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Research Article

Quality of life in patients with prostate cancer treated with hormonotherapy

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Abstract. Introduction: Most patients with advanced stage prostate cancer manifest associated lower urinary tract symptoms (LUTS). In the case of locally advanced prostate cancer (T3-4, N1), metastatic stages or relapse after radiotherapy, hormone therapy is the treatment of choice (antiandrogene therapy), but there is no clear indication regarding continuous (CADT) or intermittent (IADT) hormone therapy. The objective of our study was to show the difference in lower urinary tract symptoms and quality of life in patients treated with IADT and CADT. Materials and method: this is a prospective longitudinal cohort study of 41 patients with locally advanced non-metastatic prostate cancer with a biochemical or lymph node relapse after radiotherapy and patients with advanced metastatic cancer for which was initiated IADT or CADT between 2013-2014. We examined the change in symptoms and quality of life by means of the International Prostate Symptoms Score (IPSS). Results: there was no statistically significant difference regarding total IPSS score improvement in patients with CADT compared with those in the IADT group. For the entire group of patients there was a statistically significant improvement after treatment for IPSS score, quality of life, nocturia. Conclusions: In patients with prostate cancer treated with hormone therapy, there is no statistically significant difference between CADT vs. IADT regarding the IPSS score, irritative symptoms, obstructive symptoms. There is improvement in nocturia and quality of life. This empowers the clinician to choose any of the intermittent or continuous hormonal treatment regarding LUTS but with good advantage for nocturia and quality of life in IADT treated patients.

Key Words: continuous hormone therapy, intermittent hormone therapy, irritative score, obstructive score.

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Introduction

Prostate cancer sums up a quarter of all newly diagnosed cancer cases and accounts for the second most frequent cause of mortality from cancer (Anderson et al 2013). Most patients are elderly and manifest associated lower urinary tract symptoms (LUTS). These are in most cases the ones that bring the patient in for a consult.

After histological diagnosis and stadialization, in the cases of locally advanced prostate cancer (T 3-4, N1), metastatic or relapsed cases, hormone therapy is the treatment of choice (ADT), aimed at blocking the testosterone supply of the tumor cells in order to increase survival (Nguyen et al 2014).

Until now, studies have shown no clear indications for intermittent (IADT) or continuous therapy (CADT) (Sharifi et al 2010). Moreover, most studies included mixed cohorts of patients rather than clear subgroups (non-metastatic, metastatic, locally advanced) and have different designs (Abrahamsson et al 2017). The main reason for choosing IADT regards short term and long-term side effects of the CADT: loss of sexual functions, increased risk for cardiovascular disease and diabetes, osteoporosis, loss of muscle mass, weight gain, cognitive deficiencies, asthenia, depression, hot flushes (Crook et al 2012).

Side effects of CADT were studied for 20 years (Klotz et al 1987). In our experience, after commencement of hormone therapy (ADT) with LHRH agonists and antiandrogens, we have observed a change in LUTS (Leval et al 2002). Therefore, we started to study a group of patients with advanced prostate cancer, under CADT vs. IADT by quantifying LUTS by means of the international prostate symptoms score IPSS-8 (Barry et al 1992). The objective of our study was to show the differences in LUTS and quality of life in adenocarcinoma of the prostate patients treated with IADT and CADT.

Materials and method

This is a prospective, longitudinal, cohort study of 41 patients with locally advanced and metastatic prostate cancer, or with biochemical or lymph node relapse after radiotherapy and advanced metastatic cancer for which we have initiated continuous or intermittent hormone therapy between 2013-2014, in collaboration with a private Clinic from Cluj-Napoca.

The study has the ethics committee approval. The patients have signed the informed consent before entering the study.

Inclusion criteria for patients in the IADT subgroup were: non-metastatic stage, no bone metastasis, cancer localized in the lymph nodes, local or biochemical relapse after radiotherapy.

Table 1. Patients characteristics and IPSS score evolution

Variable			Characteristic
Age (years)			77 (68; 81)
Initial PSA (ng/dl)			38.4 (16.6; 57.1)
Control PSA (ng/dl)			1.8 (0.4; 3.6)
M			15 (36.6%)
N 1-2			15 (36.6%)
G	6		2 (4.9%)
	7		27 (65.9%)
	8-9		12 (29.3%)
T	2		8 (19.5%)
	3		29 (70.7%)
	4		4 (9.8%)
Radiotherapy			4 (9.8%)
Hormonotherapy		Intermitent	13 (31.7%)
		Continous	28 (68.3%)
Initial total IPSS			16.2±5.5
Initial IPSS	Mild		2 (4.9%)
	Moderate		28 (68.3%)
	Severe		11 (26.8%)
Total IPSS at control			13±5.9
Control IPSS	Mild		8 (19.5%)
	Moderate		25 (61%)
	Severe		8 (19.5%)
Initial irritative score			6 (6; 9)
Control irritative score			6 (5; 7.5)
Initial obstructive score			8 (6; 12)
Control obstructive score			7 (5; 10.5)
Initial nocturia			2 (2; 3)
Control nocturia			2 (2; 2.5)
Initial quality of life			2 (2; 3)
Control quality of life			2 (1; 2)

Table no. 2. Evolution of IPSS

Variable		Initial IPSS	Control IPSS	P
Treatment	Intermittent	14.9±4.2	10.6±4.9	0.1
	Continuous	16.8±5.9	14.1±6.1	
G	6	21±8.4	24±5.6	
	7	16.4±5.1	12.8±4.9	0.005
	8-9	15±5.9	11.5±6.5	
T	2	15.1±3.6	10.8±3.9	
	3	16.7±6.2	14.1±6.5	0.1
	4	14.5±0.5	9.5±1.2	
Radiotherapy		21.2±5.6	20±2.1	0.1

We excluded patients with large size tumors, multiple metastasis, PSA > 100 ng/mL because of the poor prognosis and low survival rates. These patients were referred for CADT.

