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Diagnostic and treatment methods of skeletal symptoms of haemophilia and education of patients regarding the disease – review study

Metody diagnostyczne i terapeutyczne objawów szkieletowych w hemofilii oraz edukacja pacjentów w zakresie choroby – przegląd badań

Adrianna Gorecka

https://orcid.org/0000-0003-1977-712X

Medical University of Lublin

Natalia Osial

https://orcid.org/0000-0003-2081-5592

Medical University of Lublin

Abstract

Introduction. Haemophilia is a genetic haemorrhagic disorder that characterises with extensive and prolonged bleeding. In severe stages of the disease, joint haemorrhages may occur and eventually result in joint degeneration and haemophilic arthropathy.

Aim of the study. Summary and evaluation of diagnostic and treatment methods of skeletal problems in patients with haemophilia. Review of patients' knowledge about the disease.

Material and methods. Review of the newest medical journal literature published on PubMed database.

Results. Ultrasonography is a non-invasive imaging method used to diagnose acute hemarthrosis and early stages of joint damage. Magnetic resonance is a standard tool in evaluation and scoring of haemophilic arthropathy. X-rays and computed tomography can also be additionally used, but are ineffective in imaging soft tissue and cartilage. Substitution of clotting factors is a standard treatment in haemophilia which reduces the frequency of bleeding. Arthrocentesis, synovectomy for example radiosynovectomy are effective in case of joint disorders. Intra-joint injections of hyaluronic acid are

also effective. In advanced stages of haemophilic arthropathy joint replacement is recommended. Majority of patients with haemophilia claim that they are sufficiently educated about their disease.

Conclusion. Haemophilic arthropathy is a severe joint destructing condition that causes limited mobility, chronic pain and a reduced quality of life. Its early diagnosis and proper treatment is necessary to avoid total destruction of the affected joint. Multidisciplinary care of the patient is an approach of great importance. Education of patients about their disease and up-to-date treatment methods is necessary.

Key words: haemophilia, arthropathy, haemophilic arthropathy, radiosynovectomy, clotting factors, education

Abstrakt

Wprowadzenie. Hemofilia jest genetycznym zaburzeniem krwotocznym, które charakteryzuje się nadmiernym i wydłużonym krwawieniem. W ciężkich postaciach choroby mogą wystąpić krwawienia dostawowe i w konsekwencji doprowadzić do degeneracji stawu i artropatii hemofilowej.

Cel pracy. Podsumowanie i ocena metod diagnostyki i leczenia schorzeń układu kostnego u chorych na hemofilię. Przegląd wiedzy pacjentów na temat choroby.

Materiał i metody. Przegląd najnowszej literatury medycznej opublikowanej w bazie danych PubMed.

Wyniki. Ultrasonografia jest nieinwazyjną metodą obrazowania używaną do diagnozowania ostrej choroby zwyrodnieniowej stawów oraz wczesnych stadiów uszkodzenia stawu. Rezonans magnetyczny jest standardowym narzędziem do oceny zaawansowania artropatii hemofilowej. Zdjęcia RTG i tomografia komputerowa mogą być dodatkowo używane, lecz są nieefektywne w obrazowaniu tkanek miękkich i chrząstki. Substytucja czynników krzepnięcia jest podstawowym leczeniem w hemofilii, które redukuje częstotliwość krwawień. Artrocenteza, synowektomia - np. radiosynowektomia, są skuteczne w razie zaburzeń stawowych. Dostawowe iniekcje kwasu hialuronowego również mogą okazać się korzystne. W zaawansowanych stadiach artropatii hemofilowej rekomendowana jest wymiana stawu. Większość pacjentów chorych na hemofilię uważa, że ich wiedza na temat choroby jest wystarczająca.

Wnioski. Artropatia hemofilowa jest jest ciężką chorobą wyniszczającą stawy, która powoduje ograniczoną ruchomość, przewlekły ból i obniżoną jakość życia. Wczesne rozpoznanie i właściwe leczenie jest niezbędne, aby uniknąć całkowitego zniszczenia zajętego stawu. Wielodyscyplinarna opieka nad pacjentem ma ogromne znaczenie. Konieczna jest edukacja pacjentów na temat ich choroby i nowoczesnych metod leczenia.

