



Musculoskeletal steroid injections during the COVID-19 pandemic

Mark Bugeja^{*}, Jasmine Mariani, Jessica Dowling, Giulia Stringaro, Jean Luc Portelli, Kurstein Sant, John Casaletto

Department of Trauma, Orthopaedics and Sports Medicine, Mater Dei Hospital, Triq Dun Karm, Msida, MSD2090, Malta

ARTICLE INFO

Keywords:
Covid-19
Musculoskeletal
Corticosteroid injection
Malta

ABSTRACT

Introduction: This study aims to determine whether musculoskeletal corticosteroid injections increase the risk for COVID-19.

Method: 734 patients who received a corticosteroid injection during the COVID-19 pandemic were followed and their COVID status within 30 days after the injection checked. The results were then compared with an age and sex matched control group.

Results: No statistically significant difference in the frequency of COVID-19 cases between the two groups was found.

Conclusion: It appears that the use of musculoskeletal corticosteroid injections during the COVID-19 pandemic does not confer increased risk of contracting the virus.

1. Introduction

1.1. Musculoskeletal corticosteroid injections

Corticosteroid injections are routinely used for the localised management of a broad range of painful musculoskeletal conditions, with the knee and shoulder being the two most common areas injected.^{1–3} The injection is predominantly given to patients suffering from joint arthritis, bursitis, tendinopathy, and synovitis.^{1,2} The objective is to control pain, improve the quality of activities of daily living, increase range of motion, and in some instances it may also delay or prevent surgery.¹ The injection offers a high concentration of corticosteroid at the site of injection, thus exerting its anti-inflammatory and immunosuppressive effects locally with limited systemic absorption.² The first corticosteroid injection dates back to 1950 when George W. Thorn instilled 10 mg 17-hydroxycorticosterone into the painful knee of a patient suffering from rheumatoid arthritis.⁴ Apart from improvement in knee symptoms there was coincidentally a general improvement in the condition itself, thus reflecting its systemic effects.⁴ The systemically absorbed steroid is metabolised in the liver and then excreted by the kidneys, thus, systemic absorption apart from being dependent on the size of area injected, steroid preparation used, dose and frequency of the injection, it is also dependent on liver and renal function.²

The concern with systemic absorption of the injected corticosteroid

is suppression of the hypothalamic-pituitary-adrenal (HPA) axis.² The lowest serum cortisol (maximum HPA suppression) occurs within the first two days.² Increased HPA suppression occur when multiple joints have been injected, when steroid dose is split, and when higher doses are used. The serum cortisol levels usually return to baseline after 1–2 weeks following the usual dose (40–80 mg) of methylprednisolone, 2–4 weeks in triamcinolone hexacetonide and beyond 28 days in triamcinolone acetonide.²

There is concern with the transient immunosuppression caused by musculoskeletal corticosteroid injections, which can compromise the humoral immune response, and thus, susceptibility to viral infections. In view of this Terin et al.⁵ conducted a study with the aim to determine whether musculoskeletal corticosteroid injection was associated with increased Influenza risk. This was a retrospective study of 15,068 patients who received musculoskeletal corticosteroid injection at Mayo Clinic in Rochester, Minnesota just before or within the five influenza seasons spanning from 1st August 2012 to 31st March 2017.⁵ It was noted that the risk for influenza was higher in patients receiving a musculoskeletal corticosteroid injection, even in those following the influenza vaccine. Surprisingly, women younger than 65 years had a higher risk for influenza than older individuals.⁵

On 11th March 2020, with COVID-19 cases outside China increasing 13-fold, thousands of people losing their lives and thousands more fighting for their lives in hospital, the World Health Organisation (WHO)

^{*} Corresponding author.

E-mail addresses: mark.a.bugeja@gov.mt (M. Bugeja), jasmine.mariani@gov.mt (J. Mariani), jessica.dowling@gov.mt (J. Dowling), giulia.stringaro@gov.mt (G. Stringaro), jean-luc.a.portelli@gov.mt (J.L. Portelli), kurstein-nicholas.sant@gov.mt (K. Sant), jacasaletto@gmail.com (J. Casaletto).

