Staphylococcal Osteo-Articular Infections: Anatomical Localization, Etiological Mechanism, Diagnosis and Management

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Abstract

Osteo-Articular Infections (OAI) are polymorphic, potentially serious and costly infections. The genus Staphylococcus, the first etiology of osteoarticular infections, is associated with forms that are particularly difficult to treat. Three phenotypic mechanisms have been linked to this high rate of chronicity and relapses, allowing bacterial adaptation to bone tissue life and escape to the host immune system and the action of antibiotics: the formation of biofilm, persistence of staphylococci in osteoblasts, and evolution to the morphotype of Small Colony Variant (SCV).

The diagnosis and management of OAI are very heterogeneous, due to the specificities provided by the diversity of infected sites, their evolution time, their pathophysiological mechanisms, and the presence or absence of orthopedic equipment. Consequently, the management of these infections most often requires a complex multidisciplinary approach, combining sometimes heavy surgical management with prolonged intravenous antibiotic therapy. These infections require prolonged hospitalization (average duration of each hospitalization of 17.5 days, with the need for multiple hospitalizations in 20% of cases).

Osteo-articular infections are a major public health issue, requiring the establishment of reference centers for the management of these complex infections and responding to the need to facilitate clinical and basic research in this area, to improve the quality care of the persons concerned.

Keywords: Osteo-articular infections • Genus staphylococcus • Biofilm • Small colony variant

Introduction

The osteo-Articular Infections (OAI) regroup a set of clinical entities having in common the invasion and the progressive destruction of the bone and cartilaginous tissues by microorganisms, most often bacterial. These infections constitute a very heterogeneous group of clinical situations, classified according to their anatomical location, their period of evolution, the mechanism leading to infection, and the presence or absence of orthopedic material [1].

The germs responsible for bone infection depend on many factors: the gateway, the circumstances of occurrence, and the terrain. The genus Staphylococcus, involved in more than 50% of the OAI, represents the first etiology. It includes *S. aureus*, considered the main pathogen, and Coagulase-Negative Staphylococci (CNS), the main representative of which is *S. epidermidis*. Less studied than *S. aureus, S. epidermidis*, is responsible for 30 to 43% of orthopedic equipment OAI, even outpacing *S. aureus* in terms of frequency in some series. The time to develop IOA is therefore one of the main determinants of management, impacting the type of surgery and the duration of antibiotic therapy. A simple joint lavage is thus proposed in case of acute joint prosthesis infection, while chronic forms require a complete removal of the orthopedic material [2].

The treatment of osteomyelitis or acute or chronic septic arthritis requires long-term management, often requiring iterative procedures and prolonged antibiotic treatment ranging from 6 weeks to at least 3 months. This treatment is usually systemic but the spread of antibiotics in the bone or in a joint is weak, forcing infectiologists to use high-dose, parenteral and prolonged antibiotics. Despite this long and costly medical and surgical management, staphylococcal OAI is classically associated with a high rate of treatment failure, which is responsible for chronic and recurrent infections that cause significant morbidity. This failure rate is estimated between 20 and 30% in osteomyelitis, and between 0 and 16% in spondylodiscitis. In case of *S. aureus* API, it can reach 20% in the case of acute forms under conservative treatment, but can exceed 85% if prosthesis retention is proposed outside the recommendations. In the case of a suitable indication of change of prosthesis in one or two stages, the failure rate varies between 0 and 14%. However, this rate of treatment failure and the risk factors for progression to chronicity and recurrence are difficult to evaluate because of the great diversity of clinical forms of OAI with *S. aureus*. The great heterogeneity of the clinical situations and the absence of a randomized controlled study of sufficient power do not make it possible to propose a standardized treatment of the OAI. The management of these infections is therefore based on recommendations from international infectious disease companies to harmonize practices despite the limited data available.

Osteoarticular Infections

Anatomical location

Septic arthritis: is an infection of the joint cavity, with the knee being the most frequently involved seat. The bacterial development in synovia produces an inflammatory response and the recruitment of leucocytes into the joint fluid. Local production of free radicals, and the release of proteolytic enzymes (metalloproteases, lysosomal enzymes) and bacterial toxins result in the destruction of cartilage. Due to the inextensibility of the capsule limiting the joint cavity, local inflammation causes an increase in intra-articular pressure responsible for exacerbation of the destruction of cartilage and synovia by mechanical and ischemic phenomena. In the absence of rapid management, an extension of the infection to synovia, cartilaginous tissue, and subchondral bone leads to the progressive destruction of the joint [3].

