



Effect of dutasteride treatment on reducing blood loss and in perioperative period of open prostatectomy

Dutasterid tedavisinin açık prostatektomi operasyonu esnasındaki kan kaybını azaltmadaki etkisi

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ABSTRACT

Objective: Open prostatectomy (OP) is a valid option for the surgical treatment of large prostates in the absence of holmium laser enucleation. The most frequent complication of OP is intra- and perioperative bleeding. Preoperative use of dutasteride has been shown to reduce vascularity and perioperative bleeding in transurethral resection of the prostate (TUR-P). However, there has been no study addressing this effect in OP. The aim of this study was to evaluate whether pretreatment with dutasteride for 6 weeks before OP can reduce surgical blood loss.

Material and methods: Data of 218 patients with benign prostatic hyperplasia (BPH) who underwent OP was investigated retrospectively. Of the 218 patients, 46 were treated with dutasteride for at least 6 weeks and the rest were dutasteride naive. Age, prostate volume, prostate-specific antigen (PSA) levels, coagulation tests, platelet counts, pre- and postoperative hemoglobin (Hb) levels, and transfusion history were recorded. Blood loss was estimated as follows: preoperative Hb (-) postoperative Hb (+) amount of transfusion. The 2 groups were compared by independent samples t-test and a p value of 0.05 was considered significant.

Results: The groups were similar in terms of age, prostate volume, platelet counts, coagulation tests, and postoperative Hb levels. Preoperative Hb levels were lower in the dutasteride group (13.4 vs. 14.3, $p=0.002$) and amount of bleeding (-2.72 g/dL vs. -1.93 g/dL, $p=0.01$) was shown to be significantly lower in dutasteride group.

Conclusion: Our results showed that pretreatment with dutasteride for 6 weeks before OP considerably reduces perioperative surgical bleeding. Further prospective randomized trials should be conducted to confirm the effectiveness of such treatment.

Key words: Bleeding; benign prostatic hyperplasia; dutasteride; open prostatectomy.

ÖZET

Amaç: Büyük boyutlu prostatlarda holmium lazer enükleasyon yokluğunda açık prostatektomi halen geçerli tedavi seçeneğidir. Açık prostatektominin en sık komplikasyonu intra ve peri-operatif kanamadır. Prostatın transüretal rezeksiyonu (TUR-P) operasyonu öncesi dutasterid kullanımının vasküleriteyi ve peri-operatif kanamayı azalttığı gösterilmiştir. Ancak dutasteridin açık prostatektomi uygulanan hastalardaki etkisini gösteren çalışma yoktur. Bu çalışmada cerrahi öncesi 6 hafta dutasterid kullanımının cerrahi kanamayı azaltıp azaltmadığını değerlendirmeyi amaçlandı.

Gereç ve yöntemler: Açık prostatektomi yapılan 218 hastanın verileri retrospektif olarak incelendi. Hastaların 46'sına en az altı hafta boyunca dutasterid tedavisi verilirken geri kalan hastalara dutasterid tedavisi verilmedi. Yaş, prostat hacmi, prostat spesifik antijen (PSA) düzeyi, koagülasyon testleri, platelet sayısı, pre-op ve post-op hemoglobin düzeyleri ve kan transfüzyon öyküsü kaydedildi. Kan kaybı "Preoperatif Hb - Postoperatif Hb + Transfüzyon miktarı" formülü ile hesaplandı. Her iki grup t testi ile karşılaştırıldı ve p değeri 0,05 olarak kabul edildi.

Bulgular: Her iki grup arasında yaş, prostat hacmi, platelet sayısı, koagülasyon testleri ve post-op Hb düzeyleri açısından fark saptanmadı. Pre-op Hb düzeyi (13,4'e karşı 14,3, $p=0,002$) ve kanama miktarı (-2,72 g/dL'ye karşı -1,93 g/dL, $p=0,0001$) dutasterid tedavisi alan grupta anlamlı olarak daha düşük bulundu.

