

THE EFFECT OF ANDROGEN DEPRIVATION THERAPY ON THE LIPID PROFILE AND BLOOD GLUCOSE LEVEL IN PROSTATE CANCER PATIENTS IN ADAM MALIK GENERAL HOSPITAL MEDAN

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ABSTRACT

Objective: The aim of this study is to observe the effect of Androgen Deprivation Therapy (ADT) on patients with advanced stage of prostate cancer on the lipid profile and blood glucose level. **Material & Methods:** This is a descriptive cross-sectional study and include the prostate cancer patients which were admitted to Urology Polyclinic in Haji Adam Malik General Hospital, Medan from June 2014 – June 2015 and also received ADT. **Results:** From June 2014 – June 2015, a total of 25 prostate cancer patients receiving ADT was included in this study with an average age of 67.08 ± 7.48 years old. The median prostate specific antigen (PSA) level of this group of patients is 19.6 ng/mL and the lowest and highest value of 3.4 and 278 ng/mL respectively. ADT administration is found to cause a significant elevation of 2-hour postprandial blood glucose (121.12 ± 21 mg/mL vs 134.64 ± 33.35 mg/mL, p -value=0.011) and Glycosylated hemoglobin ($5 \pm 0.5\%$ vs $5.5 \pm 0.79\%$, p -value=0.000) (HbA1c) after 6 months of therapy. Additionally, ADT administration within 3 and 6 months of duration had also significantly increased triglyceride (TG) level when compared to before treatment (104.4 ± 38.67 vs 131.2 ± 32.27 vs 127 ± 33.43 respectively, p -value=0.005). **Conclusion:** ADT treatment in prostate cancer patients increase triglyceride levels after 3 and 6 months of treatment followed by 2-hour postprandial blood glucose and HbA1C levels after 6 months of the treatment.

Keywords: Prostate cancer; androgen deprivation therapy, Haji Adam Malik General Hospital.

ABSTRAK

Tujuan: Tujuan dari penelitian ini adalah untuk mengobservasi efek dari terapi Androgen Deprivation Therapy (ADT) pada pasien dengan kanker prostat stadium lanjut terhadap profil lipid dan kadar gula darah. **Bahan & cara:** Penelitian ini merupakan penelitian deskriptif dengan subjek seluruh pasien dengan kanker prostat yang mendapat terapi ADT di RSUP Haji Adam Malik, Medan sejak Juni 2014 hingga Juni 2015. **Hasil:** Dari Juni 2014 hingga Juni 2015, terdapat total 25 pasien kanker prostat yang mendapat terapi ADT dengan rerata usia 67.08 ± 7.48 tahun. Nilai tengah Prostate Specific Antigen (PSA) adalah 19.6 ng/mL dengan nilai terendah dan tertinggi adalah 3.4 dan 278 ng/mL secara berurutan. Terapi ADT didapatkan mengakibatkan peningkatan bermakna sebelum dan 6 bulan sesudah pemberian untuk kadar gula darah post prandial (121.12 ± 21 mg/mL vs 134.64 ± 33.35 mg/mL, p -value=0.011) dan Glycosylated hemoglobin (HbA1C) ($5 \pm 0.5\%$ vs $5.5 \pm 0.79\%$, p -value=0.000). Pemberian ADT selama 3 sampai 6 bulan juga secara bermakna meningkatkan kadar Trigliserida (TG) (104.4 ± 38.67 vs 131.2 ± 32.27 vs 127 ± 33.43 , p -value=0.005). **Simpulan:** Terapi ADT pada pasien dengan kanker prostat menyebabkan peningkatan kadar TG setelah 3 dan 6 bulan pemberian. ADT juga mengakibatkan peningkatan kadar gula darah post prandial dan HbA1C setelah 6 bulan pemberian.

Kata kunci: Kanker prostat, androgen deprivation therapy, RSUP H. Adam Malik.