<https://doi.org/10.1016/j.jor.2021.07.017>

Received 15 June 2021; Accepted 20 July 2021

Available online 21 July 2021

0972-978X/© 2021 Published by Elsevier B.V. on behalf of Professor P K Surendran Memorial Education Foundation.

declared the COVID-19 outbreak a pandemic and a global health emergency.⁶ Concerns with the use of musculoskeletal injections possibly causing increased risk for COVID-19 infection from their transient immunosuppressive effects quickly gathered momentum. This led to various guidelines being issued around the globe.

1.2. Guidelines

The British Society of Skeletal Radiologists (BSSR) issued a positional statement on the 25th March 2020 stating that musculoskeletal corticosteroid injections should be avoided, and that vulnerable patients (elderly and those with comorbidities) should not receive corticosteroid injections during the COVID-19 pandemic.⁷ The Association of Chartered Physiotherapists in Orthopaedic Medicine and Injection Therapy (ACPOMIT), together with the British Association of Spinal Surgeons (BASS), the British Society of Rheumatology (BSR), and the British Orthopaedic Association (BOA) in March 2020 issued guidelines stating that musculoskeletal corticosteroid injections should only be used for inflammatory arthropathy where there is acute synovitis, and to consider using low doses.⁸ For non-inflammatory musculoskeletal pain, they advise to only consider injection if patient has debilitating pain, that has not responded to other alternatives, and if the symptoms persist will impact their health and wellbeing negatively.⁸ The Faculty of Pain Medicine of the Royal College of Anaesthetist (FPM) published a statement on 17th March 2020 stating that corticosteroid injections must not be given to patients with active COVID-19 infection, and that the clinician should be cautious when considering giving corticosteroid injection due to concern of immunosuppression, as harm might arise in those incubating or later develop COVID-19.⁹

Same guidelines were also published in America. Miller et al.¹⁰ on behalf of the Spine Intervention Society (SIS) published a clinical perspective paper stating that patients without severe pain should postpone their corticosteroid injection until after the COVID-19 pandemic abates. In March 2020, the American Society of Regional Anaesthesia and Pain Medicine (ASRA) and the European Society of Regional Anaesthesia and Pain Therapy (ESRA) issued a joint statement advising clinicians to use musculoskeletal corticosteroid injection with caution and to use a lower dose, especially in high risk individuals.¹¹ More recently on the 3rd February 2021, the American Academy of Orthopaedic Surgeons (AAOS) advised orthopaedic surgeons to consider other alternatives if possible during the COVID-19 pandemic, and if corticosteroids are deemed necessary, it advises on using the lowest dose that is clinically effective.¹²

1.3. Aim

With elective surgeries being postponed in view of the COVID-19 pandemic, it is being estimated that more patients will be in debilitating pain awaiting a date for their surgery. Therefore, we conducted a retrospective study to determine whether musculoskeletal corticosteroid injections are safe during the COVID-19 pandemic.

2. Materials and methods

2.1. Demographics

With an area of just 316 km² and a population of 514,564 individuals, Malta is one of the smallest and densely populated in the world.¹³ Due to the small geographical size of the island and 7 testing centres, Malta was able to provide extensive easy access to swabbing.¹³ The overall positivity rate of the COVID-19 Reverse Transcription Polymerase Chain Reaction (RT-PCR) tests as at 12th June 2021 was 3.21% (total number of swabs 951,303; total number of COVID-19 cases 30,581).¹³ This reflects the extensive testing done in Malta even for people with mild or no symptoms, possibly aided by the free health care system in Malta. The total number of tests per 1,000,000 population till the 12th

June 2021 was 2,149,094 in Malta, which is similar to that in the United Kingdom (2,832,849 swabs per 1,000,000 population), but higher than that in the United States of America (1,483,637 swabs per 1,000,000 population). All the COVID-19 RT-PCR tests performed in Malta are held on a centralised hospital database identifiable by a single national identity number.

