The Role of Intermittent Chemotherapy in the Survival of Patients with Hormone Refractory Prostate Cancer

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Abstract

Introduction: Prostate cancer is one of the most common cancers among males and the second factor resulting to death due to cancer among them.(1) The median age of its diagnosis is 65 years. The initial treatment includes androgen ablation or orchiectomy.(2, 3) In case of patient's hormone refractory, chemotherapy would be substituted. The objective of this study is the consideration of intermittent chemotherapy's role in patients' survival and their quality of life.

Materials & Methods: Since (1384,07,07), 25 patients with Hormone Refractory Prostate Cancer that referred to Taleghani & Imam Reza hospital were enrolled in this study, and Taxotere, Mitoxantrone and Navalbine were prescribed along with Estramustin 140 mg/m2 and Prednisolone 10 mg/BD for 4 days respectively(4, 5, 6) and the quality of life (QoL), toxicity and overall survival were evaluated. The most toxicity included grade 2 and 3 neuropathy and neutropenia that was compliant for patients. The overall survival was 22months.

Conclusion: Intermittent chemotherapy in elderly patients with hormone refractory prostate cancer provides compliant toxicity and improvement of QoL and overall survival.

Keywords: Prostate Cancer, Intermittent Chemotherapy, Hormone Refractory Prostate Cancer

Introduction

Prostate cancer is the most common cancers among males and the second fatal factor after skin cancer.(1) The median age of its diagnosis is 65 years. Generally the clinical progression of prostate cancer is different and may be from indolent to invasive progression. The most common metastatic site are lymph node & bone.(1, 2, 3) The initial treatments include androgen ablation consisting of orchiectomy and anti androgen treatments.(2, 3) The median survival of patients with symptomatic hormone refractory prostate cancer is 9- 12 months(6) and then the patient is entered to hormone refractory prostate cancer phase. The development of prostate cancer cells are stimulated by testosterone and balances hormone treatment or testosterone level or the rate of response, however it would be basically effective in 60%- 70% of metastatic patients and after approximately 9- 12 months the response,(6) would enter HRPCphase.

HRPC is described based on the increase of PSA, radiographic studies, scan isotope or clinical criteria of metastatic progressive disease. High risk patients for HRPC include those with high tumor bulk in physical examination and at stages T3 & T4, PSA higher than 20 and Gleason score 8- 10. HRPC symptoms may relate to clinical indications such as urinary track compression, bone pain development in case of bone metastasis and uncontrolled pains & fractures. After patient's refractoriness to hormone therapy, treatment options would be limited.

Chemotherapy may be considered in addition to anti- androgen withdrawal and secondary hormone therapies. We examined the effect of different intermittent therapy regimens in form of the start of treatment after 6 previous regimens or a new treatment regimen in patients that have not received sufficient response.(6, 7, 8, 9, 10, 11) Besides, the overall survival & toxicity were investigated in this trial.

Table- 1. Patients demoghraphy.

No. of patients	25
Age, years Median (range)	60 (50- 78)
Karnofsky index 90- 100% 70- 80%	 20 5
PSA, ng/ml Median range <100 >100	 114 11 14
Hemoglobin, g/dl <13 >13	 15 10
Alkaline phosphatase, U/l Normal (<120 U/l) Elevated (>120 U/l)	 6 19
Site of metastases Bone Visceral/lymph nodes	 17 7

PSA: Prostate-specific antigen

Table- 2. Toxicity of regimens.

Toxicity	Prednisone/Mitoxantron (Pt)		Docetaxel/Estramustine (Pt)		Navelbine/Prednisolone (Pt)	
	Grade 1- 2	Grade 3-4	Grade 1- 2	Grade 3-4	Grade 1- 2	Grade 3-4
Febrile neutropenia	-	-	-	2	-	2
Anemia	1	-	2	-	2	-
Trhombocytopenia	2	-	6	-	1	-
Neutropenia	8	2	5	3	-	-
Nausea/Vomitting	1	-	1	1	-	-
Diarrhea	-	-	1	2	-	-
Neuropathy, Sensory	-	-	-	-	-	-
Constipation	-	-	-	-	1	2
Neuropathy	-	-	1	3	2	5
Deep vein thrombosis	-	-	1	-	1	-

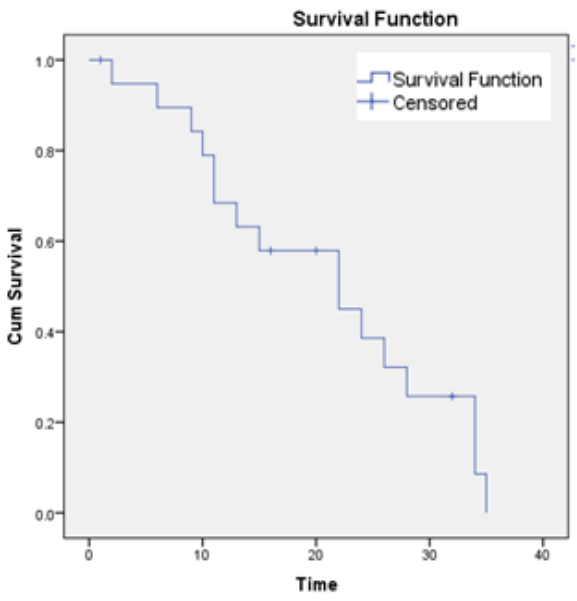

Figure- 1. The consistency of disease was more convenient with Taxotere and the overall survival was 22 months.

Materials & Methods

It is accomplished based on criteria that involve prostate cancer patients into HRPC phase including:

1. Patients with increased PSA
2. Patients with bone scan progression
3. Clinical progression of disease

Patients diagnosed with prostate cancer referred to Imam Reza & Taleghani hospital and enrolled in this study (Table- 1). Their treatment started with daily Taxorere 10 mg/m^2 and Prednisolone 10 mg/BD and Estramustin 280 mg for 4 days and continued for 6 cycles in case of their compliance, no progression of their disease and their PSA decrease. In case of disease progression and no response to treatment after 1 cycle, patient was entered secondary stage of treatment including Mitoxantrone 14 mg/m^2 and Prednisolone and estramustin with the same dose of first regime each 21 days. The secondary regime started in case of PSA increase of 20% or and outstanding decrease of PSA in the first regime that has had 50% increase. The secondary regime started for 24 patients, one patient's deaths. The third treatment regimen required the terms of the secondary regimen in order to be initiated, including

Navelbine, Prednisolone and Estramustin 30 mg/m^2 for first and second week, each 21 days for 6 cycles. The third treatment regimen started for 23 patients, one patient's deaths at time secondary regime. One patient's deaths at time the third treatment regimen.

Results

During the trial, patients encountered with toxicity including grade 3 and 4 in cases which was higher in Taxotere arm THAN Navalbine arm. Digestive symptoms including nausea and vomiting observed in two patients of Taxotere arm and one patients of Mitoxantrone arm respectively. Infections caused to hospital admission in two patients of patients with Taxotere, ZERO and two patients with Mitoxanterone and Navelbin respectively. Two patients faced DVT and treated (Table- 2). The consistency of disease was more convenient with Taxotere and the overall survival was 22 months (Figure- 1).

Discussion

Intermittent chemotherapy regimens for HRPC elderly patients do not provide a considerable toxicity that modifies their quality of life. So these regimens would be compliant for patients. An interesting point regarding Navalbine in this trial is that it would be still effective in spite of patient's resistance and disease progression.

Conclusion

Theses regimens can not still provide sufficient survival for patients. So target therapy products such as anti angiogenesis Thalidomid and Avastin and other similar drugs should be considered.

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