Improving Quality of Life during Androgen Deprivation Therapy in Prostate Adenocarcinoma Patients: Effect of Prescribed Clinic-Based Exercise Program

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Abstract

Context: The mainstay of treatment of advanced prostate adenocarcinoma is androgen deprivation therapy (ADT). ADT invariably results in a progressive loss of bone density and muscle mass and diminishing cardiopulmonary and cognitive function. Exercise is beneficial as adjuvant treatment during ADT. **Aim:** This study seeks to identify the benefit of prescribed exercise programs beyond routine physical activities of daily living in low-income patients on ADT. **Settings and Design:** Men on ADT for 12 months who were in the remission phase of the disease were recruited for a 6 week supervised aerobic and resistive exercise program. **Subjects and Methods:** The effects of the prescribed exercise on muscle strength (MS), peak expiratory flow rate (PEFR), maximum oxygen uptake (MOU) and brief fatigue inventory (BFI) were assessed. 10R max test was deployed for MS while the modified Young Men Christian Association protocol for bicycle ergometer was used for PEFR and MOU. All measures were taken pre- and post-intervention with a check for adverse events at week 3. **Statistical Analysis Used:** Simple frequency in SPSS version 21 was used. **Results:** Only 5 of 34 recruited subjects completed the study. There was 34.0% improvement in MOU, 34.9% improvement in PEFR, 130.0% increase in exercise duration, and 29.2% reduction in reported BFI. Improvement in parameters was more among those that had lower values at recruitment. Compliance with exercise prescription was a major challenge. All participants reported improvement in activities of daily living. **Conclusions:** Prescribed aerobic and resistive exercise program is beneficial during ADT for prostate adenocarcinoma. Those with poorer reserves tend to benefit more.

Keywords: Androgen deprivation therapy, muscle strength, peak exploratory flow rate, prescribed exercise, prostate adenocarcinoma

Introduction

Prostate cancer is the most frequently diagnosed malignancy and one of the leading causes of cancer death in men worldwide.[1] In Africa, an estimated pooled incidence rate of 22.0/100,000 men has been reported.[2] In Nigeria, prostate cancer is the most common cancer of men, with an incidence of 19.1/100,000 men from the combined Ibadan and Abuja Cancer Registries reports of 2010.[3]

Androgen deprivation therapy (ADT) is the recommended first-line therapy for advanced prostate adenocarcinoma.[4] First-line ADT can be achieved through bilateral total or subcapsular orchidectomy (surgical orchidectomy) or through the repeated administration of gonadotropin-releasing hormone analogs or antagonists (medical orchidectomy).[5] The addition of antiandrogens (steroidal or nonsteroidal) to orchidectomy (surgical or medical) targets to block the effects of adrenal and other extra-testicular androgens on the malignant acinar cells, thereby ensuring maximal androgen blockade.[6,7]

Androgens are physiologic anabolic hormones. Therefore, ADT is accompanied by several adverse effects such as fatigue, functional decline, increased body fat, and loss of lean body tissue.[8] Other adverse effects of ADT are increased insulin resistance, decreased libido and sexual dysfunction, hot

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flashes, gynecomastia, reduced testis size, anemia, and loss of bone mineral density.[9] These effects result from a reduction in circulating levels of androgens, mostly testosterone.[10,11] ADT is known to impair physical strength with time, resulting in increased fatigue.[12] Clearly, ADT has the potential of negatively affecting the overall quality of life (QoL) of prostate adenocarcinoma patients.

In Nigeria, ADT, in the form of surgical orchidectomy is prevalently administered due to a combination of late presentation with advanced diseases and challenges in accessing medical orchidectomy.[5,13] Although 90% disease remission rates have been reported with ADT, the aforementioned adverse effects could lead to reduced physical wellbeing.

