections. It highlights the suitability and efficacy of magnesium injection for arthropathy pain management. It indicates that magnesium injection is a safe and effective alternative to steroid injection, especially in situations warranting steroid avoidance, such as SCD morbidity, infections, immunocompromise, or immediate post-vaccination.

Magnesium is essential in the haematological, immune, cardiovascular, respiratory, musculoskeletal, and neurological systems [8]. Magnesium may benefit SCD by enhancing erythrocytes' liquid content, preventing deformation. Magnesium reduces pain and central sensitisation [4,8]. This possibly contributed to our study's pain reduction and sleep improvement.

There is controversy about steroid therapy tolerance in SCD [1]. However, our study showed that most SCD patients did not have complications after repeated periarticular dexamethasone injections. This suggests that dexamethasone injection may be safely employed in SCD patients, especially if there is no hypothermia, infection, immunocompromise, high steroid dose, or multiple joint injections. Nonetheless, magnesium injection is a better and safer alternative in situations that require steroid avoidance. Also, magnesium injection is cheaper than dexamethasone injection. Magnesium injection costs 1 USD per dose of 1000mg, while dexamethasone injection costs 2 USD per dose of 10mg.

One non-SCD patient had insomnia after initial dexamethasone injections. However, subsequent treatments were not complicated by insomnia. Chronic pain is associated with insomnia, and steroids occasionally disrupt the normal circadian rhythm, thereby aggravating insomnia. On the contrary, magnesium enhances the circadian rhythm, promotes neuromuscular homeostasis, reduces stress, and improves sleep [8]. Indeed, magnesium is beneficial for chronic pain patients. Periarticular magnesium injection therapy promotes value-based healthcare for SCD arthropathy patients.

Conclusions

SCD arthropathy pain is significant. Periarticular magnesium injection provides safe and effective analgesia in SCD. Periarticular dexamethasone injection may be employed in SCD patients if there is no hypothermia, infection, immunocompromise, high steroid dose, or multiple joint injections. Magnesium injection is a safe and reliable alternative to steroid injection for managing severe arthropathy pain, especially in situations that require steroid avoidance.

Conflict of Interest

All the authors declare no conflict of interest.

Acknowledgement

All the authors testify that all persons designated as authors qualify for authorship and have checked the article for plagiarism. All the authors were involved in writing initial and final drafts, proofreading, critical review, and approval of the final article draft.

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