Osteitis is defined as the infection of bone marrow and cortical tissue. The initial infectious process results in a local inflammatory reaction that, together with bacterial multiplication, leads to localized vascularized vascular micro-thromboses. The evolution is towards the formation of sequestra, zones of infected and necrotic bone tissue, characteristic of osteitis chronization (Figures 1). These devascularized and detached fragments of the surrounding tissue are poorly accessible to immune cells and antibiotics and behave as a foreign body inert to adhesion, bacterial colonization and biofilm formation. In untreated forms of chronic osteomyelitis, which have become rare in industrialized countries, bone sequestras can have two fates determined by their size. Small sequestrants are gradually resorbed by granulation tissue recruited by inflammatory signals from the necrotic zone. When the extent of the sequestra is too great or the inflammatory response of the host is compromised, their extension is progressively confined by a neoformation of bone from the periosteum, detached from the cortical bone by the accumulation of pus which can also fistulate to the skin. This neoformation, the involucre, makes it possible to ensure the continuity of the bone and the minimum maintenance of its function during the convalescence phase. However, the inadequate vascularization of the circumscribed tissues favors the maintenance of underlying bone sequestration, resulting in a chronic pathology in which surgical debridement is often the only option.

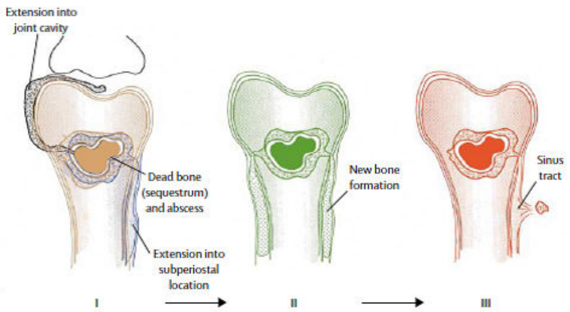


Figure 1: Steps in the progression of chronic osteomyelitis. I: From sequestrum, an area of devascularised dead bone, progression of intramedullary infection towards an intracapsular location can lead to septic arthritis; progression of infection towards a subperiosteal location can lead to periosteal elevation. II: New bone formation as a result of massive periosteal elevation. III: Extension of sequestrum and necrotic material through cortical bone creates a fistula and ultimately breaks through the skin.

Osteomyelitis classically refers to an attack of the long bones by hematogenous route without foreign body, the most frequent mechanism in the child. The bone ends (metaphyses) are then the privileged seat of infection, because of the system of bone vascularization: arteries entering the bone at the diaphyseal level are distributed to the ends where they form vascular loops, seats of a slowing of the blood flow favoring the bacterial transplant. In the Anglo-Saxon literature, osteitis and osteomyelitis constitute a single entity referred to as "osteomyelitis". The Cierny-Mader classification (Table 1) summarizes the different types of osteomyelitis according to the site, the mechanism of occurrence, and the type of bone involvement, and is directly related to the prognosis of these infections[4].

Spondylodiscitis is a particular form of osteomyelitis reaching the intervertebral disc and adjacent vertebral endplates. It is the most common location of osteomyelitis in adults. The lumbar spine is the most commonly affected, followed by thoracic and cervical vertebrae.

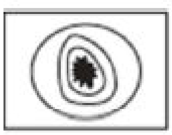
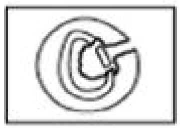
Anatomical stages	
	Stage 1: Intramedullary osteomyelitis limited to the medullary Etiology: hematogenous Treatment: antibiotic, surgical drainage
	Stage 2: superficial osteomyelitis, exposed surface necrosis Etiology: contiguity infection Treatment: antibiotic, superficial debridement, cover
	Stage 3: Localized osteomyelitis (cortical sequestration), well-individualized necrosis. Localized cortical damage, bone instability before or after debridement Etiology: trauma, evolution of stage 1 or 2, iatrogenic (screw, plate) Treatment: antibiotic, debridement, sequestrectomy Immobilization ± bone graft
	Stage 4: diffuse osteomyelitis, circumferential cortical involvement, bone instability before or after debridement Etiology: trauma, evolution of stage 1-2 or 3, iatrpgene (nail) Treatment: antibiotic, debridement, sequestrectomy ± bone graft Stabilization (ORIF, extreme fixation (llizarof), Amputation?)
Physiological state	
A: absence of anomaly B: anomalies Bs: generalized - undernutrition - hepatic and / or renal failure - diabetes - chronic hypoxemia - autoimmune disease - neoplasia - immunocompromised or immunosuppressive - end of the ages of life - smoking C: precarious state	B1: localized: - chronic lymphedema - venous insufficiency - postradic fibrosis - eschar - neuropathy