Słowa kluczowe: hemofilia, artropatia, artropatia hemofilowa, radiosynowektomia, czynniki krzepnięcia, edukacja

Introduction - epidemiology and genetics of haemophilia

Haemophilia is the most common severe hereditary haemorrhagic disorder [1]. It is a chromosome X-linked disease, so the majority of people affected by the disease are men, while woman are carriers of the defected gene and do not develop symptoms. Symptomatic haemophilia in woman is possible, when both X chromosomes have mutant allele [2]. When a mutant gene is identified in a patient, genetic tests for at-risk family members and prenatal examination for a pregnancy at increased risk are

possible to diagnose a disease [3]. Haemophilia is classified into type A, B or C and characterises with lack, deficiency or decreased activity of clotting factors – VIII, IX or XI, respectively. In Poland, the most common type of haemophilia is type A, with a prevalence of 7/100 000, then type B - 1/100 000. Type C is much rarer [4].

Clinical symptoms of haemophilia

Main symptom of haemophilia is extensive and prolonged bleeding that can occur even after minor injuries or spontaneously. The age of diagnosis and frequency of bleeding episodes are related to the activity level of clotting factor [3]. We can divide haemophilia into three groups: severe - <1% active clotting factor, moderate – 1-5 % active clotting factor and mild - >5% active clotting factor. In patients with mild haemophilia spontaneous bleeding incidents do not occur, however abnormal bleeding is reported after such interventions as tooth extractions or skin incision. Individuals with this type of the disease are often diagnosed later in life. People suffering from moderate haemophilia have prolonged bleeding after relatively minor trauma, with the frequency varying on average from once a month to once a year. Bleeding with no history of trauma can also happen.

The most severe symptoms are presented in severe haemophilia and the diagnosis is usually mad in the first two years of life. Up to five spontaneous bleeding may happen every month. Oral or soft tissue bleeding with pain and swelling are observed. Severe haemophilia is the only type in which joint bleeds are observed [3].

Haemophilic arthropathy

A characteristic symptom of severe haemophilia A or B (<1% active clotting factor, VIII or IX) is hemarthrosis, which develop due to recurrent joint haemorrhages and may lead to haemophilic arthropathy. First intra-articular joint bleedings in haemophilia A appear in early childhood and their frequency increases with age. Direct influence of iron contained in the blood provokes degeneration of synovial membrane, cartilage and subchondral constituents [5]. Inflammation caused by iron, cytokines and growth factors lead to synovitis hypertrophy, osteopenia and even cartilage and bone destruction [6]. The most frequently affected joint as a knee, followed by an ankle and an elbow [7]. The first symptom reported by patients is pain, redness and limited joint mobility, eventually followed by joint remodelling, chronic pain and a reduced quality of life.

Diagnosis of haemophilic arthropathy

X-ray is an initial imaging modality, though mainly moderate and severe arthropathic changes may be well detected. X-ray enables to visualise narrowing of the joint space due to cartilage disorders, irregular subchondral bone or subchondral cysts [8]. Computed tomography (CT) might be helpful in detecting minor defects of the cortical bone and in visualizing loose bone fragments in more advanced stages of arthropathy. As both X-ray and computed tomography are insensitive for soft tissue and cartilage changes other imaging methods should be applied in less advanced cases [8], as early recognition of joint haemorrhage and early diagnosis of haemophilic arthropathy is pivotal to prevent patients' disability.

Ultrasonography (USG) - cheap, fast and non-invasive diagnostic tool - enables the diagnosis of acute hemarthrosis and early haemophilic arthropathy as well as better monitoring of progressive joint

damage [9]. In USG, however, total joint visualization is impossible due to limited tissue penetration with high-resolution probes [10]. Other imaging method used for assessing arthropathy is magnetic resonance (MR). The method is a current standard in the evaluation of and scoring of haemophilic arthropathy, despite its limitations in imaging synovial hypertrophy [10].