Studies have reported extensively on the benefits of exercise, especially supervised exercise, in cancer patients during treatment and afterwards.[14] In a systematic review, Gardner *et al*. demonstrated benefits, to prostate adenocarcinoma patients, of aerobic and resistance training exercises on muscular strength, cardiorespiratory fitness, functional task performance, lean body mass, and on level of fatigue, but with some inconsistent effects on adiposity.[15] Supervised controlled exercise programs are reportedly safe as adjuvant therapy in ADT for prostate cancer.[16] When complied with, exercise programs, which may be group-based or home-based, have been found to significantly improve ADT-related fatigue, metabolic and cardiovascular side effects, as well as cognitive function.[17]

Do prescribed exercise programs offer additional benefits in the care of patients on ADT in our setting? The objective of this study, therefore, is to examine the effect of prescribed, clinic-based physical exercise program on muscle function, cardiopulmonary function, and fatigue in patients on ADT for prostate adenocarcinoma in our low-income setting.

Subjects and Methods

Consecutive patients diagnosed with advanced prostate adenocarcinoma who have been on ADT for a period of 12 months form the study population. The patients were recruited from the Urology Clinic of a tertiary health institution in a low-income setting, while the prescribed exercise was undertaken at the Physiotherapy department of the same institution. All patients were 12 months post bilateral total orchiectomy at recruitment. On enrollment, these patients were observed for 6 weeks as control arm before cross over to participate in the exercise program for the next 6 weeks.

The cardiopulmonary function was tested with a graded exercise test using a modified Young Men's Christian Association (YMCA) protocol for bicycle ergometer. The Karvonen formula using the age-predicted maximum heart rate and the resting heart rate was used to calculate the safe target heart rate zone. Each patient cycled on a bicycle ergometer with an inbuilt heart rate monitor regulated by the set age, height, and weight of the participant. The resistance on the bicycle was increased every 3 min by increasing the wattage to achieve 70% of the calculated target heart rate, or the subject reached a steady-state heart rate, or until signs of fatigue or exhaustion were noted according to the YMCA protocol and the American College of Sports Medicine guidelines.[18] Borg's scale was used to determine the patient's perceived extent of exhaustion. Cycling was at subject's pace as against the 50 rev/min of the YMCA protocol. The initial wattage was set at 25 watts, and the machine self-adjusted to maintain the preset target heart rate. Maximum oxygen uptake, peak expiratory flow rate (PEFR), and exercise duration were determined.

Muscle strength (MS) and endurance were assessed using the Oxford technique, where the 10R max was determined on a multi-gym resistive exercise machine. Participants were guided on how to lift weight safely through the full range in the correct form. Weights were lifted incrementally until the highest weight that could be lifted without muscle fatigue was found. This was judged by determining the weight that could be lifted ten times through full range without quivering of the muscle. When determined, each participant lifted 80% of their maximal weight progressively, starting with 8 repetitions in 3 sets.

Blood pressure and resting heart rates were measured after at least 5 min rest upon arrival for the commencement of the exercise activity of the day. Anthropometric measures were done with a standard tape rule and a stadiometer with a weighing scale attached.

Cardiopulmonary and anthropometric indices as well as brief fatigue inventory (BFI) were taken at the onset of the program and again at the end of the 6 weeks. A self-report on the change in daily activities was used to assess QoL qualitatively. It was done by asking simple questions such as, "are you able to cope with your daily activities" and "if yes, has it changed for better or worse in the last 7 days?"

Ethical clearance was obtained from the Health Research Ethics Committee of the University of Nigeria Teaching Hospital, Enugu.

