DOI: 10.1590/1809-2950/22008229032022EN

CASE STUDY

Inspiratory muscle training in quality of life and functional capacity in cardiotoxicity: case report

Treinamento muscular inspiratório na qualidade de vida e capacidade funcional na cardiotoxicidade: relato de caso

Entrenamiento muscular inspiratorio en la calidad de vida y capacidad funcional en la cardiotoxicidad: reporte de un caso

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ABSTRACT | Cancer patients develop frequent cardiac problems due to chemotherapy toxicity, which impacts functional capacity (FC) and quality of life (QoL). Inspiratory Muscle Training (IMT) may be a viable therapeutic resource since cause-effect studies have shown improvement in FC and QoL in other populations. However, its effect was not evaluated in cardio-oncology patients. The study aimed to describe the effect of an IMT program on the FC and QoL of a patient with cardiotoxicity, LDM, aged 41 years, female and, sedentary that developed heart failure after chemotherapy. The QoL was evaluated by the Minnesota test. Dynamic Inspiratory Muscle Strength (S-Index) and Glycemic Threshold (GT) of the inspiratory muscles were also evaluated. The GT was determined by capillary glycemia with a digital glucometer (*Accu-Chek – Roche*), at the lowest value of glycemia of the load corresponding to the Incremental Inspiratory Muscle Test (IIMT). The load progression was performed every two weeks. After two months, all tests were reapplied. In the Minnesota test, the values related to FC, pre and post IMT, were 36 v. 8 (78% improvement); the clinical and psychological aspects 32 v. 7 (78% improvement); S-Index was 41 v. 51cmH_2O (24% improvement). IMT improved the FC and QoL of a cardio-oncology patient, configuring itself as a possible and viable therapeutic resource for this population.
Keywords | Anthracyclines; Heart Failure; Oncology; Maximal Respiratory Pressures.

RESUMO | Pacientes oncológicos desenvolvem problemas cardíacos frequentes devido à toxidade dos quimioterápicos, com consequente impacto na capacidade funcional (CF) e na qualidade de vida (QV). O treinamento muscular inspiratório (TMI) pode ser um recurso terapêutico viável, já que estudos de causa-efeito demonstraram melhora da CF e da QV em outras populações. Contudo, seu efeito ainda não foi avaliado em pacientes cardio-oncológicos. Assim, o objetivo deste estudo foi descrever o efeito de um programa de TMI sobre a CF e a QV de uma paciente com cardiotoxicidade: LDM, com 41 anos, mulher e sedentária, que desenvolveu insuficiência cardíaca após tratamento quimioterápico. A QV foi avaliada pelo teste de Minnesota. Foram avaliados também a força muscular inspiratória dinâmica (S-Index) e o limiar glicêmico (LG) dos músculos inspiratórios. O LG foi determinado pela glicemia capilar por meio do glicosímetro digital (*Accu-Chek – Roche*) no menor valor da glicemia da carga correspondente ao teste muscular inspiratório incremental (TMII). A progressão da carga foi realizada a cada duas semanas. Ao final de dois meses, todos os testes foram reaplicados. No teste de Minnesota, os valores relacionados à CF, antes e após o TMI, foram de 36 vs. 8 (melhora de 78%); aos aspectos clínicos e psicológicos foram de 32 vs. 7 (melhora de 78%), a S-Index foram de 41 vs. 51cmH_2O (melhora de 24%). O TMI melhorou a CF

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e a QV de uma paciente cardio-oncológica, configurando-se como um recurso terapêutico viável para essa população.
Descritores | Antraciclinas; Insuficiência Cardíaca; Oncologia; Pressões Respiratórias Máximas.