2.2. Study design

This study was conducted retrospectively from 2nd March 2020 to 29th January 2021 during the COVID-19 pandemic in Malta, following approval by the institutional data protection unit. The start date was chosen with respect to the first reported cases of COVID-19 in Malta. This study consists of all patients, the firm of single orthopaedic firm reviewed and administered corticosteroid injections during this time period. The corticosteroid used was methylprednisolone acetate (Depo-Medrone® by Pfizer US) with a dosage of 40 mg mixed with bupivacaine hydrochloride. For every patient the following data was collected: identification number, sex, age, date of injection, site of injection, and their COVID-19 status during the month following the corticosteroid injection. COVID-19 status was found using the hospital's electronic patients' medical record, iSOFT Clinical Manager (iCM) version 2.4. The test used to diagnose COVID-19 in Malta was the COVID-19 RT-PCR test, taken as a nasal swab. Patients who tested positive in the COVID-19 RT-PCR test within 1 month following the corticosteroid injection were noted.

To determine whether patients testing positive for COVID-19 within 1 month of receiving musculoskeletal corticosteroid injection was related to the injection, a control group was set up. For each patient in the study group, a patient with the same age and sex, but who has not received a corticosteroid injection was randomly selected and placed in the control group. A computer program was used to randomly generate an identification number keeping the last two digits of the identification number of the corresponding patient in the study group. The last two digits of the national identity number correspond to the year of birth registration; therefore, this gave an identification number with the same age as the corresponding patient in the study group. If the identification number did not belong to an individual with the same sex as the study group, another number was generated until an individual with the same age and sex as the corresponding individual in the study group was obtained. The COVID-19 status of the individuals who underwent a COVID-19 RT-PCR test within the same study period to their corresponding matched individual in the study group, was then checked using iCM version 2.4.

2.3. Data analysis

StatsDirect Statistical software version 3.0 was used for data analysis. The study group and the control group were then compared for any statistical significance in the number of positive cases using Fisher Exact Test. Our null hypothesis (H_0) for this study was that there is no statistically significant difference in the number of COVID-19 positive individuals in both groups.

3. Results

Between 2nd March 2020 to 29th January 2021, we collected data on 734 patients that received one or more musculoskeletal corticosteroid injections by one orthopaedic team. Patients' ages ranged from 19 to 90 years ($M = 56$, $SD = 13.4$) with 56% ($n = 411$) being female and 44% ($n = 322$) being male. The site(s) of injection and the number of patients receiving the injection in this/these sites are shown in Table 1. Since the patients were under the care of an orthopaedic upper limb specialty team, most of the patients were given injections around the shoulder and elbow areas.

There were 4 patients (0.54%) who tested positive for COVID-19

Table 1
Musculoskeletal corticosteroid injection sites.

Site(s) of corticosteroid injection	No. of patients
Glenohumeral joint	404
Glenohumeral joint and subacromial bursa	91
Levator scapulae and trapezius muscle	53
Subacromial bursa	42
Acromioclavicular joint	34
Elbow – common extensor origin	33
Acromioclavicular joint and subacromial bursa	16
Trochanteric bursa	15
Glenohumeral joint, subacromial bursa, and acromioclavicular joint	10
Finger A1 pulley	5
Glenohumeral joint and peri coracoid area	4
Glenohumeral joint and suprascapular nerve	3
Peri-Coracoid area	3
Rhomboid muscles	3
Glenohumeral joint and thumb carpometacarpal joint	3
First wrist extensor compartment	3
Glenohumeral joint, subacromial bursa, and 1st wrist extensor compartment	2
Coracoid space and acromioclavicular joint	2
Plantar fascia	2
Scapulothoracic bursa	2
Knee joint	3
Elbow – common flexor origin	1

within 30-days of receiving the corticosteroid injection. Table 2 shows the details of these 4 patients. In the control group there were 3 patients (0.41%) who tested positive for COVID-19 during the same 30-day frame as their corresponding patient in the study group.