Table 1: Observed changes in cardiopulmonary function and muscular function parameters

Parameter	Mean observed change (%)
Cardiopulmonary function	
Maximum oxygen uptake	+34
Peak expiratory flow rate	+34.9
Exercise duration	+130
MS	
Pull-up	+13.3
Chest press	+13.3
Leg extension	+11.7
Leg curl	+25.0
Pull down	0.0

MS: Muscle strength

Table 2: Peak expiratory flow rate values before and after 6 weeks of prescribed controlled exercises

Participant ID	Preexercise (L/min)	Postexercise (L/min)	Interval change (L/min)	Percentage change
001	236	430	194	82.2
002	233	330	97	41.6
003	243	310	67	27.5
004	363	436	73	20.1
005	300	310	10	3.3
Mean	275.0	363.2	88.2	34.9

Table 3: Compares the tolerated duration of the first exercise session at the onset of the exercise program and at the conclusion of the exercise program, 6 weeks after, for each participant

Participant ID	First session (min)	Last session (mins)	Change (min)	Percentage change
001	10.0	30.0	20.0	200
002	10.0	20.0	10.0	100
003	5.0	20.0	15.0	150
004	10.0	20.0	10.0	100
005	10.0	20.0	10.0	100
Mean	9.0	22.0	13.0	130

Results

Of the 34 study subjects that were recruited with informed consent, only 5 completed the prescribed exercise regimen. The subjects that opted out cited logistics associated with a thrice weekly visit to the hospital's physiotherapy unit as the main reason. Hence, this is a case series of the 5 men. The mean age is 72.2 ± 3.9 years, and the mean body weight is 54 ± 8.9 kg. They are all 12 months post bilateral total orchidectomy at recruitment.

Table 1 shows the mean changes in cardiopulmonary and muscular function parameters. This table shows some positive change (improvement) in all parameters of interest except in "pull-down" MS. The positive change (improvement) in exercise duration is quite remarkable.

The observations from the peak expiratory flow rate (PEFR) for each of the participants are shown in Table 2. In all five subjects, there is an observable improvement in peak expiratory flow rate (PEFR) after the 6 weeks of prescribed controlled exercise. The improvement appears to be higher in subjects with poorer PEFR pre-exercise.

The duration tolerated per exercise session for each participant is noted. Table 3 shows the duration tolerated at the first exercise session and the duration tolerated at the last exercise session, 6 weeks after, for each study participant. Each subject tolerated the exercise longer at the conclusion of the 6-week program.

The mean weights tolerated for the various MS and endurance exercises at the first exercise session are compared against the mean weights tolerated at the last exercise session 6 weeks after, as shown in Table 4.

With the exception of pull-down exercise, there is an increase in the mean weight tolerated for all the other exercise programs over the 6-week period.

All patients reported an improvement in daily activities and overall QoL. There is also a mean improvement of 29% in the BFI, as shown in Table 5.

At the conclusion of the 6-week exercise program, each subject reported an improvement in the BFI ranging from 20% to 45%.

Discussion

ADT is generally recognized as the first-line treatment for advanced prostate adenocarcinoma.[4] ADT has recognized time dependent adverse effects consequent on withdrawing the anabolic effect of androgens. Beyond the first few years of ADT, and in the absence of any chemical, radiological, or clinical evidence of tumor progression, the adverse effects of ADT may become major contributors to poor QoL.[9,17] For instance, osteoporosis complicating prolonged ADT is known to be a cause of spinal adverse events in prostate adenocarcinoma patients.

The beneficial effects of prescribed exercise programs on cardiopulmonary function, muscle function, and bone density are known and have been leveraged upon in mitigating some of the adverse effects of cancer treatment generally.[14,19] Hence, the observed poor compliance with prescribed exercise program for the prostate adenocarcinoma patients on ADT in this low-income setting is quite worrisome. Whatever the reasons for this observation may be, the implication is that these patients fail to appreciate the suggested possible benefits from such exercise programs.