RESUMEN | Los pacientes con cáncer desarrollan problemas cardíacos frecuentes debido a la cardiotoxicidad de la quimioterapia, con el consiguiente impacto en la capacidad funcional (FC) y la calidad de vida (CV). El entrenamiento muscular inspiratorio (IMT) puede ser un recurso terapéutico viable, ya que los estudios de causa-efecto han demostrado una mejora en la FC y la CV en otras poblaciones. Sin embargo, su efecto aún no se ha evaluado en pacientes cardio-oncológicos. Por lo tanto, el objetivo de este estudio fue describir el efecto de un programa de IMT sobre la FC y la CV de un paciente con cardiotoxicidad: LDM, 41 años, mujer y sedentaria, que desarrolló insuficiencia cardíaca después del tratamiento de quimioterapia. La CV se evaluó mediante la prueba de Minnesota. También se evaluaron la fuerza muscular inspiratoria dinámica (índice S) y el umbral glucémico (LG) de los músculos inspiratorios. El LG se determinó por glucemia capilar mediante el glucómetro digital (*Accu-Chek – Roche*) al valor más bajo de la carga glucélica correspondiente a la prueba muscular inspiratoria incremental (IMI). La progresión de la carga se realizó cada dos semanas. Después de dos meses, todas las pruebas se volvieron a aplicar. En la prueba de Minnesota, los valores relacionados con la FC, antes y después de THE, fueron 36 vs. 8 (78% de mejora); los aspectos clínicos y psicológicos fueron 32 vs. 7 (mejora del 78%), el índice S fue de 41 vs. 51cmH_2O (mejora del 24%). El IMT mejoró la FC y la CV de un paciente cardio-oncológico, constituyendo un recurso terapéutico viable para esta población.
Palabras clave | Antraciclinas; Insuficiencia Cardíaca; Oncología; Presiones Respiratorias Máximas.

INTRODUCTION

Neoplasms represent the second leading cause of death in developed and developing countries[1]. Chemotherapy is one of the main treatments for neoplasm, however, it can generate cardiovascular dysfunctions that lead to heart failure (HF). Based on the values of the left ventricular ejection fraction (LVEF), the Brazilian Cardio-oncology Guideline[1] classifies the cardiovascular dysfunctions resulting from chemotherapy in neoplastic patients, called cardiotoxicity. Moreover, the treatment may trigger ventricular and supraventricular arrhythmias, acute coronary syndrome, systemic arterial hypertension, and thromboembolic events[1]. Thus, the clinical impact of cardiotoxicity results in loss of functional capacity (FC), limits daily life activities and, consequently, causes intolerance to physical exercise.

Inspiratory muscle training (IMT) is a therapeutic resource of easy application and reproducibility that presents beneficial responses for patients with heart disease. According to Bosnak-Guclu et al.[2], IMT benefits FC, respiratory and peripheral muscle strength, pulmonary function, dyspnea, fatigue, depression, and quality of life of HF patients. Therefore, IMT may be a viable alternative, but it is still little tested in patients with HF due to toxicity of neoplasia treatment. Our study aimed to describe the effect of an IMT individualized program on the FC and QoL of a patient with HF due to chemotherapy treatment for breast cancer.

Case description

The participant of the study was LMD, female, aged 41 years, sedentary, BMI of 23.7kg/m^2, diagnosed with HF with normal ejection fraction (left ventricle ejection fraction of 71%) caused by cardiotoxicity after chemotherapy for breast neoplasm. Invasive ductal carcinoma occurred in the left breast and armpits level I and II—with metastasis in two of the 12 dissected lymph nodes with no extracapsular extension.

After the chemotherapy treatment with anthracycline, the patient sought the cardiovascular rehabilitation service of the Actus Cordios Clinic, in Salvador (BA), Brazil, to treat the tiredness she felt during routine activities, such as sweeping the house. Since the participant lived in another city and could not participate in a supervised program, the research team decided to conduct a semi-supervised monitoring, with application of IMT and maintenance of physical activities that the patient already performed (domestic services). Thus, two more appointments were scheduled, totaling three for the beginning of the rehabilitation program with IMT.

