The effects of FES in Spinal Cord Injury on cardiovascular responses: A literature review

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ABSTRACT

Background: Functional stimulation (FES) is considered to be an effective method to reduce the risk factors caused by spinal cord injury and enhance the cardiovascular responses. This study involved a systematic review of the current literature to investigate whether FES application has an effect on cardiovascular responses in both quadriplegic and paraplegic people.

Methods: A systematic review of the literature identified 20 studies that met the inclusion criteria, including 51 quadriplegic and 121 paraplegic patients who received FES training. Methodological quality assessment was carried out by one researcher using the Cochrane's Methodological Quality Scale. Large clinical heterogeneity, variety in outcome measures and low methodological quality of studies precluded a quantitative analysis of the data.

Results: Methodological quality scores ranged between 6-11 (out of 24), indicating poor study design. Evidence of clinical, methodological and statistical heterogeneity was present. FES tended to render positive effects, particularly for oxygen uptake and cardiac output. Paraplegic people tended to benefit more than quadriplegic persons, but this trend was not consistent. Also, interaction between cardiovascular variables made it difficult to interpret some of these results.

Conclusion: This study showed that there is a wide diversity in studies investigating the effects of FES in spinal cord injured individuals, pointing to the need for future well-designed study. It remains unclear how the above effects are best achieved in different subgroups.

KEY WORDS: *electrical stimulation, Spinal Cord Injury and Exercise*

INTRODUCTION

Many studies have shown that exercise can be beneficial in SCI subjects (11, 12, 13). Exercises such as shoulder elevation and depression, passive and active walking, hand cycling and group gymnastics resulted in improvements in cardiorespiratory responses, physical strength, better integration into society and greater independence (11, 12, 13). Exercise recommendations for SCI presently include the use of FES to facilitate exercise either via a FES leg cycle ergometer or FES assisted treadmill gait training (11, 13).

There are several studies that report benefits of FES assisted training in SCI in areas like cardiovascular responses, haemodynamic responses, bone density, gas exchange kinetics, gait function and in psychological domains (5, 10, 14, 16). Many studies report specific improvements in the following cardiorespiratory responses: blood flow, cardiac output, heart rate, stroke volume, oxygen uptake and blood pressure (14, 17, 18). However, some studies also report that during FES intervention specific elements of cardiorespiratory responses remained the same or got worse (18, 19). For instance, blood flow remained unchanged in the Gerrits et al. study 2001(19), whereas in another study oxygen uptake and cardiac output remained the same (18).

Also, with FES assisted exercise a reduced bone loss or an increase of bone mineral density was suggested to occur (20, 21). However, in some other work it was reported that there were no convincing trends to suggest that FES can play a clinically relevant role in osteoporosis prevention (23) hrough improved kinetics of gas exchange the exercise tolerance may increase as a result of FES (24) and it appears that FES may enhance gait and muscle strength for people with SCI (25). Moreover, many patients gain function through FES programs, take part in many more activities and participate more fully in the community. However, psychological and functional improvements occur only after the first two-three years (5).

The above overview indicates that although positive effects of FES have been reported, the results are presently inconclusive. In addition, some studies show that FES may have adverse effects in some cases. Knuttson J et al (26), showed evidence that implanted electrodes in the upper limb, while remaining intact within the body, led to occurrence of inflection and granuloma. In DC Wheeler's, 1993 (27) study there was evidence of autonomic dysreflexia during FES.

Although current study suggests that enhancement of cardiorespiratory fitness is associated with the use of FES in SCI, these suggestions are at present largely based on clinical review studies referring to the potential benefits of FES. The designs of current experimental studies were mostly based on case-series designs (pre-post comparisons) including small patient groups. No earlier reviews of the literature were undertaken to evaluate the effects of FES in SCI focused on cardiorespiratory responses alone. A systematic review of evidence addressing cardiorespiratory responses of SCI subjects during FES is therefore required to enhance the field of adapted physical activity. The present study is therefore aimed at addressing the following research question:

1. Is FES assisted-training beneficial for cardiorespiratory function in paraplegic and quadriplegic patients?

METHODS

Search Strategy

Six, electronic databases (CINAHL, Cochrane, PsycInfo, Pubmed, Sport Discus and Wed of Science) were searched for relevant publications until May 2008, using the following keywords or related words in different combinations: Electrical stimulation, Spinal Cord Injury and Exercise

Selection Criteria

After the previous identification of articles, a first selection of relevant articles was done on the basis of whether the titles/abstracts addressed the research question of interest. To be included in the second selection of this review the remaining articles met the following criteria:

1. Experimental studies published in English;
2. Addressing adults with paraplegia and/or quadriplegia;
3. FES is applied as monotherapy or in addition to an exercise regime;
4. FES was applied to improve one of the following cardiorespiratory outcome measures: Oxygen Uptake, Stroke Volume, Heart Rate, Blood Flow, Blood Pressure, and Cardiac output;
5. Interventions applied to both upper or lower extremities were included;

First analysis of the results revealed large clinical heterogeneity of interventions. As this study was focused on identifying the effect of FES on cardiorespiratory responses and FES used during treadmill training is largely aimed at improvement of gait, following additional exclusion criteria were applied:

6. Studies investigating FES and walking/gait;
7. Single case studies;
8. Studies addressing one session of FES only.

Data Extraction and Quality Assessment

Data extraction was carried out on the above criteria by one researcher. Final selection was checked by an independent rater against the above mentioned inclusion criteria. Any discrepancies between researchers were resolved by consensus. Methodological quality assessment was carried out by one researcher using the Cochranes's Methodological Quality Scale, see appendix A. This score rates the quality on a scale of 0-24 (28).

Method of Analysis

Large clinical heterogeneity, variety in outcome measures and low methodological quality of studies precluded a quantitative analysis of the data. Therefore a narrative review was carried out and reported upon in the results

RESULTS

From an initial list of 673 articles, 567 were excluded based on the title and 106 articles were fully retrieved and reviewed. From these 106 articles 25 were finally selected. Forty-eight were excluded on the basis of not addressing the stipulated cardiovascular responses, 22 involved no FES, two did not evaluate an actual intervention and nine were review articles rather than experimental studies. The remaining 25 articles were checked and discussed against the inclusion criteria by the two researchers and after reading these full 25 articles again, four more of these were excluded on the second set of exclusion criteria. Two studies were excluded because they examined FES in gait/walking (n = 2). One intervention was left out because it applied FES only for one session (n = 1) and two studies were excluded because they were a single case study (n = 2). The final 20 articles were dated from 1990 until 2007 and separated into pre-post designs with control group studies (n = 9) and pre-post designs without control group studies (n = 11).

In sixteen out of twenty studies oxygen uptake was a measured outcome variable. From these studies, ten reported a statistically significant increase of oxygen uptake during FES intervention. Hooker's et al (32) reported that oxygen uptake increased by 23% in both paraplegic and quadriplegic people. In Barstow's et al (36) oxygen uptake increased during FES in both leg cycle ergometer and hybrid exercise whereas in another study (30) on paraplegic patients only, oxygen uptake increased from 0.22 ± 0.02 to 0.65 ± 0.15 L/minute. In three studies the results were not considered to be significant (18, 35, 38) and in the remaining three it was reported that either oxygen uptake remained unchanged or was significantly lower (34, 37, 40).

In seventeen studies heart rate was measured. In eight statistically significant increased rates were reported, whereas in two the results were considered to be non- significant. In five studies (41, 44) it was reported that either it remained unchanged or it was significantly decreased after the intervention

(17, 19, 24, 34, 36), and in two studies (35, 43) that heart rate was similar at rest for paraplegic and quadriplegic patients whereas during exercise there was a delayed increase

Cardiac output showed a significant increase in eight from the nine studies in which it was measured. Hooker et al (32), mentioned that cardiac output increased by 13% both in paraplegic and quadriplegic patients whereas in another study (34) it increased by 30% during FES applied at rest, 18% during 30Watt FES arm cranking exercise and 28% during 90W FES leg cycle ergometer. Raymond et al (18), showed no change in cardiac output during FES intervention.

Stroke volume was measured in nine out of the twenty one studies. In five studies the results reported a significant increase in stroke volume whereas in two the results were not clear (18, 40). In Dela's et al (43) study, stroke volume (SV) was similar at rest whereas during exercise it increased in quadriplegic people and remained unchanged in paraplegic persons. Kjaer et al (38) reported that SV also increased in quadriplegic patients but remained unchanged in paraplegic people. Also, Hooker et al (32) found that there were no significant changes in stroke volume (+6%) during FES-leg cycle exercise for neither for quadriplegic nor for paraplegic patients.

Blood flow was measured in four studies, and in two no change was noticed (31, 33). In one study (38) blood flow was twice as low both in paraplegic and quadriplegic people than in able-bodied at baseline.

