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Effect of Exercise on Muscle Strength, Pain and Functional Ability in Patients with Haemophilia: A Narrative Review

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Abstract: ***Background: Haemophilia is an inherited bleeding disorder. It is caused by an x - linked deficiency of coagulation factors VIII in haemophilia A and factor IX in haemophilia B. Haemophilia is estimated to occur in one in 10, 000 births. In haemophilia 65–80% of all bleeding episodes are intra - articular, and 80% of them are mainly localized in elbows, ankles and knees. Recurrent intra articular bleeding occur with haemophilic arthropathy which cause muscle atrophy around joint and hallmarked by chronic synovitis and cartilage destruction. Due to muscle weakness the joint become less stable and more vulnerable to stress and a vicious cycle perpetuates. Adjunctive management for haemophilia is clotting factor precipitate with PRICE principle - protection, rest, ice, compression and elevation protocol for joint and muscle bleed and another approach is POLICE - protection, optimum loading, ice, compression and elevation. Ice is used to treat acute and chronic pain. Strengthening the muscles surrounding the affected joint is a beneficial strategy to stop or delay arthropathy. Resistance training is recommended for strengthening muscles to improve joint stability. Objective: To find out the effect of exercise on muscle strength, pain and functional ability in patients of haemophilia. Study selection: This narrative review is conducted on databases from Pub med, Google scholar and ResearchGate. This review included 10 studies on the effect of resistance exercise on muscle strength, pain and functional ability in patients of haemophilia. Conclusion: it is concluded that exercise training effective in increasing muscle strength, decreasing pain and improving functional ability. But some studies show some limitations. so further studies of higher methodological quality are needed to determine the optimal type of exercise, optimal dosage and timing.***

Keywords: Haemophilia, Muscle Strength, Pain Management, Functional Ability, Exercise Training

1. Introduction

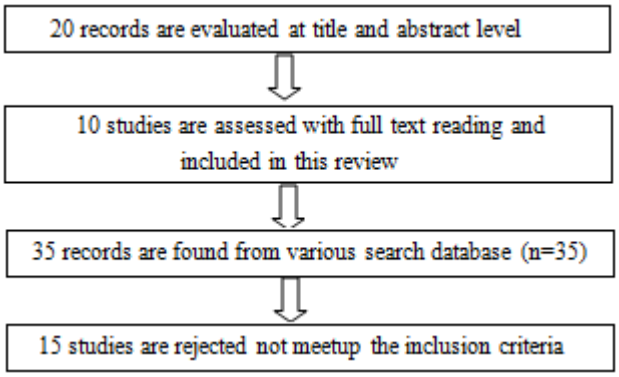
Haemophilia is an inherited bleeding disorder caused by an x - linked deficiency of coagulation factors VIII in haemophilia A and factor IX in haemophilia B.1 Haemophilia A is more common than haemophilia B, representing 80–85% of the total haemophilia population.[2] Haemophilia generally affects males on the maternal side and both F8 and F9 genes are prone to new mutations, and as many as 1/3 of all cases are the result of spontaneous mutation where there is no prior family history.[2] In haemophilia 65–80% of all bleeding episodes are intra - articular, and 80% of them are mainly localized in elbows, ankles and knees.3 Haemophilia is estimated to occur in one in 10, 000 births.2 There are three levels of haemophilia based on the proportion of the clotting factor in patients' blood are: [4]Severe: clotting factor level < 1 % of normal, characterized by spontaneous bleeding without trauma, Moderate: 1 - 5 % of normal, have risk of occasional bleeding with minor trauma, Mild: 5 - 40 % of normal, severe bleeding with minor trauma.4Most bleeding occurs internally into the joints or muscles and Some bleeds can be life - threatening line intracranial, neck, GIT and require immediate treatment. Recurrent intra articular bleeding occur with homophilic arthropathy which cause muscle atrophy around joint and hallmarked by chronic synovitis and cartilage destruction.[3] Due to muscle weakness the joint become less stable and more vulnerable to stress and a vicious cycle perpetuates.[5] The goal for prevention of arthropathy is to break this vicious circle by effective haemostatic therapy and physiotherapy. Even the haemophiliacs whose joints are free from arthropathy show a decrease in physical condition, muscular strength, aerobic resistance, anaerobic resistance and proprioception.[3] A correct diagnosis is essential to ensure that a patient gets the appropriate treatment. Principles of diagnosis are understanding the clinical features of haemophilia and the appropriateness of the clinical diagnosis. Using screening tests to identify the potential cause of bleeding, for example, platelet count, bleeding time or other platelet function screening tests, prothrombin time (PT), and activated partial thromboplastin time (APTT).[2]

Haemophilia can be managed in three different ways: through surgery, physical therapy, and medications that promote clotting while also treating pain and coexisting illnesses.6 Replacement therapy, using either clotting factor VIII for haemophilia A or clotting factor IX for haemophilia B, or cryoprecipitate or fresh frozen plasma, is used to treat haemorrhagic episodes in people with haemophilia.