Table 1: Different types of osteomyelitis according to the site, the mechanism of occurrence, and the type of bone involvement.

Etiological mechanism of osteoarticular infections

Osteo-articular infections can result:

- A haematogenous mechanism, thus constituting a septic location secondary during bacteremia;
- An inoculation occurring during a trauma (open fracture) or an invasive gesture (puncture, infiltration, surgery);
- The extension of an infectious focus of contiguity.

In adults, hematogenous OAIs occur mainly in patients over 50 years of age, with the exception of intravenous drug users. The cutaneous, pulmonary, dental and urinary entry gates are the most frequent. Their occurrence is related to the usual risk factors for bacteremia, including the presence of a central venous catheter or an indwelling urinary catheter, extra-renal cleansing, the existence of a urinary tract infection, and sickle cell disease. In the presence of a joint prosthesis, the overall risk of septic graft during bacteraemia would be low, estimated at less than 1%. However, this risk is much higher in case of *S. aureus* bacteremia, then estimated at 30-40%. Hematogenous OAIs are generally mono-microbial, whereas other etiological mechanisms more frequently cause multi-microbial infections [5].

Presence of orthopedic material

The presence of orthopedic equipment, whether it is peripheral or spinal osteosynthesis equipment or joint prostheses, increases the risk of OAI. Several mechanisms are involved:

The implantation of a foreign material is very quickly followed by its covering by a protein matrix containing in particular fibrin, fibrinogen and laminins which promote bacterial adhesion.

The interaction of foreign material with neutrophils induces dysfunction of phagocytosis, responsible for local immunodepression. Several animal models have shown that the inoculum of *S. aureus* needed to cause infection is divided by more than 100,000 in the presence of a foreign body. The diagnostic and therapeutic management of these infections on orthopedic equipment thus obeys requirements different from native OAI[6].

Chronology of occurrence

The duration of evolution of the OAI represents an essential prognostic factor, supposed to guide the type surgery and the duration of antibiotic therapy. However, the definition of acute or chronic OAI is not consensual. For the clinician, acute OAI is most often with significant local and systemic inflammatory signs, whereas chronic OAI produces only a weak biological inflammatory syndrome, with the absence of fever being common. The elements associated with chronicity at the time of diagnosis are the existence of a fistula, the importance of radiological lesions and the presence of bone sequestrants making bacterial eradication difficult because of the absence of diffusion of antibiotics in these portions. of avascular bones. For the microbiologist, biofilm formation, a dynamic entity consisting of an extracellular matrix secreted by bacteria and allowing them to adhere strongly to host tissues and material, and the morphology of colonies isolated from deep samples define chronicity. Finally, for the orthopedic surgeon, the acute infection is the one that would be likely to heal without ablation of the prosthetic material. The ambiguity of this classification is due to the imprecision of the clinical and paraclinical expression which does not translate the histological aspect of the lesions, so that in practice, there is no precise demarcation between acute and chronic OAI. The delay beyond which an OAI becomes chronic is very controversial and probably very variable depending on the situation [7]. However, in the absence of an objective definition of chronicity, an arbitrary delay of 3 to 4 weeks between the onset of clinical signs and the microbiological diagnosis is usually used to distinguish between acute and chronic OAI. In case of infection on orthopedic material, including API, the delay between the installation of the material and the infection allows to guide the mechanism and bacterial etiology [8].

In addition to the acute or chronic character, are distinguished as follows:

Eearly infections occurring within 1 to 3 months of surgery, and where the predominant mechanism is intraoperative inoculation of virulent *S. aureus* or Gram-negative bacilli germs;

Delayed surgical site infections (between 1-3 months and 1-2 years following surgery) generally related to less virulent pathogens such as SCN (including *S. epidermidis*) or Propionibacterium acnes;

Late infections, occurring beyond 1 to 2 years, most often of haematogenous origin and unrelated to surgery [9].