Blood pressure was measured in six studies. In two studies (17, 19) blood pressure didn't change and in one (43) blood pressure was lower in quadriplegic people while seated. At rest and during exercise it decreased in paraplegic patients, while there was a small decline in quadriplegic patients. In one study (35) FES leg cycle ergometer significantly increased resting blood pressure in quadriplegic patients and lowered it in paraplegic patients whereas in both groups blood pressure was significantly decreased after submaximal exercise. In one study (44) blood pressure was increased after the intervention and in one the results were not significant (41).

In the above section all the parameters were discussed separately, but it has to be recognized that cardiovascular responses are correlated to each other in a way that the change of the value of one can affect the other. It is well-known that, cardiac output is equal to stroke volume (SV) multiplied by heart rate (HR) (45).

In conclusion, the results show that FES seems to have an effect particularly in oxygen uptake and cardiac output. Moreover, results have shown that these effects were apparent in both para and quadriplegic patients. However, taking into consideration that besides the values that have been reported in studies that have been conducted for both paraplegic and quadriplegic patients, more studies were conducted on paraplegic people only and reported positive effects. Overall, it seemed that paraplegic persons tended to benefit more than quadriplegic patients. This can be easily understood from the number of patients that were also been described in this review (51 quadriplegic and 121 paraplegic patients).

DISCUSSION

This review summarized 20 effects studies of FES on cardiorespiratory responses in Spinal Cord Injury. Cardiac performance is of a great clinical importance in SCI, as cardiovascular disease is a growing concern for this population. It has been shown (46, 47) that people with SCI are at greater risk to develop obesity, lipid disorders, metabolic syndrome and diabetes. Daily energy expenditure is significantly lower in Spinal Cord Injury and that contributes to heightened cardiovascular risk including abnormalities in blood pressure, heart rate variability, and arrhythmias that can limit the capacity to perform physical activity (48). The use of various FES protocols to encourage increases in physical activity and to augment physical fitness and reduce heart disease risk is relatively new, but a growing field of investigation (49). The evidence reviewed in this study so far weakly supports its use for improving potential health benefits for patients with Spinal Cord Injury.

The available evidence found in this study was of low methodological quality. All the studies included pre-post designs rather than experimental or quasi-experimental studies. Only articles in English were included and therefore some studies may have been missed that could provide important information. There was also major heterogeneity at various levels including the methodology, population, intervention and outcome measures. Different methods of FES were included in this review such as FES cycle ergometer (38), isokinetic dynamometer with FES applied in leg muscles (17), Arm cranking combined with FES leg exercise (18, 34, 44), FES Rowing (14, 37) and FES applied to the leg muscles while seated (31). Within the intervention patients trained in different power outputs and intensities as also in different electrical frequencies. The duration of the sessions was from 2-36 and lasted from 2 minutes to thirty. For example in Gerrits et al (19), study the method was FES leg cycle exercise applied to the leg muscles, the stimulation consisted of 30 Hertz whereas the duration was 18 sessions, 3 times per week of 30 minutes per session at 50 revolutions per minute in the cycle ergometer. In another study Davis et al (34), arm cranking exercise with FES was used at varying outputs (30, 60, 90 Watt) and cycling at 60 revolutions per minute.

None of the discussed studies considered adverse events of FES. Review studies have, however, mentioned that through excessive intensity, of FES, pain, work overload and electrical frequency could have negative effects on cardiorespiratory responses and lead to autonomic hypereflexia, muscle fatigue, wounds on the skin etc. (26, 27, 50).

Taking the above limitations into consideration, this review showed that there is some evidence to support that after FES training oxygen uptake was increased. The observed increases in oxygen uptake, may have been the result of an increase in active muscle mass, as well as the effect of FES on activation of the peripheral muscle pump (44). However, the FES method and the training interventions varied across studies as well as the experience levels of the patients with FES and thus results should be interpreted with some caution. Wheeler et al (14), reported that oxygen uptake increased during FES with rowing but remained unchanged during FES upper extremity rowing or FES bilateral extremity extension and flexion. When comparing studies that used different modalities of hybrid exercise it must be recognized that that there is a fundamental difference between FES rowing and hybrid exercise, involving the FES leg cycle ergometer and the arm cranking ergometer. In the rowing exercise there was a clear relationship between upper and lower extremities which both contributed during hybrid work (voluntary upper body movements were combined with electrically stimulated movements of the paralyzed leg muscles for total body exercise), whereas in cycling plus upper extremity ergometer, upper and lower extremities worked more independently (14). Hybrid exercise elevates the metabolic demand in persons with spinal cord injury and places greater stress on the cardiorespiratory system as compared with FES leg cycle ergometer or hybrid exercise alone (14, 39, 42).