Using the Fisher’s exact test, at a p-value of <0.05 there was no statistically significant difference between the study and the control group (Table 3). Therefore, the null hypothesis of this study was not rejected.

4. Discussion

A recent literature review showed that only two studies have been published to determine the safety of corticosteroid injections during the COVID-19 pandemic.^{1,3} Mohamad et al.¹ conducted a retrospective study at the sports medicine clinic and the orthopaedic clinic in Queen Elizabeth Hospital and Queen Elizabeth II Hospital, in the state of Sabah, Malaysia, between 1st December 2019 and 30th June 2020. This study enrolled 35 patients, and these were given triamcinolone as a steroid injection with a dose of 20 mg for fingers and 40 mg for other body areas.¹ Patients were then contacted via telephone and enquired about COVID-19 symptoms, and about attendance to clinics or hospitals for COVID-19 screening.¹ None of the patients developed any COVID-19 symptoms following steroid injection.¹ The study by Mohamad et al.¹ has some limitations in view of the very small number of patients when the prevalence of COVID-19 in Malaysia was low. Another potential limitation is that none of the participants were screened for COVID-19 as they were asymptomatic, therefore, the true number of COVID-19 infections in the study performed by Mohamad et al.¹ rests unknown.

Another study similar study but with more patients was published by McKean et al.³ This was a retrospective observational study at Stoke Mandeville Hospital, Aylesbury, UK on 443 patients who received one or more intraarticular corticosteroid injection between 1st February 2020 and 30th June 2020. High risk patients were excluded. The steroid used in the study by McKean et al.³ were 6.6 mg dexamethasone for nerve root injections, 40 mg triamcinolone acetate for facet and large joint injection, and 40 mg methylprednisolone for small joints. Like the study by Mohamad et al.¹ only those symptomatic or hospitalised were screened for COVID-19. From all the 443 patients only 8 patients were screened for COVID-19, with half of them being symptomatic and the other half due to routine RT-PCR COVID swab during a hospital admission. From the 8 patients who underwent the screening, none

Table 2
Demographic data of patients testing positive for COVID-19 within 30-days of receiving the corticosteroid injection.

Sex	Age	Location of injection	Date of injection	Date of COVID-19 positive	No. of days till positive
Female	65	Right glenohumeral joint and right thumb	07/03/2020	05/04/2020	29
Female	71	Right glenohumeral joint and subacromial space and left first extensor compartment	26/08/2020	01/09/2020	6
Female	39	Right glenohumeral joint and subacromial space	05/12/2020	28/12/2020	23
Female	56	Right glenohumeral joint	06/01/2021	17/01/2021	11

Table 3
Fisher’s exact test.

	Positive	Negative	Total
Study group	4	730	734
Control group	3	731	734
Total	7	1461	1468

The two-tailed p-value equals 1.0. The association between the groups and the outcomes is considered to be not statistically significant.

tested positive for COVID-19.³

The studies by Mohamad et al.¹ and McKean et al.³ included a small number of patients and had no control group. This precluded the authors to determine the relative risk of steroid injection over the general population. Our study included more patients and made use of an age and sex matched control group. The island centralised database for RT-PCR COVID-19 results enables us to identify all positive results in both groups.

This study has its limitations. Despite having much more patients than the studies by Mohamad et al.¹ and McKean et al.,³ the numbers are still relatively small and a future large population-based studies are necessary. Another limitation that is universal to our study and the studies by Mohamad et al.¹ and McKean et al.³ is that not all the individuals in the study and control group were screened for COVID-19 prior to the infiltration. Only those who were symptomatic or hospitalised were screened for COVID-19, thus asymptomatic COVID-19 infections were not detected in these studies.

5. Conclusion

This study shows no increased risk of contracting RT-PCR diagnosed COVID-19 following musculoskeletal corticosteroid injections. Given the lengthy cessation of elective orthopaedic surgery during the COVID-19 pandemic, and the very long waiting lists, musculoskeletal corticosteroid injections are expected to be important therapeutic option for patients waiting for surgery. Based on the results of this study, it appears that the use of musculoskeletal corticosteroid injections during the COVID-19 pandemic is safe.