Sonuç: Çalışmamızda açık prostatektomi öncesi 6 hafta Dutasterid kullanımının perioperatif cerrahiye bağlı kanamayı önemli ölçüde azalttığı görüldü. Tedavinin etkinliğini kanıtlamak için başka prospektif randomize çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Kanama miktarı; benign prostat hiperplazisi; dutasterid; açık prostatektomi.

Introduction

Benign prostatic hyperplasia (BPH) is an important health problem in aging males, and despite

the development of new pharmacologic drugs, a considerable proportion of patients still require surgical intervention. Endoscopic management of prostate adenomas by electroresection or

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laser energy is currently accepted as the standard management.^[1] However, adenomas with volume >80-100 mL require open surgery when a holmium laser is not available, particularly in developing countries.

Open prostatectomy (OP) has been shown to be successful for the treatment of large adenomas.^[2-4] However, it has certain disadvantages, such as a longer hospitalization period and perioperative hemorrhage.^[5]

Dutasteride, which acts as an inhibitor of type 1 and 2 isoenzymes of 5- α reductase inhibitors (5-ARIs), has been found to reduce prostate tissue vascularity within 6 weeks of therapy.^[6] With the aid of this effect, dutasteride has been shown to reduce perioperative bleeding rates in patients undergoing transurethral resection.^[7,8]

However, to the best of our knowledge, there is no published study regarding the effect of dutasteride on reducing perioperative bleeding in patients undergoing OP. In this study, we aimed to evaluate whether pretreatment with dutasteride can reduce perioperative bleeding rates in patients undergoing OP.

Material and methods

In this retrospective study, data of 218 patients who underwent OP at our institution between May 2009 and May 2014 was evaluated. Patients were divided into 2 groups: patients in group 1 received dutasteride for at least 6 weeks prior to surgery and patients in group 2 were dutasteride naïve. Patients with bleeding diathesis and under anticoagulant or antiaggregant treatment, those with renal or hepatic insufficiency, and those who had undergone invasive procedures for prostate were excluded. Written informed consent was obtained from all patients who participated in this study.

Age, preoperative prostate volume, serum prostate-specific antigen (PSA) levels, hemoglobin (Hb) levels, hematocrit (Hct) levels, platelet counts, activated partial thromboplastin time (APTT), and international normalized ratio (INR) were recorded. Hb and Hct levels and platelet counts were also recorded within the first 24 h after surgery. The amount of blood loss was calculated as follows: preoperative Hb levels (-) postoperative Hb levels (+) amount of transfusion (estimating that 1 unit of erythrocyte suspension increases Hb levels by 1 g/dL).

Statistical analysis

Data was expressed as mean \pm SD and Student's t-test and chi-square test were used for comparison. A p value of 0.05 was considered statistically significant.

Results

The mean age of the population was 71.4 ± 7.2 years and the mean prostate volume was 135.1 ± 42.3 mL. The mean Hb and Hct levels were 14.2 ± 1.7 and 42.3 ± 5.2 respectively, and the mean platelet

count was $240,000 \pm 66,000$. The groups were similar in terms of preoperative characteristics, except for preoperative Hb levels, which were significantly higher in group 2 (14.3 ± 1.7) than in group 1 (13.4 ± 1.5) ($p=0.002$). The results are summarized in Table 1.

Transfusion was needed in 21 (45.6%) patients in group 1 and 82 (47.6%) patients in group 2 ($p=0.14$). The difference in Hb levels disappeared in the postoperative period (12.6 ± 1.2 vs. 12.4 ± 1.4 , $p=0.344$). The amount of bleeding was significantly higher in group 2 (2.72 ± 1.43) than in group 1 (1.93 ± 1.34) ($p=0.01$). The results are summarized in Figure 1.

Discussion

OP still represents an important alternative in the surgical treatment of symptomatic BPH with prostate volume >80-100 mL.