Heart Rate was significantly increased in ten out of seventeen studies. One (37) of these studies reported an increase in heart rate during both arm cranking, arm cranking combined with FES leg exercise ergometer and FES rowing, whereas during FES leg cycle ergometer heart rate was lower.

Of the seven remaining studies with mixed results, tw_0 (24, 26) studies showed similar resting values between paraplegic and quadriplegic patients. In two studies, the reported results were non significant (41,44) and in three studies, heart rate remained unchanged compared to baseline values (17, 19, 34).

Within the above mentioned result pattern there were some differences among paraplegic and quadriplegic patients. Dela et al (43), reported that heart rate was similar at rest in both groups but during the exercise and recovery phase it was lower in quadriplegic people compared to paraplegic persons. Nevertheless, heart rate did increase in quadriplegic patients but even more in paraplegic patients. A possible explanation which agrees with other findings in previous articles (30, 31, 43), is that this result can be explained by the absence of arterial baroreflex resetting in quadriplegic and paraplegic people. In the absence of the arterial baroreflex resetting, this increase is interpreted as hypertension. Baroreflex dysfunction is more likely to occur in high-level SCI and more particularly in lesions at T_3 or above (51). However the impairment in baroreceptor control may not be restricted to individuals with high-level lesions. In paraplegic people it may also be disabling in the absence of ascending and descending neural traffic. In general, in the able-bodied this reflex contributes to elevating arterial pressure and during constant exercise regulates it continuously, acting as a negative feedback system and controlling fluctuations above and below the operating point (52).

In addition, there were some other studies that reported a decrease in heart rate in quadriplegic and paraplegic patients for different reasons (35, 36). The generally lower heart rate in quadriplegic people is due to lack of sympathetic intervention to the heart and peripheral arterioles and veins resulting from cervical injury typically causing vagal dominance and reduction in heart rate (35) whereas in paraplegics this is not due to an inherent dysfunction in control of heart rate. Rather, it is likely to be specifically related to FES-induced exercise of muscle mass below the level of injury (24, 35, 36).

Cardiac output was measured in nine studies and was found significantly increased in eight after FES. In one study (35) the resting values of cardiac output were the same between the quadriplegic and paraplegic people. In addition, the exercise phase elevated these values in both paraplegic and quadriplegic patients. Thomas et al (17) also found that cardiac output was elevated in both groups during FES over rest. This can be explained by the hypothesis that because of the fact that resting heart rate did not change in SCI subjects, increased cardiac output in response to electrical stimulation exercise was driven more by the volume load imposed by augmented venous return from the leg muscles, than by neural regulation of heart rate. Differences between the effects of different FES regimes were also noticed. For example in the study by Davis et al (34) cardiac output increased by 30% during FES at rest, 18% during FES arm cranking exercise at 30 Watts and by 28% during FES Arm cranking exercise at 90 Watts. The 18-30% increases of cardiac output were apparently due to FES induced activation of the peripheral «muscle pump». The effectiveness of FES induced contractions of calf and thigh muscles to raise cardiac output in spinal cord injured people may contribute to this effect (53,54).

Stroke volume was measured in nine studies and significant increases noticed in five, whereas in two studies the results were not significant. Most of the studies reported an increase, but as above, differences between the interventions and the effect of FES were noticed. In general, reactivation of the lower limb muscle pump via electrical stimulation-induced contractions in spinal cord injury improved venous return, increased ventricular filling pressures and augmented stroke volume (40). In one study (43) stroke volume was similar at rest, whereas it increased with FES leg cycle exercise in quadriplegic patients and remained the same in paraplegic people. Similarly, in the study by Kjaer et al (38) stroke volume rose in quadriplegic patients and did not in paraplegic patients with FES exercise. These findings may be interpreted as that for quadriplegic patients an increase in cardiac output was associated with only a modest increase in heart rate, therefore a higher value of stroke volume was noticed, whereas in paraplegic patients the increase in cardiac output was affected by heart rate and therefore stroke volume was unchanged (43).

Studies measuring blood flow were limited and therefore it would be premature to say that this is affected by FES. Blood pressure was found to be enhanced only in two studies (35, 44) and differences between quadriplegic and paraplegic patients were apparent. In one study (43) blood pressure was low in quadriplegic patients while seated and a small decline noted during exercise, whereas in paraplegic people blood pressure was decreased at rest and during exercise ($p < 0.05$). In quadriplegic patients, because of the almost complete lack of autonomic innervations of the resistance vessels, it becomes difficult to increase cardiac output because of the vasodilatation associated with exercise

Quadriplegic and paraplegic patients with comparable fitness levels at baseline still produced different cardiovascular responses. Possible explanations for this might be:

a) the relative effect of the FES induced activation of the leg muscles and the concomitant increase in oxygen uptake may be greater in quadriplegic patients.

b) the supporting effect of FES on the redistribution of blood may be more pronounced in quadriplegic patients as a result of their greater impairment (44).