This study investigated the effect of a 6-week supervised, clinic-based exercise program for men on ADT of 12 months duration for prostate adenocarcinoma. These men are in clinical and biochemical remission. The study noted improvement in cardiopulmonary function and MS at the least on short-term basis, as has been observed from other studies.[19] Though these study participants are peasant farmers and traders in low-income settings, and cannot be said to have sedentary lifestyles, there are observed improvements on the study parameters [Table 1] suggesting that activities of daily living alone do not constitute adequate physical activity for optimal cardiopulmonary and muscular functions in these individuals.[5]

The mean PEFR of these participants prior to the commencement of the exercise program is 275.0 L/min [Table 2], which is

Table 4: Compares the mean weights tolerated at the first exercise session against the mean weights tolerated at the last exercise session

Muscle strength and endurance exercise	1st session mean weight (kg)	Last session mean weight (kg)	Change in mean weight	Percentage change
Pull-up	6.75	7.65	0.90	13.3
Pull-down	11.25	11.25	0.0	0.0
Chest press	6.75	7.65	0.90	13.3
Leg extension	7.65	8.55	0.90	11.7
Leg curl	1.80	2.25	0.45	25.0

Table 5: The brief fatigue inventory before and after the exercise program is shown for each of the 5 participants

Participant ID	Preexercise	Postexercise	Change	Percentage change
001	85	65	−20	23.5
002	81	65	−16	19.7
003	82	60	−22	26.8
004	60	33	−27	45.0
005	64	44	−20	31.2
Mean	74.4	53.4	−21.0	29.2

similar to values observed from studies recruiting elderly men with compromised respiratory function, but lower than values among men with optimal respiratory function.[17,20] With the prescribed exercise program, the mean PEFR increased appreciably, approaching optimal values in men. Interestingly, the increment in PEFR is seen more among participants with poorer PEFR values at recruitment [Table 2]. The implication, therefore, is that PEFR may, with further evaluation, be used as a possible indicator of patients that will benefit from prescribed exercise programs during ADT.

At the end of the 6 weeks, each participant lasted longer at exercise sessions when compared to the values at the onset [Table 3]. In addition, there is some improvement in MS of each participant, as observed with the various exercise modules [Table 4]. These observations are indicators of increased ability to perform physical functions with less fatigue and an improved sense of well-being. Fatigue is documented as one of the challenges of therapy for cancer and active measures are required to modify it.[18] Supervised exercises constitute a recognized part of such active measures.

At recruitment, the participants in this study checked in moderate to severe fatigue with the BFI [Table 5]. On the background of nadir levels of serum testosterone and serum prostate-specific antigen, tumor burden may be contributing minimally to the level of fatigue reported than at recruitment. The ongoing ADT may be contributing substantially to the observed fatigue.[12] That the exercise-related improvement in MS at the end of the 6-week program coincides with a reduction in the reported level of fatigue is in keeping with the recommendation that supervised exercise be instituted during ADT.[19,21]

In addition, a 29% reduction in the mean reported level of BFI is observed, possibly because the exercise program is for 6 weeks. There is no reason to adduce that longer durations of exercise will not result in higher values of reduction in BFI since observations elsewhere suggest that improvement in muscle function, as well as cardiopulmonary and cognitive function, with controlled exercises, correlates positively with the duration of the patient with the exercise program.[22]

Findings from this series suggest that patients on ADT in the form of bilateral total orchidectomy in low socioeconomic settings benefit from prescribed physical exercise programs. Compliance with such prescriptions, however, could be a major challenge. Undertaking prescribed exercises beyond activities of daily living improves cardiopulmonary function and level of fatigue with activities of daily living. This study is limited by high drop out rates of participants due to the need to visit the hospital physiotherapy unit frequently.

Conclusions

Prescribed exercise programs comprising aerobic and resistive components are beneficial in improving cardiopulmonary and muscle function with resultant improvement in the reported level of fatigue among persons diagnosed with advanced prostate adenocarcinoma who are in remission on ADT. It appears persons with poorer PEFR benefit more from such exercise programs. A properly funded randomized control trial is needed to further evaluate the findings thereof.

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Conflicts of interest

There are no conflicts of interest.

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