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Review Article

The knee in severe haemophilia with special emphasis on surgical/invasive procedures

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ABSTRACT

Close collaboration between haematologists, orthopaedic surgeons, rehabilitation physicians, pediatricians, pharmacist, radiologist, pain specialist, psychologists, physiotherapists and nurses is essential for the proper handling of knee problems in haemophiliac patients. The ideal scenario would be for the primary prophylaxis (prevention of the disease) to prevent major degenerative changes that we still see so frequently in this type of patients. Until we achieve this we will continue having to perform multiple invasive orthopaedic procedures, such as articular punctures (joint aspiration) to drain haemarthrosis, radiosynovectomies, arthroscopic synovectomies, tendon lenghtenings, realignment osteotomies and total knee replacements (primary and revision) on the knees of people with haemophilia. As a result of this, we will improve the quality of life of haemophiliac patients with orthopaedic knee problems. The rate of potential complications following knee orthopaedic procedures, especially in patients with inhibitors, must not be underestimated.

Contents

Introduction

For the past 50 years, the treatment of haemophilia patients has improved significantly to the point that a newborn with haemophilia living in a developed country can expect to have a normal lifespan and a high quality of life [1]. There is now a wide range of recombinant factor concentrates, and an impressive safety record with respect to pathogen transmission. However, remaining therapeutic challenges include the formation of inhibitory alloantibodies and the international disparity that exists in product availability due to differences in licensure status as well as prohibitively high costs [2]. On the other hand, a wide range of plasma derived factor concentrates are still available and used. However, orthopaedic knee problems are still very frequent in haemophilia. In fact, over the last 50 years orthopaedic surgeons have never stopped operating to resolve multiple problems, from the simple draining of a haemarthrosis (joint aspiration or arthrocentesis) to performing a total knee replacement (TKR), whether primary or for revision. In this

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article we will analyse orthopaedic knee problems in haemophilia and the surgical techniques that can be used to relieve these problems.

General Concepts

In some countries (20-30% of the world population), the orthopaedic problems of haemophilia have reduced since the prophylaxis of haemarthrosis and arthropathies was introduced in them [3–5]. In this way, in these countries, they have managed to turn serious haemophilia into a milder type of haemophilia, maintaining the factor level above 1% permanently [4–6]. This achievement has not been easy, due to the enormous economic problem it represents, as well as the difficulty in achieving intravenous lines in patients with haemophilia (catheter infection, repeated vein punctures from early childhood, etc.). Patients in primary prophylaxis can even enjoy sporting activities but not in a similar to those performed by the general population [7]. Even without inhibitor, even with prophylaxis, a severe patient still have some limitations. Sport activities particularly deleterious for the health of the knee are those including impacts and twisting of the knee (soccer, football, basket ball, volley ball, et cetera).

Other developed countries do not use the above-mentioned prophylaxis in its primary form (i.e. starting at 2 years of age before the appearance of the first haemarthrosis) but rather its secondary form (i.e. starting it as decided by each haematologist at a slightly later age, when some haemarthrosis have already occurred). According to Fischer et al., prophylaxis has become the standard mantra of care for those individuals with severe haemophilia [8]. Primary prophylaxis is advocated to prevent the occurrence of symptomatic acute spontaneous haemarthroses and to preserve joint structure and function. Typically, twice or thrice weekly infusions of factor VIII or IX concentrates are integral to this treatment approach. Secondary prophylaxis is initiated after the relentless cycle of progressive joint damage has been triggered by prior haemarthroses and is intended to preserve existing joint health by preventing additional spontaneous bleeding events. Event-driven prophylaxis involves the administration of clotting factor concentrates to prevent acute traumatic bleeds, which are anticipated to occur in association with surgical or physical trauma. This regimen enhances the effectiveness of primary or secondary prophylaxis protocols or on-demand approaches to replacement therapy. Besides the marked reduction in the so-called annual bleed rate, prophylaxis regimens frequently increase personal self-confidence to embark on a more active and physical lifestyle; however, in reality, prophylaxis must be individualized in accordance with bleeding phenotypes, with the unique pharmacokinetic profile of administered replacement clotting factor concentrates, with the specific clinical scenario, and with the degree of intensity anticipated for any physical activity. The introduction of extended half-life replacement products will also influence how these prophylaxis regimens will be accomplished. Another form of secondary prophylaxis is prophylactic treatment in adults. Makris has stated that prophylaxis in haemophilia should be life-long [9].