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INTRODUCTION

Prostate cancer is the second most common malignancies occurred in men. The number of events are varies in different countries and etnis.¹ A study

done by Globocan et al, stated that prostate cancer were the third common malignancy in Indonesia male population. Based on from Indonesian Society of Urology Oncology (ISUO) 2011, there were 971 patients diagnosed of prostate cancer in duration

from 2006 to 2010. Five years survival rate of prostate cancer were around 98.8%.² Standard treatment for advanced prostate cancer with metastasize disease are androgen deprivation therapy (ADT). ADT could be done surgically, orchiectomy or through medication using Gonadotropin-Releasing Hormone (GnRH) agonist as well as antagonist.³

The high survival rates in patients with prostate cancer were implicated to long term used of ADT. The long term used of ADT then will affect the occurrence of side effects including diabetes mellitus, hyperinsulinemia, lipid metabolism abnormality, heart disease, osteoporosis, and anemia.⁴

Sex hormones are well known has effect on serum lipid profile. An epidemiological data said that total serum testosterone and free serum testosterone were negatively related to total cholesterol (TC), Low-Density Lipoprotein (LDL), and triglyceride in non-diabetic patients. At the same time, testosterone concentration was positively related to High-Density Lipoprotein (HDL).⁵

A prospective study explained that ADT could cause dramatic alteration of body mass composition and would induce peripheral insulin resistance that would lead to diabetes mellitus and dyslipidemia.⁵ A population study showed that low testosterone serum concentration was an independent risk factors for the occurrence of diabetes and metabolic syndrome in male patients.⁶ Prostate cancer patients whom used ADT has higher risk to suffered from insulin resistance and hyperglycemia.⁷

OBJECTIVE

The aim of this study is to evaluate the effects of ADT related lipid profile and fasting glucose level in patients with prostate cancer in Haji Adam Malik Hospital Medan.

MATERIAL & METHODS

This was a descriptive analytical study with cross-sectional design done in H. Adam Malik Hospital from June 2014 to June 2015. Samples were patients with prostate cancer whom got ADT such as LHRH agonist and anti-androgen medication or subcapsular orchidectomy bilateral (SOB). Patients with complete laboratory examination before the treatment as well as 3 and 6 month after treatment were included in the study. Complete laboratory examination were PSA, testosterone, blood glucose profile, and lipid profile examination. Patients whom consumed anti-cholesterol drugs or already had diabetes mellitus at the time of admission were excluded from the study. All data were collected from patients' medical record. All data were analyzed using SPSS ver. 20.

RESULTS

Based on data taken from the patient's medical record from June 2014 until June 2015, there were 25 patients with prostate cancer who received ADT therapy either LHRH agonists and anti-androgens or bilateral subcapsular orchidectomy. The average age of patients with prostate cancer who

Table 1. Patients age and PSA level before ADT.

	N	%
Age (years old)		
≤ 70	16	64
70-80	8	32
> 80	1	4
PSA (ng/mL)		
<10	3	12
10-20	10	40
>20	12	48

Table 2. Characteristics of lipid and blood glucose profiles in prostate cancer patient with ADT treatments.

	Before treatment (mg/dL)	3 months after treatment (mg/dL)	6 months after treatment (mg/dL)	p
Fasting blood glucose	104 ± 14.6	102.3 ± 15.8	100.4 ± 16.74	0.123
2 hours post- prandial blood glucose	121.12 ± 21	126.48 ± 25	134.64 ± 33.35	0.011
HbA1c	5 ± 0.5	5.3 ± 0.71	5.5 ± 0.79	0.000
Total cholesterol	182.12 ± 29.19	181.12 ± 27.03	182.08 ± 23.95	0.989
HDL	45.76 ± 12.95	44.36 ± 10.66	42.48 ± 9.8	0.109
LDL	113.52 ± 25.56	110.56 ± 28.05	113.88 ± 24.77	0.854
Triglyceride	104.4 ± 38.67	131.2 ± 32.27	127 ± 33.43	0.005

received ADT therapy was 67.08 ± 7.48 years old. Most prostate cancer patients aged under 70 years (64%).

Median PSA level of patients before the treatments were given was around 19.6 ng/mL ranged from 3.4–278 ng/mL. Based of PSA group, patients with prostate cancer whom got ADT treatments were mostly had PSA above 20 ng/mL (48%) followed by PSA level around 10–20 ng/mL (40%).

