Observational Studies

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Risk of infection within 4 weeks of corticosteroid injection (CSI) in the management of chronic pain during a pandemic: a cohort study in 216 patients

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Abstract

Objectives: Targeted corticosteroid injections (CSI) are one of the treatments that can provide pain relief and thereby, enhance quality of life in patients with chronic pain. Corticosteroids (CS) are known to impair immune response. The objective was to evaluate the risk of developing post-procedural infection within 4 weeks of receiving depot CSI for chronic pain as part of on going quality improvement project. We hypothesised that interventional treatment with depot steroids will not cause a significant increase in clinical infection in the first 4 weeks.
Methods: Telephone follow-up was performed as a part of prospective longitudinal audit in a cohort of patients who received interventional treatment for chronic pain at a multidisciplinary pain medicine centre based at a university teaching hospital. Patients who received interventional treatment in the management of chronic pain under a single physician between October 2019 and December 2020 were followed up over telephone as part of on going longitudinal audits. Data was collected on any infection within 4 and 12 weeks of receiving the intervention. Outcomes collected included type of intervention, dose of depot steroids and pain relief obtained at 12 weeks following intervention.
Results: Over a 15 month period, 261 patients received pain interventions with depot CS. There was no loss to follow-up. Nine patients reported an infection within 4 weeks of receiving depot steroids (9/261, 3.4%). None of the patients tested positive for Covid-19. Eight patients (8/261, 3%) reported an infection between 5 and 12 weeks following the corticosteroid intervention. Although none of the patients tested positive for Covid-19, two patients presented with clinical and radiological features suggestive of Covid-19. Durable analgesia was reported by 51% (133/261) and clinically significant analgesia by 30% (78/261) at 12 weeks following the intervention. Failure rate was 19% (50/261).
Conclusions: Pain medicine interventions with depot steroids do not appear to overtly increase the risk for Covid-19 infection in the midst of a pandemic.

Keywords: chronic pain; corticosteroid injection; Covid-19 infection; immunosuppression.

Introduction

Chronic pain can cause significant dysfunction in the quality of life. Targeted corticosteroid injections (CSI) have been shown to provide pain relief and thereby, enhance quality of life in patients with chronic pain [1, 2]. Corticosteroids (CS) produce alleviation of pain by both anti-inflammatory and a direct analgesic mechanism [3–6]. CS is also used in other areas of medicine including rheumatology, dermatology, organ transplant and remains the mainstay of treatment in certain musculoskeletal conditions affecting the hand and wrist [7].

CS are known to impair immune response [8]. Epidural CSI have been shown to suppress the hypothalamic-pituitary-adrenal axis (HPA) for up to 4 weeks [9–11]. Systemic CS can impair both innate and adaptive immune response [8]. There is low quality evidence that intra-articular CSI can increase the risk of contracting influenza virus [12]. As a result, various regulatory bodies have advised against adding CS to pain interventions or to significantly reduce the dose [13–16]. This diktat could risk denying an effective treatment to patients who often have very limited options available to manage their chronic pain. On the other hand, there is some evidence that CS can enhance the innate immune response [17].

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Currently, the risk of developing clinical infection following CSI is unknown. This information is essential when discussing the risks of CSI during informed consent process. A prospective longitudinal follow-up of over 200 patients receiving CSI in the management of chronic abdominal pain had not revealed post-procedural infection as a significant risk factor [18]. We hypothesised that interventional treatment with depot steroids will not cause a significant increase in clinical infection in the first 4 weeks following CSI.

Covid-19 pandemic provided an opportunity to confirm the potential risk of developing infections in patients with chronic pain who have received CSI. The authors present a report on 261 patients who received depot CSI during the Covid-19 pandemic.

Methods

Adult patients under the care of a single pain medicine physician (GN) who received interventional treatment in the management of chronic pain from 9th October 2019 to 23rd December 2020 were included in this cohort study. The report is from a tertiary pain medicine unit based in a university hospital in the United Kingdom. The current work was performed as a part of prospective longitudinal audits that are registered with Clinical Audit and Safety (CASE), University Hospitals of Leicester NHS Trust [18, 19]. The patients provided written consent for telephone review and for the use of the de-identified data for data analysis and publication in a peer-reviewed journal.

Patients were followed up over telephone at 4 and 12 weeks following CSI. Patients were asked about any infection including influenza and Covid-19 within 4 weeks as well as within 12 weeks of receiving CSI. Specific information on the type of infection, antibiotic treatment, hospitalisation and Covid-19 testing (reverse transcription-polymerase chain reaction test, RT-PCR) were collected. Outcomes collected included diagnosis, type of intervention, dose of depot CS used and percentage pain relief obtained at 12 weeks after intervention. Data on patient's co-morbidity and current dose of opioid medication was also collected.

Effectiveness of the intervention was classified into three groups based on patient reported outcomes. Failure was defined as absence of 30% pain relief at 12 weeks following the intervention. Clinically significant pain relief was 30–40% relief at 12 weeks. Durable pain relief was ≥50 relief at 12 weeks [2].

Statistical analysis of the results was performed using Stata version 13.1 (Statacorp LC, Texas) statistical package for Windows (Microsoft Corp.).