Other classifications exist, including that of Tsukayama, which distinguishes early (<1 month), late (> 1 month), hematogenous, postoperative API, and those diagnosed with positive bacteriological specimens when replacing an aseptic presumed prosthesis [31]. MacPherson's classification takes into account the type of infection, the co-morbidities and the immune status of the patient, and the state of the wound, and is directly correlated with the prognosis of APIs (Table 2).

Type of infection
Type 1: Early postoperative IOA evolving for less than 4 weeks
Type 2: hematogenous IOA on painless functional prosthesis evolving since less 4 weeks
Type 3: Chronic infection evolving for more than 4 weeks
State of health and immunity of the patient
Type A: without risk factor * and immunocompetent
Type B: compromised by 1 or 2 risk factor (s) *
Type C: compromised by more than 2 risk factors * and at least one of the factors neutrophils <1000/mm3, CD4 <100 / mm3, intravenous drug use, chronic active infection in another site, hematology or neoplasia
Local state of the associated wound
Type 1: no local risk factor **
Type 2: Compromised by 1 or 2 local risk factor (s) **
Type 3: compromised by more than 2 local risk factors **

Table 2 : Classification of MacPherson articular prosthetic infections. * Risk factors related to the host: age ≥ 80 years, chronic dermatosis, lymphoedema, indwelling urinary catheter, malnutrition (albumin <30 g / L), nicotine addiction, diabetes, cirrhosis, immunosuppressive therapy, neoplasia (progressive with aplastic chemotherapy), respiratory failure with SpO2 in ambient air <60%, renal failure requiring hemodialysis, systemic inflammatory disease (rheumatoid arthritis, systemic lupus erythematosus), immunodepression (HIV, acquired immune deficiency syndrome).

Bacterial etiology

The distribution of infectious agents responsible for OAI is highly variable according to the studies, since it depends on the contributing factors, the geographical area, the type of infection and the age. Staphylococcus aureus is the main pathogen responsible for OAI. It is thus isolated in about 35 to 65% of native OAI, in populations of various geographical origins, although significant variations are observed depending on the recruitment of services. In the United Kingdom, the Health Protection Agency's reports on the surveillance of Surgical Site Infections (SSI) between 1997 and 2005 determined that *S. aureus* was responsible for 41.4% of total hip prosthesis infections, 59.1% of partial prosthetic infections. of hip, 33.5% of knee prosthesis infections, and 53% of infections after surgical reduction of open fracture [10].

The risk factors for *S. aureus* OAI events combine the general factors of OAI occurrence with those more specific for *S. aureus* infection including hemodialysis, rheumatoid arthritis, diabetes, and neoplasia. There are two additional specificities to mention. First, in the presence of orthopedic equipment, the risk of osteo-articular septic transplantation during *S. aureus* bacteremia is much higher (30-40%) than for other etiological agents (<1%), possibly due to the numerous virulence factors of *S. aureus*, and in particular its multiple adhesion proteins. This probably explains in part the predominance of the hematogenous mechanism in the occurrence of OAI to *S. aureus*, and especially API. Then, the permanent nasal carriage of *S. aureus*, detected in about 20% of the general population, is a risk factor for staphylococcal infection. On the other hand, intermittent carriers (30% of the population) have an infectious risk equivalent to that of non-colonized subjects. Although not clearly associated with the general risk of AOA, nasal carriage of *S. aureus* is a well-identified risk factor for ISO in orthopedic surgery, a recent study showing the similarity of isolated clones ISO and portage.

While Coagulase-negative staphylococci are responsible for only 5 to 15% of native IOAs, their frequency increases in the event of a material infection. Staphylococcus epidermidis is the most frequently isolated SCN, although other species are sometimes incriminated. Thus, the etiologies of postoperative OAI are dominated by S. aureus, SCN, and non-fermenting BGN of the Pseudomonas aeruginosa type. In the immunocompromised, the diabetic, and in the course of procedures or infections concerning the digestive or urinary tract, the BGN must be taken into account. Finally, streptococci and enterococci are associated with dental and digestive entry gates, respectively.

