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Review

Facioscapulohumeral distrophy and physiotherapy: a literary review

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Abstract. [Purpose] The purpose of this review was to critically evaluate the literature concerning the physiotherapy of facioscapulohumeral dystrophy, and to determine an effective protocol for physiotherapy treatments, which can be adapted to patient characteristics. [Methods] A bibliographic research was carried out of research papers held in the following databases: PUBMED, PEDRO, MEDLINE, EDS BASE INDEX. The inclusion criteria for acceptance of the studies to the review were randomized controlled trials (RCTs) concerning a sample no smaller than 10 people and a medium- or long-term report of the results achieved. [Results] Just six of the works satisfied the inclusion criteria, and just three of them were useful for the review. However, these studies were difficult to compare. [Conclusion] At present, there are few studies concerning facioscapulohumeral dystrophy in the literature, and the few that are available rule out the utility of the techniques used. Therefore, more RCTs of new treatment strategies are needed.

Key words: Facioscapulohumeral dystrophy, Rehabilitation, Treatment

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INTRODUCTION

Facioscapulohumeral dystrophy (FSHD) is a genetic neuromuscular disorder, currently the third most diffuse in the world[1)]. This myopathy is linked to a dominant autosomic pattern and it begins in the second or third decade with an estimated prevalence of 1:20,000[2)].

FSHD initially involves the facial muscles and the scapula stabilisers, and it often progresses breaking down the forward musculature of the lower limbs and of the pelvic girdle, often developing abdominal weakness and lumbar hyperlordosis[3)]. The pathological involvement of the muscles is generally slow and often asymmetric, and the clinical development of the disease varies considerably, with sudden periods of fast progression. About 20% of the patients require wheelchairs[4)]. Life expectancy of FSHD patients is almost average, even though breathing complications can occur wich may progress all the way to respiratory disease[5)].

Quality of life (QoL) is strongly compromised in FSHD. In a recent Italian work it was shown that the QoL of FSHD patients was considerably lower than that of the population average, and the main complaints were on the motor side[6)]. It is important to emphasize that, to this day, a definitive therapy for FSHD doesn't exist, and that symptomatic surgical, pharmacological and rehabilitative interventions have to be considered. Regarding surgery, the use of scapula setting to improve upper limb control has long been confirmed in the literature[7–9)]. Yet, on the pharmacological side, trials with conflicting results have been reported. The first drugs to have been tested were corticosteroids for musculature inflammation. The literature, however, shows that even if administered in high doses, corticosteroids do not have any effect on muscle mass or muscular strength[10)]. Recently, the experimental use of salbutamol for FSHD has been reported, but in this case also it hasn't been approved for routine use[11)]. Moreover, no clinical benefits have been found in the use of monohydrate creatine[12)] or myostatine[13)], while a new generation of inhibitors haven't been tested, yet.

The rehabilitative aspect deserves a different treatise, and evidence in favour of physiotherapy treatments is not lacking[14)]; however a standardized protocol for FSHD patients doesn't exist. The objectives of the present review were to evaluate works in the literature concerning physiotherapy treatments for FSHD, focusing on the methodology of the studies, and recommendations arising from them; and to verify if the treatment recommendations were sufficiently validated, in order to design an effective protocol for physiotherapy treatment, by adapting the programme to patient characteristics.

METHODS

A bibliographic search of physiotherapy treatments used for FSHD was conducted of the following databases: PUBMED, PEDRO, MEDLINE, EDS BASE INDEX. The search of the EDS BASE INDEX was conducted using the database of the University Federico II of Naples. Due to the different terminology used to name the pathology, the search

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Table 1. Key words used in the literary research

Key word 1	Key word 2	Key word 3	Boolean operand
Facioscapulohumeral distrophy	Rehabilitation	Physiotherapy	And/Or
Facio scapulo humeral distrophy	Rehabilitation	Physiotherapy	And/Or
Fshd	Rehabilitation	Physiotherapy	And/Or

Every word in the first column has been alternatively linked to the correspondent in the second and third columns, thus selecting the results in which the words appeared together (booleano operand And) or singularly (booleano operand Or). The research has been repeated in all the databases: PubMed, Medline, Pedro, Eds base index.

was conducted using the key words specified in Table 1. The target of the search was all studies performed from 1988 to 2014, and the inclusion criteria were: controlled randomized trials with a sample size no smaller than 10 patients; and, where possible, studies with results obtained over the medium to long term.

