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Updating the Power of Your Pen in Managing Pain

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Bexinfo pain is decorated with some recent pain related news which are collected from most authentic sources. We hope this small endeavor will help you in your daily practice.

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Pain: A potential New Pathway of COVID-19

The current coronavirus disease (COVID-19) pandemic led to a significant disruption in the care of pain. The spike protein on this virus binds the angiotensin-converting enzyme 2 (ACE2) receptor, mediating entry into human cells. It has been found SARS-CoV-2, induced a decrease of membrane ACE2 receptors on host cells, resulting in an imbalance of ACE/ACE2 and triggering severe lung injury. However, multiple studies have also detected SARS-CoV-2 in the cerebrospinal fluid of infected patients. Neurological symptoms such as disturbance of consciousness, epilepsy and neuralgia may indicate invasion of SARS-CoV-2 into the central nervous system. Previous studies showed that the angiotensin-converting enzyme/Angiotensin II/Angiotensin II type 1 receptor (ACE/Ang II/AT1 receptor) receptor pathway facilitated pain transmission in the spinal dorsal horn, while the ACE2/angiotensin (1–7)/Mas receptor (ACE2/Ang (1–7)/Mas receptor) receptor pathway might alleviate pain through the inhibition of p38 mitogen-activated protein kinase phosphorylation. Researchers suggest that SARS-CoV-2 might infect the ACE2-positive cells in human spinal dorsal horn; the decrease of functional ACE2 then results in the accumulation of Ang II and the decrease of Ang (1–7); consequently, SARS-CoV-2 infection in the spinal cord could induce pain. In addition to the spinal dorsal horn, SARS-CoV-2 also attacks ACE2-positive cells in other tissues, such as the alimentary canal, kidney and heart, leading to damage to these tissues. Besides the direct attack, SARS-CoV-2 may cause “cytokine storm”, involving interleukin (IL)-6, IL-10 and tumor necrosis factor (TNF)-α. This cytokine storm may induce or aggravate damage in various tissues such as joints and muscle, triggering pain-related symptoms. Because of the effect of spinal ACE2 on pain sensation and the direct or indirect tissue damage induced by SARS-CoV-2, the potential burden of pain induced by COVID-19 cannot be ignored, especially considering the extent of the infected population.

Medications in COVID-19 patients: From an orthopedic perspective

Currently, the literature is abundant with publications about COVID-19, including the effects of various medications on COVID-19. Regarding the use of medications in orthopedic perspective during this COVID 19 pandemic, a systematic review was performed by using the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. This review aims to provide a summary of the current literature regarding common medications prescribed in orthopedic surgery and their potential implications in COVID-19 patients. The following are some important recommendations and take-home messages in the field of orthopedics from the review. Firstly, paracetamol remains the first line of analgesia and antipyretic for COVID-19 patients. Paracetamol has been stated to be the first-line analgesia according to the World Health Organization (WHO) pain ladder. No studies published have reported a untoward effect of paracetamol on COVID-19 patients. Secondly, there is no need to avoid NSAIDs for COVID-19 patients based on the current available literatures. Thirdly, opioids have the potential for immunosuppression in addition to respiratory depression and, therefore, should be prescribed with care in COVID-19 patients, with buprenorphine appearing to be the safest for use in the immunocompromised or elderly patients susceptible to infections. Fourthly, patients with conditions where steroids are proven to be efficacious can continue to receive their steroids; otherwise, systemic steroids are not recommended for COVID-19 patients in view of the potential risks. Fifthly, orthopedic surgeons following up on patients with COVID-19 who are using steroids should continue following up these patients for a longer duration in view of possible avascular necrosis. Sixthly, whenever possible, oral anticoagulation should be converted to parental heparin to minimize overtreatment or undertreatment with oral anticoagulation. Seventhly, common orthopedic antibiotics including penicillin and clindamycin are safe to continue for COVID-19 patients. Lastly, vitamins B, C and D potentially have therapeutic benefits for COVID-19 patients, and therefore, prescription for these vitamins should continue as per usual clinical practice.