Diagnosis of bone infections

Clinical data

IOA are classically manifested by the association of fever, osteoarticular pain of inflammatory schedule with stiffness and functional impotence, and signs local inflammatory. In the aftermath of the placement of a joint prosthesis, a scarring and / or abnormal scarring should lead to suspicion of early IPA. In the case of spondylodiscitis, the spinal syndrome (pain, stiffness and contracture of the para-vertebral muscles) is present in more than 90% of cases. Medullary or radicular neurological deficits are reported up to 38% of cases. They are most often related to an epidural or para-vertebral abscess, present in 17% and 26% of patients respectively. Clinical suspicion of OAI is difficult in many situations. In case of chronic infection, fever and local inflammatory signs are absent or limited in about 40% of cases. However, a fistulization of the infected home to the skin may then exist, signifying the chronicity of the OAI. The evolution can then be done by repeated episodes of abscess evacuated by the fistulous path.

Conversely, in the immediate aftermath of prosthesis placement, the presence of fever is not very specific, a febrile spike secondary to the intervention may occur. On the other hand, the onset of fever beyond 5 to 7 days after surgery becomes discriminant for the clinical suspicion of early infection with orthopedic equipment. Finally, the involvement of "deep" sites (hip, pelvis, spine, etc.) frequently leads to delayed diagnosis because of the possible absence of local inflammatory signs and the difficulty of measuring the joint effusion clinically.

Biological data

A biological inflammatory syndrome, associating leukocytosis with neutrophils and elevation of the C-Reactive Protein (CRP), must be systematically sought. The absence of inflammatory syndrome is however possible, especially in chronic OAI. Conversely, hyperleukocytosis and elevation of CRP are of little value in cases of early API suspicion, a postoperative rise of CRP normalizing in one month can be observed in the absence of any ISO. On the other hand, their kinetics could be interesting, since a rise in CRP or in leukocytosis should suggest an IPA.

The cytological and biochemical examination of the articular fluid obtained by puncture provides an important diagnostic aid, usually found an "inflammatory" fluid, exudative, rich in proteins (> 30 g / L) and neutrophils. The leukocyte count made it possible to establish different diagnostic thresholds, which vary according to the clinical situation, of correct sensitivity and specificity.

Radiological data

Radiological examinations, including conventional radiography, scaner and magnetic resonance imaging (MRI) are of great help in the diagnosis of OAI. They are looking for images of osteolysis, a periosteal reaction, joint effusion, local abscess, and possible sequestrations. The role of functional imaging (technetium-99m bone scintigraphy, indium-111 polynuclear scintigraphy and 18F-fluorodeoxyglucose positron emission tomography) is not yet well defined [53-55]. The sensitivity of these examinations is excellent, but their accessibility is still limited and they can be faulted for the diagnosis of early API, due to post-operative tissue inflammation induced by the material and surgery. Finally, a search for infective endocarditis should be considered by transthoracic and possibly trans-esophageal echocardiography in the presence of at risk heart disease or heart failure, the positivity of blood cultures, and Gram cocci infections positive, particularly in the context of spondylodiscitis.

Microbiological and histological data

Blood cultures represent the first means of the etiological diagnosis, positive in about 50% of the acute OAI, thus making it possible not to carry out a deep sampling if the isolated seed (s) is (are) susceptible of generate an OAI. The positivity of blood cultures is of course more frequent in case of haematogenous mechanism, as well as in certain localizations such as the clavicle, the pubis, and the rachis with a sensitivity reaching more than 70% in the spondylodiscites. In the absence of positive blood culture, osteoarticular bacteriological specimens should be taken, as far as possible, at least 15 days after discontinuation of any antibiotic therapy. They must be sown on various enriched solid and liquid media, and kept in culture for a prolonged period (14 days) so as not to ignore slowly growing seeds [60]. In the case of a surgical diagnostic procedure, 5 to 6 intraoperative samples must be taken in order to optimize the sensitivity of the microbiological analysis. Standard articular fluid cultures and synovial or bone biopsies have a sensitivity of 60-80%.