RESULTS

Figure 1 shows the selection procedure and the progressive selection of the results of the search. The initial search yielded 1,311 results. In the first evaluation, publication types not complying with the research criteria (acts of congresses, extracts of textbooks, etc.), and studies recorded in more than one database were eliminated.

Through this selection 1,273 results were rejected. Then, a second filter was applied to the remaining 38 articles, eliminating all those that did not directly concern the rehabilitation treatment. This left just 24 works in the final stage of the review.

Among these studies, six had the highest level of methodological quality, as they were controlled randomized trials, while another six works were prospective studies without a control group. There were also six systematic reviews (concerning FSHD case management), a case report and a controlled study. For four studies, the nature of the work could not be verified, due to lack of information.

Considering the inclusion criteria basis, just six works of the first group were admitted to the final review. In Table 2 the main characteristics and the indications of the selected studies are summarized.

The first study[15] was a RCT, attempting to verify the aerobic training (AET) effect and the cognitive-behavioural therapy (CBT) effect on chronic fatigue of FSHD patients which had already been theoretically proposed in the FACTS-2 protocol[18]. The authors collected 57 patients affected by FSHD from different Dutch study centres, and randomly divided them into three groups: an AET group, a CBT group, and a group which continued with traditional treatments. The patients were evaluated after 16 weeks of intervention and 12 weeks of follow-up.

Outcome measures were: the Short Fatigue Questionnaire, Checklist Individual Strength-Fatigue, Nottingham Health Profile-Sleep, Sickness Impact Profile 68-Social Behaviour, Visual Analogue Scale.

A lower fatigue level and better physical performance was shown by the AET and CBT groups, and the CBT group also showed better sleep quality and better social participation.

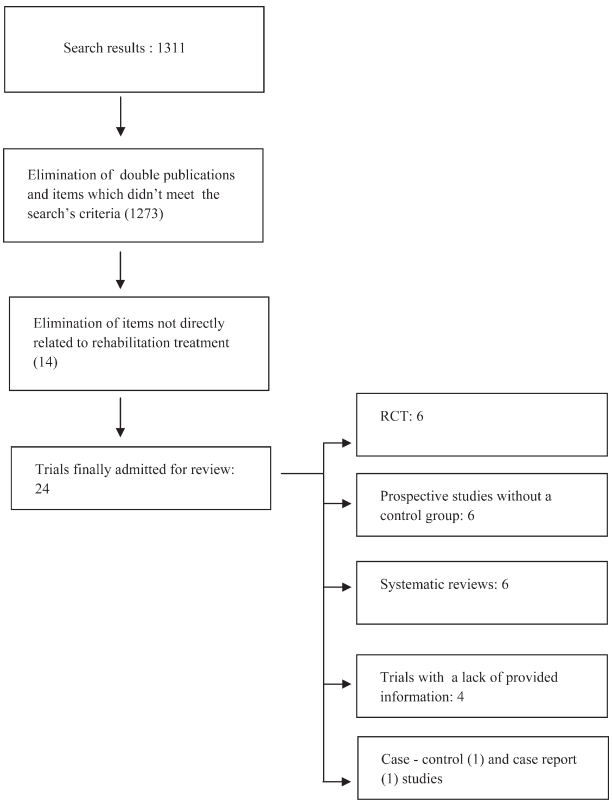

Fig. 1. Selection and progressive selection of the literary research results, which yielded 1,311 results

After considering all the publications reported more than once, the trials which did not satisfy the inclusion criteria or the trials concerning diagnosis/surgery aspects, just 24 studies were admitted to the final stage of the review. Among these six were RCT, 6 were prospective studies without any control group, 6 were systematic reviews, 1 was a case report, 1was a case/ control study, and 4 were not identified.