The above review of the literature has clearly shown that the evidence for the benefits of FES is at present limited. Therefore, unlike in the current clinical literature (47, 48), in this review caution is advocated to suggest that FES might be of benefit for cardiorespiratory fitness. Wide clinical application of the method may be not warranted at the present time and should be further investigated. Therefore, recommendations for future studies are that the completion of RCTs in this area will allow more definite conclusions to be drawn. RCTs will control for trends in time and ensure balanced groups for comparison, thereby ensuring that the outcomes measured are more likely to be due to the intervention and not open to bias.

CONCLUSION

The purpose of this study was to determine the effectiveness of Functional Electrical Stimulation on the cardiorespiratory responses in spinal cord injured people. This systematic review showed that studies into FES effects on cardiorespiratory responses are heterogeneous at various levels including methodology, population, intervention, and outcome measures, making a meta-analysis not feasible. The qualities of the studies evaluating some of the clinical benefits of FES are low with no RCTs having been conducted. Although there is some positive evidence supporting the beneficial use of FES on cardiorespiratoty responses in individuals with SCI with a tendency for paraplegic patients to benefit more, it remains unclear how these effects are best achieved in different subgroups, whether there may be adverse effects and what the long-term consequences are.

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APPENDIX A

Cochrane's scale for Methodological Quality Scoring

Methodological Quality

Study

Items and possible scores	Score
Was the assigned treatment adequately concealed prior to allocation?	
2 = method did not allow disclosure of assignment	
1 = small but possible chance of disclosure of assignment or unclear	
0 = quasi-randomised or open list/tables	______
0 = non Randomistion applied	______
Were the outcomes of patients/participants who withdrew described and included in the analysis (intention to treat)?	
2 = withdrawals well described and accounted for in analysis	
1 = withdrawals described and analysis not possible	______
0 = no mention, inadequate mention, or obvious differences and no adjustment. Not relevant	______
Were the outcome assessors blinded to treatment status?	
2 = effective action taken to blind assessors	
1 = small or moderate chance of unblinding of assessors	______
0 = not mentioned or possible	______
Were the treatment and control group comparable at entry?	
2 = good comparability of groups, or confounding adjusted for in analysis	
1 = confounding small; mentioned but not adjusted for	______
0 = large potential for confounding, or not discussed	______
Were the participants blind to assignment status after allocation?	
2 = effective action taken to blind participants	
1 = small or moderate chance of unblinding of participants	______
0 = not possible, or not mentioned (unless double-blind), or possible but not done	______

Were the treatment providers blind to assignment status?	**Score**
2 = effective action taken to blind treatment providers	
1 = small or moderate chance of unblinding of treatment providers	______
0 = not possible, or not mentioned (unless double-blind), or possible but not done	______

Were the inclusion and exclusion criteria clearly defined?

2 = clearly defined
1 = inadequately defined ______
0 = not defined ______

Were the interventions clearly defined?

2 = clearly defined interventions are applied with a standardised protocol
1 = clearly defined interventions are applied but the application protocol is not standardised ______
0 = intervention and/or application protocol are poorly or not defined ______

Were the outcome measures used clearly defined?

2 = clearly defined
1 = inadequately defined ______
0 = not defined ______

Were tests used in outcome assessment clinicaly useful?

2 = optimal
1 = adequate ______
0 = not defined, not adequate ______

Was the surveillance active, and of clinically appropriate duration (i.e. at least 3 months)?

2 = active surveillance and appropriate duration-3months follow up or more
1 = acrive surveillance, but inadequate duration-less than 3 months follow up ______
0 = surveillance not active or not defined ______

Were point estimates and measures of variability presented for the primary outcome measures?

2 = yes
1 = point estimates, but no measures of variability presented ______
0 = vague descriptions ______

Was the compliance rate in each group likely to cause bias? **Score**

2 = compliance well described and accounted for in analysis
1 = compliance well described but differences between groups not accounted for in analysis ________
0 = compliance unclear ________

Was there a description of adverse effects of the intervention(s)?

2 = well described
1 = poorly described ________
0 = not described ________

Total score

____

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