In case of removal of orthopedic material, sonication of the prosthesis or osteosynthesis material would allow better detection of Small Colony Variants (SCV) and bacteria strongly adhering to the material, especially in the presence of biofilm, but is not currently available. in all bacteriology laboratories. This technique also seems to improve the sensitivity of cultures of samples taken under antibiotic therapy or after a therapeutic window of less than 14 days. Ulcerative swabbing or fistula removal should no longer be used because of their non-correlation with deep osteoarticular samples in more than 50% of cases, with the exception of the positivity of the sample of S. aureusZX z . This point remains debated since a recent study showed that the positivity of two positive fistula-positive fistulas with the same germ had a sensitivity of 94% compared to the surgical biopsy in 77 patients with chronic mono-microbial osteomyelitis [68]. This figure decreased to 79% in the case of poly-microbial OAI. Molecular methods (universal or specific PCR) can help the etiological diagnosis in case of negative cultures, especially during previous antibiotic therapy.

The bacteriological methods must be supplemented by a histological analysis of the biopsies. The presence of signs of tissue inflammation, including neutrophils, has a sensitivity of 43 to 100% and a specificity of 81 to 98% for the diagnosis of OAI.

Diagnostic features of staphylococcal osteoarticular infections

The clinical, biological and radiological presentation of *S. aureus* OAI does not differ from other etiologies and is generally not a problem in the absence of prior antibiotic therapy. It should be noted, however, that the frequent involvement of biofilm and SCV can make bacterial isolation difficult, as these phenotypic variants show slow growth in culture. In the case of infections on equipment, sonication here would be of interest. The positivity of a *S. aureus* fistula specimen may be the only situation where this examination would be cost-effective. Numerous molecular methods are now being evaluated in the diagnosis of *S. aureus* OAI. Specific "house" PCRs have been developed for the detection of *S. aureus* in osteoarticular samples. Commercial kits such as the GeneXpert MRSA/SA SSTI are currently available, capable of simultaneously detecting the presence of *S. aureus* and meticillin resistance directly on specimens within one hour. The diagnosis of OAI with *S. epidermidis* is more delicate. Indeed, this germ is a frequent source of contamination of the samples, from the patient's carrying strains, the sampler, and the laboratory agents in charge of the sampling. Thus, the positivity of at least two concordant samples is required.

Osteoarticular infections support

The treatment of OAI is particularly complex, taking into account the issues of efficacy, intraosseous diffusion and tolerance of antibiotic therapy, preserving the functional prognosis and quality of life of the patient. It imposes a multidisciplinary medico-surgical care long and expensive. The great heterogeneity of the clinical situations and the absence of a randomized controlled study of sufficient power do not make it possible to propose a standardized treatment of the OAI. The management of these patients is based on recommendations from international infectious disease companies to harmonize practices despite the limited data available.

Surgical treatment

Decrease of the bacterial inoculum is a prerequisite for the success of antibiotic therapy in OAI. The question of the surgical indication must therefore be systematically asked. The technique to be used in septic arthritis on native articulation is not clearly established. Although not validated by any prospective and questionable study according to many teams, the iterative evacuation of needle pus by puncture has been proposed for peripheral arthritis reaching superficial joints (knee, shoulder, elbow, ankle, wrist) and could give the same results as a surgical wash. A surgical lavage is to be proposed in case of failure of iterative punctures, or immediately in the presence of factors of poor prognosis: chronic and /or complicated infection (abscess, associated osteitis), extreme age, presence of numerous comorbidities, joint pathology underlying, and immunosuppression.

Surgical intervention must be systematic in case of API. For acute API, defined arbitrarily by a time of progression of less than 3-4 weeks, arthrotomy-lavage should be performed systematically.

. The success of this treatment depends directly on how early the procedure is compared to the diagnosis, with a cure rate of approximately 90% for surgery within 10 days of symptom onset, whereas more than 50% at 3 weeks of evolution. The other factors predictive of therapeutic success are the absence of fistula, the good sensitivity of the germ to antibiotics, and low preoperative CRP (<15 mg / L). Conservative treatment (surgical lavage with debridement of all infected tissues, and preservation of material) is therefore currently recommended in case of acute IPA in the absence of fistula, if the integrity of the soft tissues is confirmed intraoperatively, and whether antibiotic therapy adapted to good bioavailability and bone diffusion is available. In other cases, the optimal attitude would be to remove the infected prosthesis. A one-time change is possible in case of API documented pre-operatively to a germ on which bioavailable antibiotic is available and with good bone diffusion (excluding APIs with SASM without possible use of rifampicin, MRSA, enterococci, non-fermenting BGN, and yeast). In addition, bone and soft tissue should not require bone grafting or covering. In the absence of these criteria and if the patient can undergo two surgeries, the French and North American recommendations recommend a two-step change. In case of knee API, a spacer impregnated with antibiotic is then generally set up to limit the tissue retractions and facilitate the rest. The use of these spacers is still subject to debate for two reasons: i) the risk of persistence of infection on this material, especially in case of infection involving MRSA, SCV, or yeast; and ii) the risk of diffusion of the antibiotic creating a concentration gradient that may favor the emergence of SCV and /or resistant strains. The delay between the two operating times is also discussed. Reimplantation within 4 to 6 weeks under the cover of antibiotic therapy may be considered, especially if the germ involved is not MRSA, enterococcus or BGN multi-resistant. An alternative is a reimplantation 2 weeks after stopping antibiotic therapy for 4 to 6 weeks.