The study concluded that AET and CBT showed positive indications for FSHD patients.

The second work[16] was a RCT that analysed the efficiency of Kinect in the range of motion of the upper limbs of FSHD patients. Twenty-two patients in an experimental group and 24 age-and height-matched patients in a control group were examined. The evaluation of the reachable space in all of the quarters was normalized to each of the upper limb lengths. While there was a general reduction of the working space with regard to the controls ($p<0.0001$), there

Table 2. Main characteristics of the included trials

Year of publication	Authors	Kind of study	Number of patients	Conclusions
2014	Voet N, Bleijenberg G, Hendriks J et al.[15]	RCT	77	Aerobic training and cognitive behavior therapy can reduce fatigue in FSHD
2014	Han JJ, Kurillo G, Abresch RT et al.[16]	RCT	46	Use of Kinect to explore the working space of the upper limb of FSHD patients
2014	Bankole LC, Millet GY, Temesi J et al.[17]	RCT – only academic databases	16	Effectiveness of a home-based program of exercises
2010	Voet NB, Bleijenberg G, Padberg GW et al.[21]	RCT	---	Designing an intervention protocol for FSHD
2007	Kooi, E., Kalkman, J., Lindeman E et al.[22]	RCT	65	Exercise and administration of albuterol didn't affect pain or fatigue
2001	Kilmer DD, Aitkens SG, Wright NC et al.[24]	RCT	32	Eccentric contractions useless in the short term

In the first column, the publication year is shown; in the second, the authors; in the third, the kind of study; in the fourth, the number of patients; and in the fifth, the authors' conclusions.

were no differences between the two sides according to the dominant hand. The main indication that comes from it is the use of the Kinect for the evaluation and exploration of the working space of the upper extremity.

The third study considered[17] was a trial reported only in academic databases concerning a domestic rehabilitation treatment for FSHD patients. Domestic physiotherapy has yielded positive results in many neurological[18, 19] and orthopaedic[20] pathologies. In the study[17], 16 patients performed exercise for three weeks (to be cyclically repeated), but the exercises prescribed weren't described. The outcome measures cited by the authors included: clinical tests, muscular fatigue, evaluation of strength and quality of life questionnaires. The study concluded that there was a positive indication for the use of home therapy.

The fourth study[21], as noted above, was a theoretical proposal to conduct a study of FSHD in accordance with the protocol FACTS-II, and the authors were the same as those of the first described study[15]. This study followed the rules proposed 4 years earlier.

The fifth study selected[22] was a RCT in which the authors had examined the efficacy of a pharmacological therapy (albuterol) and strengthening exercises for the flexor muscles of the elbow and rear hip flexor on the reduction of pain and fatigue in FSHD. The sample examined was composed of 65 patients, who were divided into a group that received physiotherapy and another one that did not. After 26 weeks, albuterol was randomly introduced, for another 26 weeks. The outcome measures were: the maximum voluntary isometric concentration (MVIC) of the muscular groups examined, the resistance to the muscular effort, and the strength during the motion, for the evaluation of effect of manual therapy; and the MVIC of eight muscular groups, including those under manual therapy, for the evaluation of the effect of albuterol.

A series of evaluation scales (VAS, McGill pain questionnaire, scale SCL, Daily Observed Fatigue score, Daily

Observed Activity score) were also used to evaluate subjective sensations of pain and fatigue.

There were no changes in the different groups in fatigue and pain felt within the day reported by patients. Moreover 80% of the patients reported having felt back, shoulders, leg and neck pain. The authors of the study concluded that these pains could persist because of postural and myalgic components associated with the pathology, as reported by other studies[23].

Finally, we report the results of a study conducted in 2001[24] of eccentric high density contractions performed by myopathy patients. In the experimental group (14 patients) there were two cases of FSHD, while most of the remainder of the sample had diagnoses of myosis dystrophy (9 participants). The control group was composed of eighteen-year-old subjects who were not affected by any pathology.