Results

Over a 15 month period between October 2019 and December 2020, 261 patients received CSI under a single physician. The pain medicine service was temporarily suspended from 14th March 2020 to 26th June 2020 as well as between 5th November 2020 and 4th December 2020 due to a surge in Covid-19 pandemic.

There was no loss to follow-up and telephone follow-up data was available for 261 patients (100%). Demographic data are provided in Table 1. All patients received depot methylprednisolone. The mean (range) dose of depot methylprednisolone used was 74 mg (60–100 mg).

Nine patients reported an infection within 4 weeks of receiving CSI (Table 2). None of the patients tested positive for Covid-19, required organ support or hospitalisation.

Eight patients reported an infection between 5 and 12 weeks of receiving CSI (8/261, 3%). Four patients developed pneumonia, needed hospitalisation but did not require mechanical ventilation. Although none of the patients tested positive for Covid-19, clinical and radiological features were suggestive of corona virus infection in two patients with significant respiratory co-morbidities (Table 3).

Interventions included ultrasound guided (USG) trigger point injection, abdominal plane blocks (chronic abdominal pain), USG trigeminal nerve block, cervical plexus block and greater occipital nerve block (facial pain), USG cervical plexus block (whiplash-associated disorder), fluoroscopy guided sacroiliac joint injection (sacroiliac joint dysfunction) and USG peripheral nerve blocks (greater occipital, genito-femoral, lateral cutaneous nerve of thigh, erector spinae plane block) for peripheral neuropathy.

Co-morbid conditions were reported by 61% (160/261) patients. Ninety-seven patients reported being on opioid medication (37%, 97/261). This included weak opioid

Table 1: Demographic data, clinical diagnosis and type of interventional treatment with corticosteroids (CS).

Demographics	**Patients (n=261)**
Age, years (mean ± SD)	50.4 ± 16.2
Gender, n, %	
Male	102 (39%)
Female	159 (61%)
Diagnosis, n, %	
Chronic abdominal pain	112 (42.9%)
Trigeminal neuropathic pain	36 (13.8%)
Sacroiliac joint dysfunction	39 (14.9%)
Chronic headaches	11 (4.2%)
Whiplash associated disorder	38 (14.6%)
Peripheral neuropathic pain	25 (9.6%)
Intervention performed, n, %	
Abdominal plane block	66 (25.3%)
Trigeminal nerve block	37 (14.2%)
Cervical plexus block	38 (14.5%)
Peripheral nerve block	35 (13.5%)
Sacroiliac joint injection	38 (14.5%)
Trigger point injection	42 (16.1%)
Erector spinae plane block	5 (1.9%)

Table 2: Type of infection, management of infection, co-morbidity and Covid-19 test in nine patients with infection within 4 weeks of corticosteroid injection.

Age, years, gender	Time since CSI	Type of infection	Antibiotic treatment	Hospital admission	Covid-19 RT-PCR	Co-morbidity
51, F	3 weeks	UTI	Yes	No	Negative	Hypertension
25, M[a]	2 weeks	Flu like	Yes	No	Not tested	None
24, F[a]	1 week	Injection site infection	Yes	No	Not tested	Raised BMI
68, F	4 weeks	Herpes Zoster	No	No	Negative	Multiple sclerosis
57, M	2 weeks	Flu like	No	No	Negative	Bronchiectasis, Asthma
43, F	4 weeks	UTI	Yes	No	Negative	None
79, M	2 weeks	Chest Infection	Yes	No	Negative	Asthma, Diabetes Mellitus
67, F	3 weeks	UTI	Yes	No	Negative	Hypertension
22, F	4 weeks	UTI	Yes	No	Negative	None

CSI, corticosteroid injection; Covid-19, corona virus 2019; RT-PCR, reverse transcription polymerase chain reaction; UTI, urinary tract infection; BMI, body mass index. [a]Prior to the onset of corona virus 2019 pandemic.

Table 3: Type of infection, management of infection, co-morbidity and Covid-19 test in eight patients with infection after 4 weeks and within 12 weeks of corticosteroid injection.

Age, years, gender	Time since CSI	Type of infection	Antibiotic treatment	Hospital admission	Covid-19 RT-PCR	Co-morbidity
58, F	7 weeks	Pneumonia	Yes	Yes	Negative	IHD, COPD, DM, PVD, cardiac failure
75, F	8 weeks	Pneumonia	Yes	Yes	Negative	Scleroderma, Sjogren's, lung fibrosis
33, M[a]	6 week	Pneumonia	Yes	Yes	Negative	Myasthenia gravis, recurrent thymoma, on immunosuppressant
68, F	8 weeks	Flu like	No	No	Negative	Hypertension, raised BMI
75, M[a]	10 weeks	Pneumonia	Yes	Yes	Negative	Multiple myeloma, COPD, bowel cancer
70, M	5 weeks	Flu-like	No	No	Negative	None
68, F	5 weeks	UTI	Yes	No	Negative	None
36, F	8 weeks	Ear infection	Yes	No	Negative	None

CSI, corticosteroid injection; Covid-19, corona virus 2019; RT-PCR, reverse transcription-polymerase chain reaction test; IHD, ischaemic heart disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; PVD, peripheral vascular disease; BMI, body mass index; UTI, urinary tract infection. [a]Clinical and radiological feature suggestive of Covid-19 although RT-PCR test was negative.