Table 1. Comparison of the 2 groups with respect to demographic characteristics and blood levels

Parameter	Group 1	Group 2	p value
Age (mean \pm SD)	71.3 ± 7.8	71.4 ± 7.2	0.97
PSA (ng/mL)	10.27 ± 8.22	10.01 ± 9.06	0.861
Prostate volume (mL)	142.1 ± 42.3	133.2 ± 41.8	0.204
Preoperative Hb (g/dL)	13.4 ± 1.5	14.3 ± 1.7	0.002
Preoperative Plt count (mean \pm SD)	256000 ± 65900	235000 ± 65800	0.06
Postoperative Hb (g/dL)	12.6 ± 1.2	12.4 ± 1.4	0.344
Amount of bleeding (mean \pm SD)	1.93 ± 1.34	2.72 ± 1.42	0.01

SD: standard deviation; Hb: hemoglobin; Plt: platelet; PSA: prostate-specific antigen

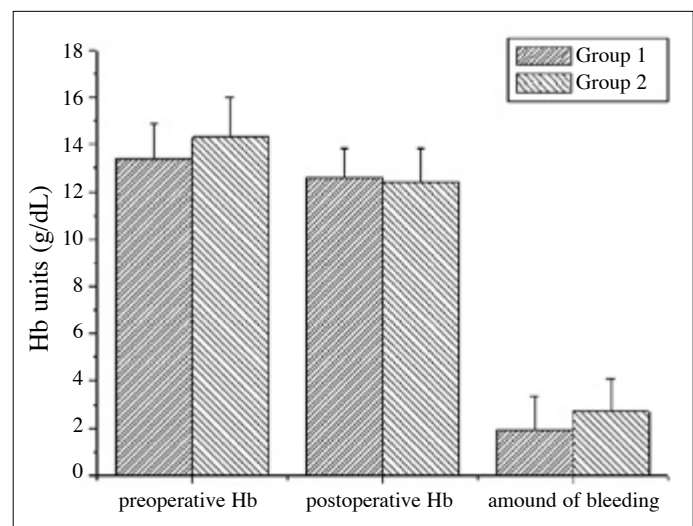


Figure 1. Comparison of the 2 groups with respect to hemoglobin levels and amount of bleeding
Hb: hemoglobin

One of the most important and prevalent complications of OP is perioperative bleeding, which sometimes requires transfusion and leads to urine retention because of blood clots.

Increased gland vascularity (neoangiogenesis) supports the development of BPH through increased proliferation of stromal and acinar cells around the urethra. 5-ARIs block the conversion of testosterone to dihydrotestosterone, reducing the activity of androgen-controlled growth factors responsible for angiogenesis.^[8]

This feature was tested for effectiveness in the prevention of intraoperative bleeding in patients undergoing transurethral resection of the prostate. Some studies have supported the pharmacological use of 5-ARIs to reduce surgical blood loss.^[9-12] However, this effect of 5-ARIs has never been studied in patients undergoing OP. Our study is the first to evaluate the effect of preoperative dutasteride in reducing surgical bleeding in patients undergoing OP and has shown that the amount of bleeding was significantly lower in patients receiving dutasteride for at least 6 weeks.

The results of the present study showed that treatment with dutasteride for at least 6 weeks prior to OP reduces surgical bleeding. No differences were found with respect to patient age, prostatic volume, or PSA levels. None of the patients were under antiagregant or anticoagulant treatment.

The most important drawback of this study is its retrospective nature and the relatively low number of patients in the group under dutasteride treatment. In addition, postoperative complications were not documented in this cohort to evaluate the role of dutasteride use in prevention of complications. However, further randomized controlled trials may be conducted on patients receiving 5-ARIs and undergoing OP.

In conclusion, at least 6 weeks of pharmacological treatment with dutasteride prior to OP appears to reduce the amount of bleeding. Further randomized prospective controlled trials are needed to confirm the use of dutasteride to decrease prostate tissue vascularity and amount of bleeding in patients undergoing OP.

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

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