In the first appointment, anthropometric and clinical data of the patient were collected, and the Minnesota Living with Heart Failure Questionnaire (MLHFQ) was applied, developed for patients with HF. The dynamic inspiratory muscle strength (S-Index) was also evaluated, using the digital device POWERbreathe®

K5 for inspiratory muscle training (POWERbreathe International Ltd., Warwickshire, UK). This equipment measures the peak of inspiratory flow that reflects the strength of the inspiratory muscles, called stress index or S-Index. A professional specialized in pneumofunctional evaluation and experienced with handling the collection instrument performed the measurement. To obtain the S-Index, the patient was positioned in a comfortable chair, with the feet supported, and oriented to perform—with the nostrils occluded by a nasal clip—slow expiration followed by a quick and strong inspiration. The movement was repeated three times, and the S-Index was determined by the highest value among the three repetitions. In this test, if the last repetition is the highest, new repetitions are performed until the highest value does not occur on the last attempt. Considering that in this case the highest value was during the second repetition, new repetitions were unnecessary.

In the second appointment the incremental inspiratory muscle test (IIMT)—developed by our research group[3]—was performed to determine the glycemic threshold (GT) of the inspiratory muscles. The IIMT is performed in an interval and composed of up to 10 stages of 19 incursions, with a respiratory cycle of five seconds, guided by the beep of the device. At the end of each stage, the load is increasingly imposed, and a passive rest of two minutes is established. The test, performed with the POWERbreathe® K5, started with 10% resistance of the S-Index obtained, increasing the load by 10% at each stage. The equipment only prints the load determined on the fourth inspiration. Therefore, 19 incursions were required at each level, with a five-second respiratory cycle. The test was interrupted when the patient could no longer overcome the resistance imposed by the device. Since the patient's S-Index was 41cmH_2O, the initial load of the IIMT was 4cmH_2O, with an increase of 4cmH_2O at each stage. To determine GT, capillary glycemia was collected by the digital glucometer *Accu-Chek* (*Roche*) at rest and immediately at the end of each stage. GT was determined by the lowest blood glucose value obtained in the corresponding stage. GT load was used for the patient's IMT. Since the GT of this patient was obtained in the first stage, she started the IMT with a 4cmH_2O load. During the performance of the IIMT, the perceived (subjective) effort was also collected by the traditional Borg scale (6 to 20) referring to the end of each stage. To evaluate the patient's FC, the six-minute walk test (6MWT) was applied in the third meeting, following all recommendations of the American Thoracic Society[4].

After the third meeting, the patient was instructed to perform IMT at home for two months. The protocol used was five weekly sessions with three sets of 10 inspiratory incursions, with passive rest of one minute between sets. The initial training load corresponded to the GT obtained in the TMII (4cmH_2O and Borg of 13) and was adjusted every two weeks using the Borg scale value identified at the GT point. Therefore, every two weeks—when the patient returned to the rehabilitation sector—she was asked whether the perception of exertion regarding the load she was performing, decreased or remained at 13. If the perception of exertion decreased, then the load was adjusted. The patient was advised to avoid any physical exertion different from the usual during this intervention period.

At the end of the two months of training, the MLHFQ, the IIMT, the 6MWT and a new echocardiogram were reapplied. The results of the first and second evaluation were described in absolute numbers and, later, the percentage of change was calculated between the first and second collection.

The patient participated in the project entitled "*Influência do exercício físico sobre a capacidade funcional aeróbica de idosos com comorbidades cardiovasculares e metabólicas associadas* (Influence of physical exercise on aerobic functional capacity of elderly with associated cardiovascular and metabolic comorbidities – free translation)," signing an informed consent form. However, the patient did not qualify for the research and was relocated to this study case. After consent, data collection continued.

RESULTS

On the echocardiogram, we observed changes in the thickness of the ventricular septum (6 vs. 8mm) and LVEF (71% vs. 69%). However, the patient's quality of life strongly improved. Initially, the Minnesota test obtained a score of 68 points, against 16 points at the end of the study, reflecting a 77% improvement. The questions regarding functional capacity and clinical and psychological aspects presented the greatest changes. Table 1 shows the tests results.