Treatment of haemophilic arthropathy

There is no specific treatment for haemophilic arthropathy, thus prevention from joint bleeding is essential to reduce synovitis and progression of joint damage. Standard treatment for haemophilia is substitution of coagulation factors [9]. Factor replacement therapy provides missing coagulation factors to prevent patients with haemophilia from joint bleeding and decreases their risk for haemophilic arthropathy [6].

If the haemorrhage persists, evacuation of the blood from the joint (arthrocentesis) is recommended and synovectomy is mandatory in the case of synovitis [11]. It is a procedure consisting of the destruction of the inflamed synovium with radiation. Radioisotopes such as Yttrium-90, Rhenium-186 or Rhenium-188 can be used in this method [11,12]. Radiosynovectomy might be a treatment of choice in treating haemophilic arthropathy as it has been shown to reduce bleeding by 65% [11]. It is important to remain a 1-metre distance from the patient treated with radiation to decrease other people's exposure to radiation [12].

Nowadays, more joint-specific methods, are additionally applied. It was observed that intra-articular injections of hyaluronic acid can relieve joint pain even for a few months [5]. Platelet-rich plasma single, administered in intra-joint injections alone or together with hyaluronic acid, is a safe and effective method in treating haemophilic arthropathy. In the 6-month follow-up after administration in the knee joint pain reduction, less bleeding episodes and delaying total knee arthroplasty were observed in both methods [13]. Intra-joint corticosteroids injections, though commonly used in the treatment of osteoarthritis, are not recommended in haemophilic arthropathy, as pain relief after the procedure is controversial and the haematologic treatment required to perform the procedure is costly [14].

In advanced condition of haemophilic arthropathy, joint replacement (endoprosthesis) is necessary, although risk of infection in patients with haemophilia is higher than in patients with osteoarthritis (1-2 vs. 7%) [9,11].

Rehabilitation and physiotherapy are also important to delay patient's disability. Every patient should be taken care of individually. Cooperation of a multidisciplinary team consisting of haematologists, rheumatologists, orthopaedic surgeons, and physiotherapists is necessary [8].

Education of patients

Majority of patients have ample knowledge about haemophilia [15]. It is due to the fact that they often interact with health workers. Moreover, knowledge is gained through personal experience with the disease. It was observed that the more bleedings a person experiences, the higher the knowledge about their health status is. Almost 70% patients fell capable of making decisions regarding their health. More than half of the respondents was satisfied with the care received. Similar results were obtained in cross-national survey covering Central Europe [16]. Over 70% of patients with haemophilia or their caregivers were satisfied with their level of knowledge about the disease. More of them acquired

necessary information from physicians. However, almost all of the respondents were interested in obtaining additional information, particularly about treatment options.

French scientists developed a plastic knee model to educate patients with severe haemophilia about the major complication - haemophilic arthropathy [17]. They aimed to improve care management and self-treatment skills in both adults and children using hemarthrosis-simulating artificial knee. There was a statistically important increase of the mean disease knowledge score in all age groups. Knowledge about the treatment also increased in children and teenagers. These findings suggest that using a hemarthrosis-simulating knee tool may be helpful in educating patients about haemophilic arthropathy.

Conclusion

Haemophilic arthropathy is a severe joint destructing condition that restricts mobility, causes chronic pain and a reduced quality of life. Its early diagnosis is necessary to avoid a complete destruction of the affected joint. Different imaging methods, such as USG, X-ray, MR and CT can be complementary in the evaluation of the disease, especially in solving diagnostic dilemmas. Patient management should be based individual risk assessment of arthropathy progression. Proper haematological treatment, such as substitution of clotting factors is highly effective in minimalizing the risk of joint bleeding. Joint-specific methods such as arthrocentesis, synovectomy, intra-joint injections of hyaluronic acid or platelet-rich plasma are also effective. All patients should be collaboratively cared for by multidisciplinary teams of haematologists, rheumatologists, orthopaedic surgeons and physiotherapists. Multidisciplinary care of the patient is an approach of great importance. Although the majority of patients report that they are sufficiently educated about haemophilia, there is a need for constant education about haemophilia and newest treatment methods to enable patients to react appropriately to their health condition.

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