Treatment with clotting factor concentrate is recommended.[7] Adjunctive management for haemophilia is clotting factor precipitate with PRICE principle - protection, rest, ice, compression and elevation protocol for joint and muscle bleed and another approach is POLICE - protection, optimum loading, ice, compression and elevation. Ice is used to treat acute and chronic pain.[2] Strengthening the muscles surrounding the affected joint is a beneficial strategy to stop or delay arthropathy. Resistance training is recommended for strengthening muscles to improve joint stability.5 Resistance training is a viable option for boosting muscle strength because the resulting joint stability could lessen bleeding episodes' frequency and severity as well as the pain and contracture they cause.[8]

2. Methods

Studies are search from the following search engine PubMed, Google scholar, ResearchGate and Cochrane library to review the literature. Studies include that muscle strength, pain and functional ability. Key words used to search studies are exercise training, pain, functional ability and haemophilia.



Authors, Journal, Year	Objectives	Design	Characteristics of participants sample size	Material and Methods	Outcomes Measures	Results
TIKTINSKYet al.2000[5]	The effect of resistance training on the frequency of bleeding in hemophilia patients	pilot study	3 patients, 1 patient age is 21 years and other 2 patients 11 years	Both patients participated in progressive resistance training 3 times week) 1, 45–60 min at each session, patient 1 for 2 years, and patient 2 for 1 year. Patient 3 began training at the age of 9 years, and has been training for 21 years. He has been engaged in resistance training 3 times week) 1, although at certain periods he trained 4–5 times week) 1, for 45 min	ROM, Muscle strength and bleeding profile	the range of motion remained unchanged while muscle strength, as evaluated manually, clearly improved.
Mulvany et al.2010[6]	Effects of a 6 - Week, Individualized, Supervised Exercise Program for People with Bleeding Disorders and Haemophilic Arthritis	Single group, pretest - post - test clinical design	Thirty - three patents with mild to severe hemophilia, 3 female, 30 male, age: 7 - 57 years	6 weeks, twice a week, individualized supervised exercise program	Muscle strength, joint rom, joint and extremity circumference, distance walked in 6 minutes	Significant improvement occurred in joint motion, strength, and distance walked in 6 minutes, with no change in joint circumference
Eid et al.2013[4]	Effect of resistance and aerobic exercise on bone mineral density, muscle strength and functional ability in children with haemophilia	Experimental study	30 boys with haemophilia, age: 10 - 14 years Selected from Abo El - Rish paediatric hospital	Subject divided into 2 groups control and study group. Control group received physical therapy program and aerobic exercise, study group received same program as control group and resistance training program. Treatment sessions 3 times per week for 3 successive months.	Bone mineral density, muscle strength (Knee flexors and extensors), functional capacity (6MWT	There was no significant difference between both groups in the pre - treatment mean values of all measured variables. Significant improvement was observed in Bone mineral density, knee extensors and flexors strength and functional ability in the study group when comparing pre and post treatment measurements
Zaky et al.2013[9]	Effect of partial weight bearing program on functional ability and quadriceps	Experimental study	30 male patients moderate haemophilia,	Patients divided into 2 groups, control group received quadriceps exercise and study group	6MWT, Muscle strength	Both groups demonstrated a significant increase in function, as