Table 1. Evolution of variables evaluated pre and post inspiratory muscle training

Characteristic	Pre IMT	Post IMT	Improvement percentage
Minnesota (points)	68	16	77%
S-Index (cmH_2O)	41	51	24%
Glycemic threshold load (cmH_2O)	8	15	53%
6MWT (m)	435	514	18%

cmH_2O: centimeters of water; S-Index: dynamic inspiratory muscle strength; 6MWT: six-minute walk test; IMT: inspiratory muscle training.

DISCUSSION

We observed significant improvements in QoL and FC of a patient with HF due to toxicity caused by chemotherapy treatment of a breast cancer in this case study. Therefore, the IMT can be a viable resource in the treatment of this population.

The reduction of metaboreflex (MTB) is possibly the greatest benefit of IMT. MTB is the redistribution of blood flow from active peripheral muscles to the diaphragm, and in healthy individuals it corresponds to 14–16% of cardiac output[5]. This response directly interferes on the FC, which is lower in the presence of a higher MTB. Thus, the better the aerobic performance of energy production of the diaphragm, the lower and later the MTB. In a randomized clinical trial, Dal Lago et al.[6] demonstrated that an IMT program reduced MTB and improved the FC of HF patients by up to 30%.

When MTB is activated, the action of phrenic nerve afferents increases, increasing sympathetic activity and peripheral vasoconstriction with consequent reduction of O_2 transport to the active musculature, leading to muscular fatigue[5,7]. IMT attenuates and slows MTB by increasing the oxidative capacity of the diaphragm muscle, which consequently delays fatigue of skeletal muscles[7]. The IMT decreases the request of the secondary inspiratory muscles, reducing the sending of blood ordered by the respiratory muscles, which directly affects the increase in the perfusion of peripheral muscles[5,7,8].

However, the use of IMT as a therapeutic tool to improve FC in cancer patients who had HF is still incipient, possibly due to the lack of studies evaluating the effect of the test in this population. This study opens a promising strand. For example, the S-Index and the GT of the inspiratory muscles improved at the end of the treatment, reflecting the progress of diaphragmatic function and secondary inspiratory muscles (Table 1), possibly responsible for the improvement of FC and QoL, which we observed, respectively, by the 6MWT distance (18%) and by the MHLFQ score (77%) (Table 1).

Notably, we prescribed the IMT differently than the traditional model. We used the glycemic threshold[9] instead of the percentage of maximal inspiratory pressure (MIP). This change may have affected the outcome, since the GT-based prescription seems to be more accurate and generate better results of diaphragmatic function. In one of the studies developed by our group, we observed a lower MIP reduction in patients after cardiac surgery who used the GT of the inspiratory muscles as the basis for the prescription of IMT compared to those who used MIP as reference[9]. In the first group, the reduction in MIP was 12% and in the conventional group (based on MIP), 32%. The predominance of type I fibers in diaphragmatic muscles is a possible physiological explanation for these results. These fibers have resistance characteristics, with lower strength and power levels when compared to type II fibers. Therefore, type I fibers can benefit the most from actions with loads closer to GT. We observed that the loads used for IMT in the traditional prescription (based on MIP) are on average twice as those used by the GT of the diaphragmatic musculature[8,9]. In this case, if we used the traditional prescription to determine the load of the IMT, i.e., 30 to 40% of the MIP, the load would be 12 to 16cmH_2O. However, based on the IIMT, in which the GT occurred in the first stage, the load used was 4cmH_2O.

IMT performance with more adequate loads, recommended for type I fibers, possibly improve the oxidative capacity of the diaphragm, attenuating fatigue and consequently delaying the MTB more efficiently and with fewer risks[8]. This benefit reflects in the improvement of FC and in the performance of functional activities that are usually performed in aerobic intensity ranges.

Therefore, this study emphasizes the importance of longitudinal controlled studies evaluating the benefit of IMT for the evaluated population, more specifically comparing the effect of different prescriptions.

CONCLUSION

Inspiratory muscle training improved the functional capacity and quality of life of a patient with grade III cardiotoxicity, constituting a viable therapeutic resource for this population.

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