The alternatives consist in the definitive ablation of the prosthesis with or without arthrodesis, or amputation, to be reserved for the most complex situations and risk of high failure. In case of osteitis, surgical debridement should always be considered in order to flatten lesions and remove necrotic tissue, especially in the presence of bone sequestra, or soft tissue or periosteal abscess. In the presence of osteosynthesis equipment, it must be removed in its entirety as soon as possible, which may require, in the case of early ISO, the establishment of an external fixator to stabilize unbound bone lesions [8]. In case of flattening resulting in significant bone loss, the filling is usually done by bone graft in one or two times. In the context of spondylodiscitis, surgery is reserved for cases of serious local complications such as spinal cord compression, epidural or para-vertebral abscess, and uncontrolled infections despite appropriate antibiotherapy. In case of spinal infection on osteosynthesis equipment, the latter must be removed as soon as possible, especially in case of delayed infection (> 1 month after installation of the equipment). In total, more than 40% of patients with spondylodiscitis require spinal surgery.

Medical treatment

Unlike the majority of infections, antibiotic susceptibility of the organisms involved is not sufficient to predict treatment efficacy in OAI. Indeed, many other parameters come into play, such as the spread of antibiotics in bone tissue, and their ability to penetrate and remain active in the bacterial biofilm .

The choice of antibiotic therapy in the treatment of OAI has been evaluated by only one randomized clinical trial, justifying the importance of rifampicin in the management of staphylococcal APIs, especially in the case of conservative treatment. The choice of the nature and duration of OAI treatment is therefore mainly based on low-level studies, grouped in two meta-analyzes that failed to show a preferential therapeutic option for these infections.

Conclusion

Antibiotic therapy of the OAI is usually double, initially intravenous, and prolonged. It is based, if possible, on the use of high doses of molecules with good bone diffusion. The duration of initial parenteral antibiotic therapy is not validated by any study. An oral relay may be considered, usually after two weeks of intravenous treatment, but requires molecules with good bioavailability and bone diffusion, and perfectly active on the isolated germ. The development of parenteral antibiotic therapy at home remains an option that is increasingly being used in cases where oral treatment is not possible.

Method

A qualitative exploratory evaluation study was conducted with six participants purposively selected from a city in the State of São Paulo, Brazil. There were four nurses, who were selected as members of one of the 17 PEH in FHTs, one coordinator of a randomly selected PEH and the business/administration manager for PHE in FHT for all the groups in the city.

The participants answered semi-structured questions in on-line interviews conducted via the Google Meet platform at a convenient day and time chosen by each respondent. Only professionals who signed an informed consent form participated in the study. The respondents received and read and signed this form in advance and before the interviews. This study was approved by the Research Ethics Committee of UNICAMP, under CAAE 31563420.7.0000.5404 and report number 4.027.257.

All interviews were audio-recorded and transcribed immediately after the interview. Thematic analysis was used to identify the main themes in the transcripts.The transcribed interviews were read several times by ERC to become familiar with the data and to identify meanings and patterns. The analysis continued until saturation was reached. The identified themes were validated by discussion with the other members of the research team.