	muscle performance in hemophilic knee arthritis		age: 8 - 12 years	received weight bearing exercise, supine wall push, wall push against Swiss ball, supine half bridging exercise for 6 weeks, 3times per week		measured by the six - minute walk test, Quadriceps isometric muscle strength was significantly improved in both groups
Parhampour et al.2014[8]	Effects of short - term resistance training and pulsed electromagnetic fields on bone metabolism and joint function in severe hemophilia A patients with osteoporosis	randomized controlled trial	48 patients with severe haemophilia, age 20–35 years	Patients randomly assigned to resistance training (RT, n = 13), combined resistance training with pulsed electromagnetic fields (RTPEMFn = 12), pulsed electromagnetic fields (PEMF n = 11) and control (n = 12) groups	Joint function, using the modified Colorado Questionnaire and Bone - specific alkaline phosphatase, N - terminal telopeptide of type 1 collagen,	After six weeks, the RT and RTPEMF groups showed a significant increase in muscle strength (one repetition maximum), There was no significant difference in these changes between the RT and RTPEMF groups
Goto et al.2014[3]	Self - monitoring has potential for home exercise programmes in patients with hemophilia	randomized controlled trial	Subjects 32 male outpatients, aged 26–64 years without an inhibitor, 8 weeks at four hospitals in Tokyo	Subjects randomly allocated to a self - monitoring group and a control group, both groups received home exercise guidance, self - monitoring group with Feed - back system and activity monitoring and control grp with no displaying activity	modified Marcus scale, visual analogue scale and muscle strength (hand held dynamometer),	home exercise improved their physical function without increased bleeding frequency and pain
Calatayud et al.2019[1]	Upper - Body Exercises with External Resistance Are Well Tolerated and Enhance Muscle Activity in People with Hemophilia	cross - sectional study.	12 patients with haemophilia, A and B, age above 18	Patient performed 2 exercises (shoulder abduction and elbow flexion) with 3 different conditions: 2 types of external resistance (elastic bands and free weights) and without external resistance (conventional).	Surface electromyography signals recorded for the biceps brachii, triceps brachii, upper trapezius, and middle deltoid muscles, kinesiophobia scale	Externally resisted exercises provided greater muscle activity than conventional no resisted therapeutic exercises. The exercises generally well tolerated and there was no change in kinesiophobia following the session.
Calatayud et al.2019[10]	Electromyographic and Safety Comparisons of Common Lower Limb Rehabilitation Exercises for People with Hemophilia	cross - sectional study.	11 patients with severe haemophilia, age above 18	single experimental session, participants performed knee extension and ankle plantar flexion during 3 conditions: elastic band - based resistance, machine - based resistance, and no external resistance. Once per week.	surface electromyography (EMG) for the rectus femoris, biceps femoris, gastrocnemius lateralis, and tibialis anterior muscles, exercise tolerability test	In the knee extension exercise, rectus femoris RMS nEMG values during the elastic resistance and machine resistance conditions similar; 29% to 30% higher activity (P <.01) and a large effect size were obtained than the non - external resistance condition. All the exercises performed tolerated by the participants with a general reported high tolerance
Calatayud et al.2020[11]	Safety and Effectiveness of Progressive Moderate - to - Vigorous Intensity Elastic Resistance Training on Physical Function	randomized controlled trial	20 patients (17 with severe, 1 with moderate, and 2 with mild haemophilia), age: 21 - 53	Subject divided into 2 groups: intervention and control group, intervention group trained 2 days per week during 8 weeks with elastic resistance, Intensity during the first 2 weeks	primary outcome - muscle strength, Secondary outcomes: Timed “Up and Go” Test (TUG), sit - to - stand, ROM, Haemophilia Joint	intervention group showed greater strength improvements than the control group in almost all of the joints, also showed

	and Pain in People with Hemophilia.		years, 8week follow up	was a 20 - repetition maximum (RM) and increased progressively toward 15RM, 12RM, and finally 10RM.	Health Score (HJHS), kinesiophobia score, global impression of pain change, general self - rated health status and desire to exercise	better TUG and sit - to - stand scores and showed greater overall pain reduction
Montecinos et al.2023[12]	Effectiveness of progressive moderate - vigorous intensity elastic resistance training on quality of life and perceived functional abilities in people with hemophilia	randomized controlled trial	18 - 60 years, with severe haemophilia	Two groups: intervention and control group. The intervention group performed progressive moderate - vigorous elastic resistance training (2 days/week, a total of 8 weeks), focusing on the muscles of the knee, elbow, and ankle joints. The control group continued its usual daily activities for 8 weeks.	Quality of life (A36 Haemophilia QoL) and perceived functional abilities (Haemophilia Activities List)	improved the quality - of - life dimension of joint damage perception and functional abilities in comparison to the control group

3. Discussion

The muscle strength, pain and functional abilities improved by resistance exercise training. The main objective of this review is to find out the effect of resistance exercise on muscle strength, pain and functional abilities. Recurrent intra articular bleeding occur with haemophilic arthropathy which cause muscle atrophy around joint and hallmarked by chronic synovitis and cartilage destruction.[3] Due to muscle weakness the joint become less stable and more vulnerable to stress and a vicious cycle perpetuates.[5] Strength training, among other forms of exercise, is advised to help people with chronic arthropathy regain their physical function; its importance increases with age and the severity of the arthropathy. Strength training can reduce the amount of circulating inflammatory cells, minimising or preventing bleeding and the discomfort that goes along with it.[11]Exercise programs based on elastic resistance bands are especially interesting due to minimal impact forces and low risk of accidents compared with traditional heavy weight.[11]A study by Calatayud et al. proven that externally resisted exercises provided greater muscle activity than conventional therapy.[1] A study by Montecinos et al. proven that progressive moderate - vigorous intensity elastic resistance training improve functional abilities, quality of life and dimension of joint damage. Calatayud et al. presented results that Progressive Moderate - to - Vigorous Intensity Elastic Resistance Training reduce overall pain, improve functional ability, joint health and muscle strength.[11]Eid et al. presented result that significant improvement was observed in bmd, knee extensors and flexors strength and functional ability in the study group when undergone resistance training and aerobic exercise.[4]

Through above studies, it is found that the exercise improves muscle strength, pain and functional ability.

4. Conclusion

Resistance exercise training is effective method for improvement of muscle strength, pain and functional ability. All the above mention studies have multiple limitations such as inadequate sample size, short intervention period, the lack of descriptions of side effects and the safety of the reported intervention is compromised by the included trials' insufficient reporting on the coagulation treatment regimen. No study revealed that training - related bleeding occurred. Optimal types of exercise and optimal dosage have yet to be determined. Hence, in order to establish a definitive protocolto overcome all these limitations.

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