The application of neuromuscular electrical stimulation (NMES) technologies in cancer care

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Abstract- **Despite the increase in long term cancer survivors, successful treatment is associated with significant sequelae. As a result, participation in voluntary exercise becomes difficult highlighting the need for pragmatic alternatives. Neuromuscular electrical stimulation (NMES) has been shown as effective in pathological conditions for improving muscle strength. However, its use in cancer care is sparse and has provided equivocal results. This paper outlines a proposed approach to the design, development, evaluation and implementation of NMES technology into cancer pathways. The proposed process comprises four stages; 1) understanding the clinical challenges faced by survivors, 2) identify the benefits of NMES in this cohort, 3) the design of the NMES protocol, 4) the evaluation of the protocol in cancer survivors, and 5) the implementation of the protocol into cancer care pathways. In this paper, we outline advancements in NMES technology which may be utilised to simultaneously improve indices of cardiovascular exercise capacity and skeletal muscle strength.**

Keuwords: Cancer, cachexia,NMES

1. INTRODUCTION

The rapid increase in the percentage of long-term cancer survivors in developed countries has been attributed to improved prognosis based on progression in screening, earlier detection and more effective treatment [1]. Current cancer treatments, although efficacious are associated with long-term side effects such as fatigue, deterioration in muscle strength, and low cardiorespiratory capacity [2]. Thus, cancer is no longer a fatal illness with mortality as the end outcome, but rather a chronic disease with significant sequelae. The sequelae to either the disease or treatment in addition to conditions predating diagnosis add to the complex rehabilitation needs of cancer survivors.

2. THE CHALLENGES FACED IN CANCER CARE

Cachexia, a complex metabolic syndrome characterised by systemic inflammation and increased muscle protein breakdown resulting in the loss of muscle mass with or without fat loss [3] is seen in approximately 40% of cancer survivors and makes participation in voluntary exercise difficult. Nutritional support and drug therapy are common strategies used in cancer cachexia management [4] However, additional strategies may help attenuate the loss of muscle mass, strength and function and be used as part of a multi-functional approach. In cancer survivors experiencing exercise-limiting symptoms, Neuromuscular Electrical Stimulation (NMES) may be a pragmatic alternative to voluntary exercise.

3. NMES: A BRIDGE TO VOLUNTARY EXERCISE?

NMES involves the controlled contraction and relaxation of superficial skeletal muscles via a pre-programmed stimulation unit and one or more surface electrodes positioned in proximity to the muscle motor point [5]. The use of NMES as a therapeutic intervention in pathological conditions such as chronic obstructive pulmonary disease (COPD) and chronic heart failure (CHF) has been shown to attenuate the loss of muscle mass and/or strength of large lower limb muscles [6], highlighting its potential as an anabolic stimulus. Furthermore, as NMES is a passive form of exercise, it allows it to be used in an unsupervised, home-based setting making NMES particularly beneficial for those unable and unwilling to take part in voluntary exercise [7]. NMES therefore has the potential to bridge the gap between immobility and the participation in voluntary exercise for cancer survivors.

4. NMES IN CANCER CARE

NMES use in cancer care is relatively sparse and results are equivocal. A case study in a patient with metastatic lung cancer found a 44% increase in physical performance following 20, 60-min NMES sessions (Pulse frequency: 63.3 Hz, pulse duration: 400μs, on/off time: 3.5/4.5-s) over 4 weeks [8]. However, conversely Windholz et al [9] despite concluding that NMES can be a feasible and acceptable intervention for home use, found no improvements in physical performance measured via a 6-minute walk test (6 MWT) and a sit-to-stand (STS) test in 10 patients with advanced cancer following 30-min of daily stimulation (pulse frequency: 50Hz, pulse duration: 300μs, on/off time: 5/5-s) for 6 weeks. Furthermore, a pilot study in 16 lung cancer patients showed that a muscle strengthening NMES protocol (Pulse frequency: 50 Hz, pulse duration: 350μs, on/off time: progressed from 2/18-s to 10/30-s) was well tolerated, with high adherence, but showed no significant improvements in muscle strength and function following 30-60 min of daily stimulation of both thighs for 4 weeks [10]. In a follow up study, no improvements in quadriceps strength and poorer than expected adherence were reported, prompting the authors to suggest that NMES may not be a suitable treatment for cancer patients [11]. To date, studies in NMES cancer care have utilized basic tetanic muscle strengthening protocols. These sustained contractions are associated with discomfort which is considered a major limitation to the use of electrical stimulation [12]. Furthermore, current exercise

guidelines for cancer survivors recommend both aerobic and resistance training. However, traditional tetanic protocols have been shown to have negligible influence on aerobic capacity [13]. Therefore, novel NMES protocols which incorporate both aerobic and strength training phases are required which can induce both an aerobic and strength response whilst addressing some of the limitations associated with NMES use.