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COVID-19: Revisiting Inflammatory Pathways of Rheumatoid Arthritis

Coronavirus disease 2019 (COVID-19) is an infectious disease, caused by severe acute respiratory syndrome coronavirus 2, which predominantly affects the lungs and, under certain circumstances, leads to an excessive or uncontrolled immune activation and cytokine response in alveolar structures. The pattern of pro-inflammatory cytokines induced in COVID-19 has similarities to those targeted in the treatment of rheumatoid arthritis. Both diseases lead to profound inflammation of structures that form the inner surfaces of the body and induce tissue destruction and responses that lead to organ failure. COVID-19 is characterized by an excessive or uncontrolled host immune response, elicited by alveolar epithelial cell damage and T cell activation in the lungs that triggers exaggerated local production of pro-inflammatory effector cytokines and leads to the attraction of large numbers of neutrophils and macrophages to the lungs. Barrier damage, T cell activation, effector cytokine production and neutrophil influx are also key features of synovitis, and some of the mediators are shared between COVID-19 and RA. The bulk of inflammation and structural damage in COVID-19 is limited to the lungs, which are progressively destroyed. Furthermore, and most likely owing to robust IL-6 activation, COVID-19 leads to systemic acute-phase responses, which are shared with RA. Whether cytokine inhibition can block this process remains to be determined, but a rationale exists for this approach. Surprisingly, the original widespread concerns about using cytokine inhibitors in a potentially life-threating infectious disease such as COVID-19 have been balanced by the recognition that a pathological hyper-inflammatory state is driving the pathology and might require therapeutic cytokine inhibition. These concepts will also affect our advice to patients with arthritis about whether to stop or continue anti-rheumatic therapy. Given that most of these treatments do not increase the risk of viral pneumonia, that glucocorticoids, which are often used to treat flares, are potentially deleterious in COVID-19, and that preliminary data from high-risk areas do not suggest an increased risk of COVID-19 in patients with arthritis, anti-rheumatic therapy should be continued during the pandemic and not be pre-emptively stopped.

During COVID-19 Isolation Exercise is Key to Improve Disease Symptoms of Rheumatic Disease

Patients with rheumatic disease should be encouraged to undertake appropriate exercise programs to combat the physical inactivity imposed by self-isolation during the COVID-19 pandemic. In commentary published in *Nature Reviews Rheumatology*, Bruno Gualan, Ph.D., of the Universidade de SÃ£o Paulo in Brazil, and colleagues have discussed the effects of both physical inactivity and activity on patients with rheumatic diseases, along with appropriate exercise regimes for these patients. Sustained hypoactivity is associated with poor physical and mental health and increased mortality risk. In patients with rheumatoid arthritis, hypoactivity is associated with poor disease-related outcomes, including high disease activity, fatigue and pain, along with cardiometabolic risk factors, such as obesity and insulin resistance. In children with rheumatic disease, prolonged inactivity may lead to muscle atrophy, fatigue, obesity, insulin resistance, dyslipidemia and poor quality of life. In contrast, structured physical activity improves disease symptoms, cardiovascular risk factors, physical capacity and function, mental health and quality of life for patients with rheumatic diseases. The author also said that-“Imposed physical inactivity and sedentary behavior can be disruptive to disease parameters, cardiovascular risk profile, physical capacity and function and mental health in patients with rheumatic diseases, resulting in poor quality of life, whereas maintaining more optimal physical activity levels can help to ameliorate these detrimental effects.” Exercise is also encouraged by the European League Against Rheumatism for patients with inflammatory arthritis and osteoarthritis, and has been shown not to trigger inflammation in patients with systemic lupus erythematosus. During the COVID-19 pandemic, home-based exercise programs designed for the general population should prescribed for patients with rheumatic diseases. Meanwhile, physically active patients can either maintain their exercise routine, such as walking, or they can adapt their activities to be performed at home. However, unsupervised, home-based exercise programs designed for the general population might not be ideal for patients with rheumatic diseases with physical limitations, uncontrolled disease activity and/or at high injury risk.