All of the study subjects performed two sets of eight maximal eccentric concentrations of the elbow flexors for seven days. The outcome measures were the maximum serum levels of creatine kinase in the concentric contraction, the circumference of the arm, and the reported pain levels. The measurement was repeated three times at: baseline, and at three and seven days later. The creatine kinase serum levels in both groups were high ($p<0.05$), while the control group showed a better response to fatigue. Concerning response to the eccentric contractions, there were no differences between the experimental group and the control group at the end of the short experimental period. The study concluded that the supposed efficacy of the eccentric contractions in FSHD would only appear after a long intervention period.

DISCUSSION

Literary reviews are exposed to a double risk bias, one related to the single study and one related to the comparison of studies.

Bias related to a single study

Bias selection risk is avoided by the choice of age-matched controls without any pathology[16, 24] or FSHD subjects of the same experimental group coming from the same territory[15, 17, 22]; this consideration does not have to be considered for the study[21] as it is a theoretical working protocol.

The controlled-randomized nature of the studies avoided a randomization bias risk.

Measurement bias is possible, meaning we cannot directly compare single measurements in the outcome.

None of the authors emphasized their results in a specific way thereby avoiding the publication bias.

Bias of comparison with other studies

The comparison possibility among the selected evidence was considered lacking, as it concerns the employed treatments and the results described. So, it is possible to exclude a systematic error.

The present review followed the guidelines reported by the study group PRISMA in a document relevant to meta-analysis and literature revisions[25]. Before discussing our results it is important to make some comments. First, it is difficult to find high level scientific work on the rehabilitation of FSHD patients, since the attention of scientists in this pathology concerns other aspects (mostly medical and surgical ones). It should also be noted that in studies conducted of the pathology, in some cases the sample studied in the intervention group does not always yield a result exclusively based on FSHD patients[24]. The few methodologically correct works identified by our research show an extremely heterogeneous treatment profile, regarding the methods used and the results obtained. Excluding theoretical protocols and not yet validated[17] procedures[21] there were three other studies admitted to the final stage of our review. In the first of these[16] the theme of the instrumental evaluation of FSHD is faced, validating with RCT the use of the Kinect for the upper limbs. This instrument has already been validated in the literature for use with stroke patients[26]. The conclusions reported by the authors for FSHD, are not useful for rehabilitation.

A true comparison can be made among the last three studies not yet mentioned[15, 22, 24] but with many difficulties. In all studies, the theme of the rehabilitation for FSHD were reported, even if in one study[22] the treatment was linked to the use of the drug, albuterol. The aims of the studies were similar: to test if physical therapy was effective for FSHD with regard to muscular strength, pain and fatigue. Nevertheless the trials are only partially comparable, as in the last study[24] only two of the patients of the intervention group were affected by FSHD.

Below is a summary of the comparison of the studies:

The interventions were different among the studies, spanning aerobic exercise[15], eccentric contractions[24], and strengthening of specific muscular groups[22].

One study did not have a clinical follow-up period, and those that did ranged from one[24] to 52 weeks[22].

The results described were conflicting: in the first study[15] the authors supported the use of AET and CBT, whereas in another study[22] the treatment was rejected. As for the last study[24], the authors hypothesized there would be positive effects in the long term, but this was not tested.

Two of these three studies[22, 24] were performed many years ago, so their indications have to be interpreted in the context of the etiological knowledge of FSHD being less advanced than it is today[27].

The only outcome measure shared was the VAS[15, 22], but since the treatments were different it was not possible to compare it.

In conclusion we can say that currently, there are too few studies concerning physiotherapy for FSHD; the results of treatments with AET and CBT need more scientific confirmations as they have only been tested in a RCT; and the while other intervention strategies were excluded, because they were rare and isolated data, we should not ignore the utility of other rehabilitative approaches.

Our final conclusion is that there is insufficient data for an EBM judgement on the role of rehabilitation in FSHD. It is desirable that future studies should conduct new RCT based on the current knowledge including different experimental protocols. These studies should pay particular attention to: pain and fatigue control in FSHD patients; the maintenance of articular mobility levels, specifically that of the scapula girdle; the early identification of postural and muscular problems of the lower girdle; and maintenance of independence in the ADL for the achievement of the best possible functional level.

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