The huge economic cost of primary prophylaxis means that 70-80% of the world's haemophiliac population does not have access to that treatment; what is more, some regions of the world do not even have access to the on-demand treatment, that is, the deficit factor replacement therapy when a haemorrhagic episode occurs (haemarthrosis) [5,10].

We live in a world in which we know quite a lot about the ideal treatment of the disease, but in which we cannot always carry it out. Prophylaxis was initially used in Sweden, but very soon it extended all over the developed world [6]. Currently it is the gold standard of treatment [4]. In the developed world, the health authorities do not restrict the treatment of people with haemophilia, and nowadays, haemophiliac children display a much better musculoskeletal situation than 50 years ago; however, the children of that time are now adults, who, despite being lucky enough to have survived the HIV epidemic, suffer serious articular knee complications, which often require an orthopaedic surgeon. In developing countries, low-dose prohylaxis is being currently used [11]. The most problematic patients are those who develop inhibitors, although we can now perform orthopaedic knee procedures on them with a high success rate [1–3,5,6,12–14]. The exact rate of success in terms of infection of TKR in non-haemophilia patients is 1% on average; however, in haemophilia patients without inhibitors the rate is 6% on average, while in haemophilia patients with inhibitors the rate is 10-12% on average [15–17].

In haemophilia it is essential to carry out an individual treatment plan for each patient. In the case of a surgical procedure, the haematological standard must be extremely careful, whereby it is the haematologist's mission to assess the benefit of treatment in bolus or in continuous infusion. Haematological standard means that when performing a major surgical knee procedure, the ideal level of the deficient factor must be 100% for about 2 weeks, although lower levels can be enough (Table 1). In other words, the multidisciplinary team basically formed by a haematologist, orthopaedic surgeon, rehabilitation physician, pharmacist, radiologist, pain specialist, pediatrician, psychologist, physiotherapist and a nurse is essential for the correct treatment of musculoskeletal knee problems in the haemophiliac patient. All the orthopaedic procedures that will analysed in this article are considered major procedures from the haematological point of view, except for joint aspiration, and chemical synovectomy and radiosynovectomy.

The whole musculo-skeletal problems (not only the knee problems) represent 80-90% of the problems that people with haemophilia suffer throughout their lives [5,18].

The role of subclinical bleeding episodes in the development of the knee arthropathy is not well known, but there is no doubt that subclinical bleeds may have an influence in cases of severe arthropathy associated with a small number of recurrent bleeding episodes [10].

Although the knee was previously the main problem in young children with haemophilia, they currently experience more problematic issues with ankles than their older counterparts because of the extensive use of prophylaxis that allow them to play contact sports, mainly soccer [19].

Anti-inflammatory medications, mainly COX-2 inhibitors, are commonly used in cases of articular pain associated with swelling of the joint, with good results [20].

Sometimes it may be recommendable to perform double or triple surgery in one surgical act, in order to resolve the patient's functional problem globally (due to the fact that the pathology is usually polyarticular). Undoubtedly this increases the risk of anaesthesia, although, on the other hand it can produce savings in the clotting factor and avoid repeated surgeries [21]. All surgery must be carried out with intravenous antibiotic prophylaxis for 24–48 hours.

The potential impact of other orthopedic procedures on the health of the knee is not well known but seems to be low. For example, there is a

Table 1
Plasma factor trough levels and duration of administration in patients with haemophilia A and B without inhibitors undergoing major orthopaedic procedures. Ideally, levels should be 100 for the 15 first post-operative days.

HAEMOPHILIA A		
	LEVEL (IU dl-1)	DURATION (days)
PRE-OPERATIVE	80-100	
POST-OPERATIVE	60-80	1-3
	40-60	4-6
	30-50	7-14
HAEMOPHILIA B		
	LEVEL (IU dL-1)	DURATION (days)
PRE-OPERATIVE	60-80	
POST-OPERATIVE	40-60	1-3
	30-50	4-6
	20-40	7-14