Results

Three main inter-related themes were identified:

Major change in usual PHE approach

The weekly face to face multidisciplinary PEH meetings were significantly disrupted and it was important to maximize opportunities to maintain the regular conversation space:

'Today, as we had a reduction in the team meeting time, it used to be from 2 pm to 4 pm, and today it is from 3 pm to 4 pm, because part of the team is no longer present …. so we try to optimize this time as much as possible. [Respondent 3 – nurse]

The conversation space was also increasingly used for information exchange in response to the COVID-19 crisis:

' The team really wants to be up-to-date, and they seek us to answer their questions, find out about new protocols, because everything is new, everything is very scary, and in this sense we've tried to support them.' [Respondent 1 – nurse]

' So we had more people looking for information as it was a new pandemic, there were different questions, several types of doubts, about the disease itself, the use of PPE, medication, and everything else. So, because of all these things, we had a collective approach with them.' [Respondent 3 – nurse]

Increased use of familiar technologies to maintain PHE

The face to face conversation space was augmented virtually and also maintained by the increased use of social media:

'I think that today, social media have been a very important tool to help us work.' [Respondent 4 – nurse]

There was increased use of familiar technologies, especially WhatsApp for communication and You Tube for information:

'We use WhatsApp very often, which is probably the most common tool today, so everything we receive and then share with the team, so I think this is the most frequently used tool.' [Respondent 2– nurse]

' [Before COVID-19], we had no access to channels like YouTube, to watch some videos, but now during the COVID-19, we can access a lot of materials.' [Respondent 1– nurse]

The focus of PHE moved towards meeting information needs, with a change in the role of the Coordinator to identify information needs and share information using familiar social media:

'Facebook and Instagram were fed every day with .. content, and we felt people were using these social channels. In some situations, I used to do some Instagram polls, for example, asking if they had any doubt, and I got more feedbacks than from the form … by email. So, apparently, social media have been a very important tool for us to send this content to a large number of people.' [Respondent 4 – nurse]

Major change in the role of the coordinator

There was a major change in the role of the coordinator, with increasing responsibility to navigate the complexity of information about COVID-19 on behalf of the FHT.

Usually this interest is more individual. They usually hear some information on the television, read news or an article, and come to ask questions to me. And many times the employees are not aware, so it generates a demand for us, nurses, to answer these questions.' [Respondent 5 – coordinator]

"And there's no time, there's no such thing, I often see that, when they see a situation… They say: "Look, there's something going on, how can we handle this situation?' [Respondent 6 – business/administration manager]

Discussion

There was a major impact of the COVID-19 pandemic on PEH by FHTs in early and mid-2020, with less opportunities for face to face meetings but there was also a change in the processes of PHE. In response to the challenge, the meetings were maintained but also virtually augmented by the use of social media. The focus of PEH and the role of the coordinator moved towards meeting the urgent and increasing information needs.

Three inter-related lessons learned were noted that have important implications for future PEH in LHT in Brazil but there are also important lessons for primary care educators in other contexts.

Importance of agile organizations in rapidly changing and complex environments

The importance of the ability of an organisation to rapidly respond by transformation and change to unexpected and sudden dramatic events, especially related to external factors, was highlighted. An essential feature of an agile organisation is rapid information management through the use of technology and this feature was also noted in the study. A strength of small organisations, such as PHT, with long term experience of making 'bottom up' decisions is that they can more rapidly and effectively respond to crises than when faced with 'top down' commands.

Importance of information brokers in rapidly changing and complex environments

Making decisions about when and how to make organisational change requires access to appropriate information and the importance of an information broker was highlighted in the study. Information brokers have an essential role in identifying information needs and disseminating information, including providing a synthesis of conflicting information. These actions reduce the time burden on other team members for making sense of the information, which is important when there is a high workload.

Appreciation of socio-technical system for technology adoption

A socio-technical framework highlights the importance of the user perspective in successful adoption of technology in an organization and this was noted in the study. Users prefer using familiar technologies since they are not only useful for their needs but also have ease of use, which is essential when rapid adoption is required in a crisis. The ubiquitous use of social media outside of healthcare is important in Brazil since many nurses in PHT do not use technology in their daily practice, especially for information seeking.

Conclusion

The COVID-19 pandemic in Brazil had a major impact on face to face PHE in FHTs. However, FHTs rapidly and successfully transformed their process for PHE by implementing an online approach using social media. The role of the PHE coordinator also changed from being a facilitator to become an information broker for navigating the large volume of conflicting information and misinformation. The lessons learned are highly relevant in other contexts, and include the importance of being an agile organization, with a 'bottom-up' approach to innovation: key role of having an information broker in rapidly changing and complex environments: and an appreciation of the importance of the socio-technical system for technology implementation in an organization, with the use of familiar technologies.

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