Sources of funding

The research did not receive any specific grant from funding agencies in public, commercial or non-profit sectors.

Declaration of competing interests

The authors have declared no conflict of interest.

Acknowledgements

None.

References

- 1 Azwan Aziz M, Abu Hanifah R, Mohd Nahar AM. Musculoskeletal corticosteroid injection during COVID-19 pandemic in Sabah: is it safe? *Adv Orthop*. 2021;2021: 1–6. <https://doi.org/10.1155/2021/8863210>.
- 2 Johnston PC, Lansang MC, Chatterjee S, Kennedy L. Intra-articular glucocorticoid injections and their effect on hypothalamic–pituitary–adrenal (HPA)-axis function. *Endocrine*. 2015;48(2):410–416. <https://doi.org/10.1007/s12020-014-0409-5>.
- 3 McKean D, Chung SL, Fairhead R, et al. Corticosteroid injections during the COVID-19 pandemic. *Bone Jt Open*. 2020;1(9):605–611. <https://doi.org/10.1302/2633-1462.19.BJO-2020-0130.R1>.
- 4 Hollander JL, Brown EM, Jessar RA, Brown CY. Hydrocortisone and cortisone injected into arthritic joints: comparative effects of and use of hydrocortisone as a local antiarthritic agent. *J Am Med Assoc*. 1951;147(17):1629–1635. <https://doi.org/10.1001/jama.1951.03670340019005>.
- 5 Sytsma TT, Greenlund LK, Greenlund LS. Joint corticosteroid injection associated with increased influenza risk. *Mayo Clin Proc Innov Qual Outcomes*. 2018;2(2): 194–198. <https://doi.org/10.1016/j.mayocpiqo.2018.01.005>.
- 6 WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. Accessed May 9, 2021 <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-11-march-2020>.
- 7 British Society of Skeletal Radiologists. The safety of corticosteroid injections during the COVID-19 global pandemic. Accessed April 28, 2021 <https://bssr.org.uk/position-and-policy/safety-msk-corticosteroid-injections-covid19>; 2020. March.
- 8 ACPOMIT BASS, BSR BOA. Corticosteroid use for musculoskeletal and rheumatic conditions during COVID-19 pandemic. Published online <https://www.boa.ac.uk/uploads/assets/30a67bae-1e3a-4b76-bf97b7f86600230b/Corticosteroid-use-for-musculoskeletal-and-rheumatic-conditions-during-COVID-19-Pandemic-V1.pdf>; 2020, 1-4.
- 9 Faculty of Pain Medicine of the Royal College of Anaesthetist. COVID-19: FPM response to concerns over safety of injected steroids for pain procedures. Published <https://fpm.ac.uk/sites/fpm/files/documents/2020-03/FPM-COVID-19-Steroid-Statement-2020-v2.pdf>; 2020. Accessed April 28, 2021.
- 10 Miller DC, Patel J, Gill J, et al. Corticosteroid injections and COVID-19 infection risk. *Pain Med*. 2020;21(8):1703–1706. <https://doi.org/10.1093/PM/PNA1199>.
- 11 Shanthanna Harsha, Cohen Steven P, Strand Natalie, et al. Recommendations on chronic pain practice during the COVID-19 pandemic. Published https://www.asra.com/content/documents/asra_esra_covid-19_and_chronic_pain.pdf; 2020.
- 12 American Academy of Orthopaedic Surgeons. Guidance summary: use of corticosteroids for musculoskeletal pain during the COVID-19 pandemic. Published <https://www.aaos.org/about/covid-19-information-for-our-members/guidance-for-elective-surgery/use-of-corticosteroids-for-musculoskeletal-pain-during-the-covid-19-pandemic/>; 2021.
- 13 Government of Malta. Government of Malta services and information. Accessed June 12, 2021 <https://www.gov.mt/en/Pages/home.aspx>.