

# Intra-articular injections in people with haemophilia in the COVID-19 era

Given the current SARS-CoV-2 pandemic, many patients with haemophilia will have close contact with a confirmed case or suffer from coronavirus 2019 respiratory disease (COVID-19) and will need medical attention. Considering that this situation is exceptional, it is necessary to carry out integrated assistance for patients with haemophilia patients and their relatives, focusing such assistance on all the dimensions of life. In this regard, the WFH's recommendations to optimize haematological prophylaxis and its adherence should be emphasized to minimize the risk of bleeding and thus reduce the need to visit healthcare facilities.<sup>1</sup>

Many patients with haemophilia will require assistance that can only be provided in a hospital setting. Although some procedures can be postponed, a significant number of them are unavoidable, such as laboratory tests, placement or removal of central line access devices (Port-a-Cath) or intra-articular injections to relieve haemophilic arthropathy, among others.

The suspension of scheduled care activity is generating a growing waiting list. These visits and procedures must be resumed quickly to cause as little harm as possible to patients. However, due to the epidemiological situation, special measures are needed to minimize the possibility of infection in patients and professionals.<sup>2</sup> In this letter, we aim to provide guidance on what measures should be taken to care for patients with haemophilia who require intra-articular injections in the current COVID-19 context.

It should be noted that, today, there are no solid references or experiences on how to undertake the normalization of care. In any case, the adoption of the recommended measures will have to be individualized for each patient and adapted to the guidelines of the government, professional associations and care centres, to ensure the safety of patients and professionals.

The most common intra-articular injections performed on haemophilia patients are arthrocentesis, infiltration (with corticosteroids, local anaesthetics, hyaluronic acid or platelet-rich plasma—PRP) and synoviorthesis (chemical or radioactive).<sup>3,4</sup> All of these invasive procedures require a prolonged period of contact with the patient and a recovery period before discharge. Therefore, all these techniques must be performed with the same level of protection. As a general rule, before the procedure and whenever possible, face-to-face contact should be minimized by previously reviewing the electronic history and having a telematic consultation. It will also be necessary for the patient to sign an informed consent form adapted to the current epidemiological scenario, so that the risks/benefits can be weighed.<sup>5,6</sup>

Since invasive procedures involve close contact, it is highly advisable to know the exact situation of the patient in relation to

COVID-19.<sup>7</sup> For invasive techniques, admissions or tests that generate aerosols, polymerase chain reaction (PCR) is recommended to be performed within the previous 48 hours. The cost-effectiveness and significance of the tests will depend on the stage of the disease and on the quality and origin of the sample.

The following guidelines are provided to help you understand the level of personal protection needed in this care environment. In general, it is necessary to minimize the time of exposure and limit the number of people in the room to the minimum personnel needed. An assistant who has not had any contact with the patient should be present.<sup>8</sup> In addition, consideration should be given to replacing professionals who have a higher risk of complications from COVID-19<sup>9</sup> (those who are immunosuppressed, who have cardiac or chronic respiratory diseases, those over 60 years of age, etc) with others who are at lower risk. In all cases, healthcare personnel must use complete personal protection equipment (PPE) [waterproof gown, filtering facepiece (FFP)2 mask, double gloves, goggles or screens, caps and tights]. FFP3 should be used if the airway is to be handled or aerosols are required. All personnel must be specifically trained to put on, take off and dispose of PPE.<sup>5,6,9</sup> In centres where there is an occupational hazards department, updated standards should be available to all personnel.

With regard to patients, to provide the necessary protection, their epidemiological situation must be considered. However, given the difficulty of classifying patients, all patients should be considered as potentially infected with COVID-19 for the purposes of preventive measures. Therefore, patients should wear a surgical mask, gloves and tights during their care. Known COVID-19-positive patients should be postponed for the procedure whenever it is not essential, until elimination of the infection is confirmed. There are techniques that should not be delayed, because of their risk of producing irreversible damage, such as the aspiration of an acute painful major haemarthrosis or the suspicion of septic arthritis. In these cases, the patient will also use an FFP2 mask without a valve. Patients who present a clear risk (with symptoms or epidemiological contacts) and in whom the tests cannot be performed should be treated with the same level of protection as a COVID-19 patient.<sup>6,9</sup>

The circuit of entry, stay and exit of the patient must avoid contact with other patients and non-healthcare personnel. The administration of coagulation factor prior to the technique, as well as subsequent monitoring during recovery, will be done in the same room as the procedure to avoid travel through the health centre. There should be separate pathways to keep suspected/infected patients separated from non-infected patients.<sup>9</sup>

It is necessary to disinfect the puncture area with a hydroalcoholic chlorhexidine solution. If anaesthesia is required, local techniques should be used whenever possible, with the patient wearing a surgical mask.<sup>8</sup>

All potential medication should be prepared and placed on a large tray (coagulation replacement factor, intra-articular drugs, anaesthetics, etc) avoiding the manipulation of medication carts as much as possible. In the same manner, all the material potentially necessary for the procedure (disinfectants, syringes, needles, bandages, etc) should be available inside the room to avoid opening doors after the patient has entered.<sup>8</sup> All material used should be sterile and for single use only. The waste generated is considered class III and must be disposed of as special biosanitary waste, in accordance with the regulations of each country. If technical equipment is used, such as ultrasound to facilitate the intervention, it must be adequately protected to minimize the possibility of contamination. All centres must have adequate cleaning, disinfection and waste management protocols, following official recommendations and in accordance with their Occupational Health and Preventive Medicine departments. Whenever possible, the patient should be called in late in the day and ideally in a room prepared for COVID-19. Cleaning and disinfection with viricides should be carried out between patients, although it is not possible to establish a minimum time between them at this time.<sup>5,6,8,9</sup>