(codeine, tramadol) consumption in 64 patients (24.5%, 64/261) and strong opioid (morphine, oxycodone, methadone) use in 33 patients (12.6%, 33/261).

At 12 weeks follow-up, durable analgesia was reported by 51% (133/261) and clinically significant analgesia by 30% (78/261). Failure rate was 19% (50/261).

Discussion

Corticosteroid injection (CSI) does not appear to overtly increase the risk of developing Covid-19 infection within first 4 weeks of intervention for chronic pain. Nine patients (3.4%, 9/261) developed an infection within 4 weeks of CSI that were managed conservatively. All patients except two (pre-Covid-19 onset) underwent testing and none tested positive for Covid-19. This is despite 61% of patients having one or more co-morbid condition(s) known to increase the risk of developing severe Covid-19 infection and 12.6% of patients on potent opioid medication recognised to cause immunosuppression. We base our statement on the current evidence that suggests CSI induced impairment in immune response is the highest within in the first 2 weeks and thereafter tapers significantly at 4 weeks after treatment [10, 11]. Although immunosuppression may persist beyond 4 weeks, there are often other patient factors that could increase the susceptibility to secondary infections (Table 3).

Between 5 and 12 weeks post CSI, eight patients reported an infection (8/261, 2.3%). Although none of the eight tested positive, two patients with significant respiratory co-morbidities presented with clinical and radiological features suggestive of Covid-19 infection (2/261, 0.7%). However, despite the significant co-morbidities and CSI induced immunosuppression, it is encouraging to note that patients were managed conservatively and did not require mechanical ventilation.

During the Covid-19 pandemic, rheumatoid arthritis patients on prednisone (>10 mg/day) were reported to have a higher risk for hospitalisation [20]. In our cohort, none of the patients required hospitalisation within first 4 weeks of CSI (Table 2). Although there is evidence that CS can depress the HPA axis and suppress endogenous cortisol production, in our cohort, it did not translate into clinically significant immunosuppression in the midst of a highly infective viral pandemic. Covid-19 susceptibility is reported to be greater in the elderly population. The mean age of this cohort was 50 years and this may have afforded some protection.

There are questions on the role as well as the efficacy of steroids in the interventional management of patients with chronic pain. Steroids appear to alleviate pain by reducing inflammation through inhibiting the synthesis or release of a number of pro-inflammatory substances. Steroids also cause a reversible local anaesthetic effect [3–6]. The role of steroids has been explored primarily in chronic axial spinal pain. The evidence in this cohort ranges from limited to strong [21]. However, our cohort did not include any patient with axial spinal pain. Addition of CS to local anaesthetic can provide durable pain relief in chronic abdominal pain, trigeminal neuropathic pain and whiplash-associated disorder [18, 19, 22]. In patients with chronic abdominal pain, local anaesthetic alone failed to provide clinically significant pain relief at 12 weeks [2]. In the present cohort, intervention with depot steroids produced durable analgesia (≥50%) at 12 weeks in 51% of patients (133/261). CSI had a failure rate of 19%.

There are limited options available in the management of chronic pain. Medications once considered effective and safe have now fallen into disrepute. These include anti-depressants, opioids and gabapentinoids. A recent meta-analysis found anti-depressants to increase mortality by a third [23]. The evidence for opioids in patients with chronic non-cancer pain is limited and there is emerging evidence of significant harm from long-term use [24, 25]. Although gabapentinoids are effective in neuropathic pain, there are concerns with respect to misuse, abuse, diversion and mortality [26, 27]. A significant proportion of patients are unable to tolerate medications or refuse medications [19]. Neuromodulation techniques offer hope but are limited to selected tertiary centres in the UK. Psychological interventions, though beneficial, have limited efficacy in the management of moderate-severe pain [28].

A practise based evidence approach has shown that targeted interventions with depot CS can provide durable analgesia, reduce opioid consumption, improve quality of life and enhance satisfaction with pain management in a fair proportion of patients. [2, 18, 19]

In our practise, we limit CSI to two per year. Although there is a potential risk of developing infections, when given an informed choice, our patients prefer to have steroids. Over two-thirds of patients in this cohort were treated during the pandemic. All of them preferred to have steroids after an informed discussion on the benefits and risks including a high risk of developing severe Covid-19. We advised patients to self-isolate for 2 weeks following CSI.

Limitations of this report include single centre, single physician practise in a limited number of patients. A further limitation is that interventions with CSI were suspended and not performed during two periods of significant increase in Covid-19 infections. The authors are aware that the study design does not allow the relative risk to be estimated from the presented data. However, we believe this report could add further evidence in quantifying the risk of infection after CSI.

In conclusion, pain medicine interventions with depot steroids can produce clinically significant analgesia and does not appear to overtly increase the risk for Covid-19 infection during a pandemic.

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Informed consent: The authors' state that written informed consent was obtained from all patients.

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