American College of Rheumatology Guidance for the Management of Adult Patients with Rheumatic Disease during the COVID-19 Pandemic

General statements for patients with rheumatic disease

- The risk of poor outcomes from COVID-19 appears to be related primarily to general risk factors such as age and comorbidity (H).
- Patients should be counseled on general preventive measures, e.g., social distancing and hand hygiene (H).
- As part of a shared decision-making process between patients and rheumatology providers, select measures to reduce healthcare encounters and potential exposure to SARS-CoV-2 (beyond general preventive measures) may be reasonable, e.g., reduced frequency of lab monitoring, optimal use of telehealth, increased dosing intervals between intravenous medications) (M/H).
- If indicated, glucocorticoids should be used at the lowest dose possible to control rheumatic disease, regardless of exposure or infection status (M/H).
- Glucocorticoids should not be abruptly stopped, regardless of exposure or infection status (H).
- If indicated, angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) should be continued in full doses or initiated (M/H)

Ongoing treatment of stable patients in the absence of infection or SARS-CoV-2 exposure

- Hydroxychloroquine or chloroquine (HCQ/CQ), sulfasalazine (SSZ), methotrexate (MTX), leflunomide (LEF), immunosuppressants (e.g., tacrolimus, cyclosporine, mycophenolate mofetil, azathioprine), biologics, Janus kinase (JAK) inhibitors and non-steroidal anti-inflammatory drugs (NSAIDs) may be continued (this includes patients with giant cell arteritis with an indication, in whom IL-6 inhibitors should be continued, if available) (M/H).
- Denosumab may still be given, extending dosing intervals to no longer than every 8 months, if necessary to minimize healthcare encounters (M)
- For patients with a history of vital organ-threatening rheumatic disease, mmunosuppressants should not be dose-reduced (M). In newly diagnosed disease, HCQ/CQ should be started at full dose, when available (H).

In patients with SLE

- In pregnant women with SLE, HCQ/CQ should be continued at the same dose, when available (H).
- If indicated, belimumab may be initiated (M).

Treatment of newly diagnosed or active rheumatic diseases, in the absence of infection or SARS-CoV-2 exposure

Active Inflammatory Arthritis:

- For patients well-controlled on HCQ/CQ, this disease-modifying anti-rheumatic drug (DMARD) should be continued, when available; when unable to access (including in patients with active or newly diagnosed disease), switching to a different conventional synthetic DMARD (either as monotherapy or as part of combination therapy) should be considered (M/H).
- For patients well-controlled on an IL-6 inhibitor, this DMARD should be continued, when available; when unable to access the agent, switching to a different biologic should be considered (M). The panel noted uncertainty regarding the use of JAK inhibitors in this situation.
- For patients with moderate to high disease activity despite optimal conventional synthetic DMARDs, biologics may be started (H). The panel noted uncertainty regarding the use of JAK inhibitors in this situation.
- For active or newly diagnosed inflammatory arthritis, conventional synthetic DMARDs may be started or switched (M).
- If indicated, low-dose glucocorticoids (≤10 mg prednisone equivalent) or NSAIDs may be started (M/H).

Other Rheumatic Diseases:

- In patients with systemic inflammatory or vital organ-threatening disease (e.g., lupus nephritis or vasculitis), high-dose glucocorticoids or immunosuppressants may be initiated (M).
- In the context of a drug shortage due to COVID-19, new HCQ/CQ prescriptions for non-FDA approved indications should be avoided (H).

Ongoing treatment of stable patients following SARS-CoV-2 exposure (without symptoms related to COVID-19)

- HCQ, SSZ, and NSAIDs may be continued (M/H).
- Immunosuppressants, non-IL-6 biologics, and JAK inhibitors should be stopped temporarily, pending a negative test result for COVID-19 or after 2 weeks of symptom-free observation (M). The panel noted uncertainty re: temporarily stopping MTX or LEF in this situation.
- In select circumstances, as part of a shared decision-making process, IL-6 inhibitors may be continued (M).