As for the drugs to be used, the potential influence of the most commonly used drugs in intra-articular injections on the predisposition to contract the disease and its complications is not yet known. Extreme precautions should be taken in patients without acquired immunity. Considering interactions of oral drugs with other viral diseases (such as influenza) for which there is more evidence, the following considerations can be offered. The use of steroids should be discouraged if possible, given they can modify the hyperthermic response (a well-proven natural defence) and act as a potential immunosuppressant.<sup>10</sup> Other options should be pursued whenever possible. For local anaesthetics, electrocardiogram (ECG) monitoring (PR interval and QTc in addition to arrhythmias) is recommended, given post-COVID-19 heart disease has not yet been accurately characterized. Regarding the intra-articular use of hyaluronic acid, rifampicin or radioisotope, no data are currently available for specific recommendations. Regarding the use of PRP, in the absence of further studies, its use cannot currently be recommended.<sup>4,6</sup>

Patients with acquired immunity to COVID-19 and without active antiviral treatment, in principle, are not at added risk and should be treated whenever their clinical situation (previous illnesses and possible sequelae derived from COVID-19 infection) allows. It is essential to make a complete evaluation before indicating any new procedure. However, it should be noted that the acquisition of immunity after COVID-19 infection has not been fully defined, and a low number of re-infections have been described. It remains to be clarified whether these are false-positive PCR tests (or previous false negatives) or whether they are new mutations of the virus.<sup>6</sup> Table 1 summarizes the additional measures that should

**TABLE 1** Additional measures that should be undertaken when performing intra-articular injections in PWH in the COVID-19 era

#### Preprocedure

Known COVID-19-positive patients or those who present a clear risk (with symptoms or epidemiological contacts) should be postponed for the procedure whenever it is not essential

Make a complete evaluation before indicating any new procedure. Whenever possible, face-to-face contact should be minimized by previously reviewing the electronic history and having a telematic consultation

The patient should sign an informed consent form adapted to the current epidemiological scenario

Consider replacing professionals who have a higher risk of complications from COVID-19

All personnel must be specifically trained to put on and dispose of PPE

There should be separate pathways to keep suspected/infected patients separated from non-infected patients

The patient should be called in late in the day and ideally in a room prepared for the rest of the patients

#### During procedure

Minimize the time of exposure and limit the number of people in the room to the minimum personnel needed

Healthcare personnel must use complete PPE

Patients should wear a surgical mask, gloves and tights during their care

All potential medication should be prepared and placed avoiding the manipulation of medication carts

The infusion of coagulation factor prior to the technique will be done in the same room as the procedure

The use of corticosteroids should be discouraged if possible

All the material potentially necessary for the procedure should be for single use and be available inside the room

It is necessary to disinfect the puncture area with a hydroalcoholic chlorhexidine solution

If anaesthesia is required, local techniques should be used whenever possible

If technical equipment is used, such as ultrasound, it must be adequately protected

#### Postprocedure

All personnel must be specifically trained to take off the PPE

The subsequent monitoring during recovery will be done in the same room as the procedure

The waste generated is considered class III and must be disposed of as special biosanitary waste

Cleaning and disinfection with viricides should be carried out between patients

All centres must have adequate cleaning, disinfection and waste management protocols

Abbreviations: PEE, personal protective equipment; PWH, people with haemophilia.

be undertaken when performing intra-articular injections in PWH in the COVID-19 era.

Everything previously mentioned leads us to the following conclusions:


- There is a need to establish precise and well-established plans for performing intra-articular injections in patients with haemophilia and acquired arthropathy, considering the current context of the COVID-19 pandemic.
- Hospitals and clinical units must prepare specific internal protocols and organize appropriate training for the staff and patients involved.
- These action protocols must include preprocedure, during procedure and postprocedure measures.
- Due to the current insufficient knowledge of COVID-19 behaviour, it is essential to establish a flexible framework that can be adapted to the epidemiological reality of each specific environment.

## DISCLOSURES

HC-R has received reimbursement for collaborating as a speaker and researcher from Pfizer and Roche; and honoraria for consulting or collaborating as a speaker from Sobi, Takeda, NovoNordisk and Bayer. ECR-M has received reimbursement for collaborating as a speaker from Pfizer, Roche, Sobi, Takeda, NovoNordisk, Octapharma and Bayer. MTA-R has received reimbursement for attending symposia/congresses and/or honoraria for speaking and/or honoraria for consulting, and/or funds for research from Takeda, Bayer, CSI-Behring, Grifols, Novo Nordisk, Sobi, Roche, Octapharma and Pfizer. VJ-Y has received reimbursement for attending symposia/congresses and/or honoraria for speaking and/or honoraria for consulting, and/or funds for research from Takeda, Bayer, CSI-Behring, Grifols, Novo Nordisk, Sobi, Roche, Octapharma and Pfizer.

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