Exclusion criteria were: loss of follow up, hormone resistance with increase in PSA and Testosterone levels (mCRPC), change in oncological therapy throughout follow up.

The changes in lower urinary tract symptoms were quantified by means of the International Prostate Symptoms Score (IPSS), upon initiation of therapy and 6 months later.

We divided the IPSS in an irritative subscore (questions 2, 4 and 7) and obstructive subscore (questions 1, 3, 5, 6). Quality of life was included in question 8 of the IPSS.

The statistical analysis was performed with the MedCalc Statistical Software version 19.0.3 (MedCalc Software bvba, Ostend, Belgium, https://www.medcalc.org, 2019). Continuous variables were expressed by mean and standard or median deviation and percentiles 25 and 75, depending on the distribution normality (verified with the Shapiro-Wilk test). The qualitative variables were characterized by frequency and percentage. The t for paired variables or the Wilcoxon test were used for comparison between the measurements. The ANOVA Repeated Measurement Test was used to verify the evolution of the IPSS score. A value of $p < 0.05$ was considered statistically significant.

Results

Characteristics of patients in the study can be found in Table 1. Patients' age was advanced, median being 77 years. Approximately one-third of patients had metastasis or lymph node involvement at the time of onset of hormone therapy. T3 status was the most represented in the study. Intermittent hormone therapy was followed by one-third of patients. Most patients had a moderate IPSS score.

Age of patients did not influence the evolution of the IPSS score ($p=0.8$). Evolution of the IPSS score from initiation of therapy to control versus various parameters is described in Table 2. Patients with intermittent hormone therapy had a greater decrease in IPSS score, but the difference from those with continuous therapy was not statistically significant, and the threshold of significance was slightly exceeded. Patients with higher tumor grading had a significantly better improvement in the IPSS score. Patients with larger tumors had the greatest improvement in the IPSS score, although the limit of statistical significance was slightly exceeded.

The irritative score changed statistically significantly between baseline and control ($p < 0.001$). Obstructive score significantly changed between baseline and control ($p < 0.001$). The number of nocturnal micturitions was significantly reduced ($p = 0.01$). Quality of life has significantly statistically changed ($p = 0.003$).

Discussions

Lower urinary tract symptoms (LUTS) are the ones that determine the patient to come in for a consult and contribute most to the patient's quality of life (Hymanet al 2001). Our study showed no statistically significant differences in IADT vs CAD. Treatment regarding LUTS, regardless of the irritative score, obstructive or mixed score. This allows us to conclude that the symptoms will be similar, whichever treatment type is chosen.

Significant improvement comes from reducing nocturia and improving quality of life.

Most frequently, prostate cancer coexists with symptomatic prostate hyperplasia. Lahrer et al reported a distribution of LUTS in 55 % light symptoms, 37.1 % moderate symptoms and 7.3 % severe symptoms (Lehrer et al 2002). Due to the fact that 70 % of prostate cancers develop in the periphery, they are frequently asymptomatic until they reach an obstructive volume for the urethra, vescial neck or neurovascular tracts or lead to symptomatic metastasis (Hamilton et al 2004).

Hamilton et al. (2004) reported a significant improve in LUTS after 3 months of ADT treatment with a reduction in postmictional residue and prostate volume in patients with prostate cancer. ADT reduces total prostate volume, tumor volume and therefore has an effect on postmictional residue, LUTS (IPSS) and urine flow markers Qmax (Sun et al 2015).

Although it is generally accepted that ADT has a reduction effect on the IPSS in the case of patients with LUTS within a 3-6 months interval (Mason et al 2013; Axcrona et al 2012), a group of Japanese authors pointed out the fact that in the case of patients with light LUTS, ADT lead to a worsening of nycturia with an increase with an average of one episode per night after 3 months of therapy (Washino et al 2018).

In our study population the majority of the patients are moderate IPSS, nocturia improved in the two subgroups of patients, statistically significant in favor of IADT.

Regarding the quality of life, results are favorable for IADT being statistically significant.

In a systematic review from 2017 which included 7 studies comparing IADT and CADT (JPR.7, SEUG 9401, SEUG 9901, TAP 22, FinnProstate, TULP, and SWOG 9346), Abrahamson concludes they show a slight advantage concerning quality of life for IADT without this being statistically significant. We must note however that these studies did not use the same instruments to quantify quality of life (Abrahamsson et al 2017).

Conclusions

In prostate cancer patients treated with hormone therapy, the quality of life and nocturia improved after six months of treatment. Although intermittent hormone therapy provided better results than continued therapy, the difference was not statistically significant. This allows us to assert that regardless of the type of hormone therapy (IADT vs CADT) chosen by the patient along with the oncologist, the profile of lower urinary tract symptoms will be similar but with better results in terms of nocturia and quality of life.

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