Rheumatic disease treatment in the context of documented or presumptive COVID-19 infection

- Regardless of COVID-19 severity, anti-malarial therapies (HCQ/CQ) may be continued, but SSZ, MTX, LEF, immunosuppressants, non-IL-6 biologics, and JAK inhibitors should be stopped or held (M/H).
- For patients with severe respiratory symptoms, NSAIDS should be stopped (M). The panel demonstrated low consensus with regards to stopping NSAIDs in the absence of severe symptoms.
- In select circumstances, as part of a shared decision-making process, IL-6 inhibitors may be continued (M).

Abbreviations: H= High Recommendation, M=Moderate Recommendation, L= Low recommendation

Study Found Significant Reductions in Traffic Accidents during the COVID-19 Pandemic

The severe disruptions caused by the SARS-CoV-2 have necessitated a redistribution of resources to meet hospitals' current service needs during this pandemic. Regarding the impact of the COVID-19 pandemic on an emergency traumatology service, an observational study was conducted in Spain. The aim of this study was to provide an overview of the impact of the pandemic, and its corresponding State of Emergency, on a tertiary traumatology emergency service. Four different periods were studied, including the first 20 days of Spain's State of Emergency, from March 14 to April 02, 2020 (Period 4). This period was compared to the 20-day period prior to the State of Emergency (Period 3), and to matching periods in the two previous years (Periods 1 and 2). A total of 6,565 patient visits were analyzed: 1909 in Period 1 (29.1%), 2161 in Period 2 (32.9%), 1983 in Period 3 (30.2%), and 512 in Period 4 (7.8%). Variables collected included patient age and sex, insurance type, discharge destination and reason for hospital admission. The patients' mean age was 55.1 years old and mejority of them were women. During the COVID-19 pandemic, there were significant reductions in total visits to the trauma emergency department, workplace accidents, traffic accidents and number of hospital admissions, particularly during Period 4. However, no statistically-significant differences were found in the number of osteoporotic hip fractures admitted between the four periods. The numbers of hospital admissions for osteoporotic hip fracture were 42 during Period 1, 41 during Period 2, 43 during Period 3 and 36 during Period 4. While most traumatological presentations decreased in frequency over the course of the outbreak, the number of osteoporotic hip fractures remained stable.

During the COVID-19 pandemic, there were significant reductions in total visits to the trauma emergency department, workplace accidents, traffic accidents and number of hospital admissions

In Era of COVID-19 Therapeutic Interventions are Essential for Reducing Osteoporosis

Coronavirus disease (COVID-19) pandemic has had a significant effect on how organizations deliver health care. COVID-19 has resulted in restriction of face to face consultations and mechanisms to access health care. Osteoporosis and fragility fractures forms a significant proportion of adult trauma and orthopedic workload even during the pandemic. A comprehensive literature review was done in India in the first week of May 2020 to assess the challenges and strategies used in the management of osteoporosis and fragility fracture care during the COVID-19 pandemic. The vertebral fractures due to osteoporosis can lead to chronic pain and deformity with advanced disease. Hip and spine fractures in the elderly are associated with increased mortality, reduction in quality of life, and functional limitations along with substantial economic burden to the health sector which further compromises the COVID-19 related treatment. A patient with osteoporosis requires complete care, multidisciplinary intervention, and patient centric rehabilitation plan; all these will be affected due to COVID-19. Osteoporosis and fragility fractures in elderly individuals pose a real challenge for an appropriate diagnosis and management, during the COVID-19 pandemic. A clinical decision along with use of clinical prediction tools for osteoporosis should be used to direct treatment. Obligatory fractures such as hip fractures require operative intervention. Non-obligatory fractures such as distal radius fractures can be managed conservatively with use of telemedicine applications in monitoring both types of patients. Therapeutic interventions that mitigate fragility fracture in era of COVID-19 are therefore essential for reducing the consequences in the future.

Osteoporosis and fragility fractures in elderly individuals pose a real challenge for an appropriate diagnosis and management, during the COVID-19 pandemic.