5. Technological advancements in NMES

Advancements in NMES technology have allowed for the successful implementation of NMES protocols which can induce aerobic adaptations. These developments have seen the successful implementation of aerobic training protocols (rhythmical continuous contraction at a frequency of 4Hz for 1-hr) with an increase of 10% in maximum aerobic capacity (VO_{2max}) following daily stimulation over a 6-8-week period seen in both CHF patients [6] and in sedentary populations [12]. In addition, a hybrid protocol (strength phase: 15-mins, frequency: 25Hz, on/off time: 5/10-s, aerobic phase: 45mins, constant rhythmical contractions at 4Hz) has been shown to improve both aerobic capacity and strength simultaneously in healthy elderly participants [14], suggesting that these protocols may be adapted to meet the specific needs of cancer survivors and meet currently recommended exercise guidelines to improve muscle strength and cardiovascular exercise capacity.

6. Evaluating NMES in cancer care pathways

Although experimental evidence in different populations highlight the efficacy of NMES, there is a need to evaluate its safety, comfort, ease of use and efficacy in cancer survivors before it can be implemented into cancer care pathways. Previous work in NMES and cancer has focused on tetanic, muscle strengthening protocols and therefore the next phase is to examine the efficacy of an aerobic and muscle strengthening hybrid protocol in the target population. The efficacy of the protocol should be established through a controlled study aimed at identifying its impact on indices of cardiovascular exercise capacity and strength. Participants should be randomly allocated to one of two groups: Group A will complete a NMES training intervention followed by a 2-week washout period followed by an 8-week control period where they will maintain habitual activity levels. Group B will undergo the same intervention but in a reversed schedule i.e. habitual activity followed by the NMES training intervention. Primary outcomes measured at baseline and at 8-weeks include exercise capacity (6-minute walk test) and lower (quadriceps muscle strength) and upper (handgrip strength) body strength. Secondary outcomes include measures of adherence and health related quality of life.

7. Conclusions

As both cardiovascular exercise capacity and muscle strength are fundamental for physical function and maintaining quality of life, a need exists to develop novel strategies to target those unable to benefit from traditional voluntary exercise programmes. This paper outlines an approach which may be considered when developing a rehabilitation/training programme in cancer care pathways.

References

[1] Mewes et al, 2012. Effectiveness of Multidimensional Cancer Survivor Rehabilitation and Cost-Effectiveness of Cancer Rehabilitation in General: A Systematic Review. *Oncologist*. 17(12), pp.1581-1593.

[2] Courneya and Freidenreich. 2001. Framework PEACE: an organizational model for examining physical exercise across the cancer experience. *Annals of Behavioural Medicine*. 23(4), pp. 263-272..

[3] Aoyagi et al, 2015. Cancer cachexia, mechanism and treatment. *World Journal of Gastrointestinal Oncology*. 7(4), pp. 17-29.

[4] Tazi and Errihani, 2010. Treatment of Cachexia in Oncology. *Indian Journal of Palliative care*. 16(3), pp. 129-137.

[5] Maffiuletti, 2010. Physiological and methodological considerations for the use of neuromuscular electrical stimulation. *European Journal of Applied Physiology*. 110, pp. 223-234.

[6] Banerjee et al, 2009. Prolonged Electrical Muscle Stimulation Exercise Improves Strength, Peak VO2 and Exercise Capacity in Patients with Stable Chronic Heart Failure. *Journal of Cardiac Failure*. 15(4), pp.319-326.

[7] Jones et al, 2016. Neuromuscular electrical stimulation for muscle weakness in adults with advanced disease. *Cochrane Database of Systematic Reviews*. 31(1).

[8] Crevenna et al, 2006. Neuromuscular electrical stimulation for a patient with metastatic lung cancer--a case report. *Supportive Care Cancer*. 14(9), pp. 970-973.

[9] Windholz et al, 2014. The feasibility and acceptability of neuromuscular electrical stimulation to improve exercise performance in patients with advancedcancer: a pilot study. *BMC Palliative Care*. 13(23).

[10] Maddocks et al, 2009. Randomized controlled pilot study of neuromuscular electrical stimulation of the quadriceps in patients with non-small cell lung cancer. *Journal of Pain and Symptom Management*. 38(6), pp. 950-956.

[11] Maddocks et al, 2013. Neuromuscular Electrical Stimulation of the Quadriceps in Patients with Non-Small Cell Lung Cancer Receiving Palliative Chemotherapy: A Randomized Phase II Study. Plos One. 8(12). Epub 2013, Dec 30.

[12] Banerjee et al, 2005. Prolonged electrical muscle stimulation exercise improves strength and aerobic capacity in healthy sedentary adults. *Journal of Applied Physiology*. 99(6), pp.2307-2311.

[13] Porcelli et al, 2012. Lack of functional effects of neuromuscular electrical stimulation on skeletal muscle oxidative metabolism in healthy humans. *Journal of Applied Physiology*. 113(7), pp.1101-1109.

[14] Caulfield et al, 2013. Self-directed home based electrical muscle stimulation training improves exercise tolerance and strength in healthy elderly. *Conference proceedings: Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society*. pp.7036-7039.

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