DISCUSSION

There were 25 patients enrolled in this study that diagnosed with prostate cancer and underwent ADT. The average age of patients was 67.08 years old with most of them were age more than 70 years old (64%). This condition showed that most of patients whom underwent ADT were in group of age with life expectancy more than 10 years. With longer life expectancy, patients will undergo long term ADT exposure. This condition associate with higher mortality rate due to side effects of ADT, such as diabetes mellitus, hyperinsulinemia, lipid metabolism abnormality, heart disease, anemia, and osteoporosis.⁴ In this study, most of patients whom underwent ADT had PSA score more than 10 ng/ml (88%).

In this study, TC were decreased in the first 3 months of ADT (181.12 ± 27.03 mg/dl) and rebound in next 3 months (182.08 ± 23.95 %). However, even though TC concentration was rebound, this concentration did not as high as initial concentration (182.12 ± 29.19 mg/dl). These results were differed from study done by Dockery et al. Dockery et al showed that TC concentration was significantly increase in the first 3 months of ADT. Other studies also showed increased of TC concentration after 6 months of ADT.⁸⁻¹⁰

Besides TC, concentration of triglyceride also changes after the administration of ADT. There were significant elevation of triglyceride after 3 and 6 months of ADT. These results were similar with previous studies.^{8,10,11} However, other study done by Nishiyama et al, did not show any changes in term of triglyceride concentration.⁹

Reduction of HDL concentration occurred after 3 and 6 months administration of ADT, but it's not significant. These results were related to condition of HDL concentration that is positively associated with testosterone concentration. Saglam et al showed that HDL concentration were increased in 3 months after ADT but then decreased in the next

3 months.⁴ However, these results were differed from study done by Morote et al. Morote et al showed continuous increased of HDL concentration, even though they were not statistically significant.¹¹

In this study, LDL concentration were decreased in the first 3 months of ADT, and increased after 6 months of ADT administration, however it were not significant. These results were similar with other studies done by Saglam et al, and Hamilton et al.^{4,10} Those studies showed that LDL concentration were increased after 6 months of ADT.^{4,10}

The effect of ADT also occurred on patients' fasting glucose level. Decreased levels of fasting glucose level occurred after 3 and 6 months of ADT administration, however these reductions were not significant. Roayaei et al showed that fasting glucose levels were increased after 3 months of ADT.⁸ Other study done Nishiyama et al showed a significant elevation of fasting glucose level after 6 months of ADT.⁹

Significant improvement occurred in term of post prandial glucose levels and HbA1c levels after 6 months of ADT. These results were similar with study done by Hamilton et al, that showed a significant increase of HbA1c levels after 6 months of ADT.¹⁰ Hamilton et al, explained that ADT lead to increase of subcutaneous and visceral fat, as well as an increase of insulin resistance after 6 months of ADT.¹⁰ These condition were explained by the theory that ADT may cause changes in body compositions in which there is elevation of fat deposits while the LBM decreased. However, the mechanism is still unexplained. Another study also explains that testosterone reduces the occurrence of lipolysis in adipose tissue. These increase of lipid is believed to be caused of the increased of insulin concentration. In other side, reduced of muscle mass lead to decreased of glucose uptake.

These information regarding the side effects of ADT are expected to be taken into consideration before giving the treatment for patients diagnosed with prostate cancer, thus "over treatment" can be reduced. Patients should also be given clear information about the side effects of this information. Additional routine examination for lipid and blood sugar levels should also be performed for patient diagnosed with prostate cancer that undergoing ADT. These examinations are advised to be taken especially in patient with abnormal lipid and glucose level. By paying attention to these side effects, mortality rates in prostate cancer caused by ADT can be reduced.

CONCLUSION

Patients diagnosed with prostate cancer whom underwent ADT were mostly aged less than 70 years old. The used of ADT in prostate cancer patients lead to elevation of TC concentration after 3 months of administration. The used of ADT also lead to increase concentration of HbA1c and post prandial glucose level.

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