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Effect of one month treatment with dutasteride on transurethral resection of the prostate

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A B S T R A C T

Objective: Evaluate the effect of dutasteride in perioperative bleeding during Transurethral Resection of Prostate (TURP).
Materials and Methods: Forty consecutive patients with criteria for TURP were included. Finasteride/dutasteride use, renal impairment, prostate <30cc, age <50 were excluded. Patients were divided in 2 groups. Group 1: 24 consecutive patients treated with dutasteride 0.5mg/day/30-days prior TURP. Group 2: 16 without treatment. Prostatic volume, difference in hemoglobin pre/post TURP, duration and amount of resected tissue were recorded. Surgeon was blinded. Statistical analysis: Multiple linear regression, Mann-Whitney and student t-tests were used.
Results: In group 1, 33%(8) improved their lower urinary tract symptoms and skipped TURP. Mean Hemoglobin loss difference between groups was 0.11gr/dl (CI 95% –0.55; 0.77, p=0.88). There was no statistical difference among variables. No positive or negative predictive values in the linear regression model.
Conclusion: Dutasteride did not significantly impact the studied variables in these non randomized and small sample size settings.

Efecto en el sangrado perioperatorio durante la resección transuretral de la próstata tras un mes de tratamiento con dutasteride

Palabras clave:
Hiperplasia prostática benigna
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R E S U M E N

Objetivo: Evaluar el efecto del dutasteride en el sangrado perioperatorio durante la resección transuretral de la próstata (RTU-P).
Material y métodos: Un total de 40 pacientes fueron incluidos. Los pacientes recibiendo finasteride o dutasteride, creatinina > 2 mg/ml, con volumen prostático < 30 cc, edad < 50 fueron excluidos. Los pacientes fueron divididos en 2 grupos. En el grupo 1: 24 pacientes consecutivos que aceptaron recibir dutasteride 0,5 mg/día durante 30 días previo a la RTU-P. En el grupo 2, 16 pacientes consecutivos sin tratamiento adicional

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Resección transuretral
de la próstata
Dutasteride

(control). Los valores de hemoglobina previos e inmediatamente posteriores a la RTU-P y el peso del tejido resecado en gramos fueron recolectados. El cirujano estuvo cegado. El análisis estadístico utilizado fue la prueba t de student, la prueba no paramétrica de Mann-Whitney y una regresión linear múltiple.

Resultados: En el grupo 1, 33% (8) mejoró su sintomatología obstructiva urinaria baja y no evitaron la RTU-P. La media de la diferencia, entre los grupos 1 y 2, de la Hb en los valores antes y después de la RTU-P fue 0,11 g/dl (IC 95% –0,55; 0,77, valor de la p 0,88). No hubo diferencias estadísticamente significativas en las variables del modelo de regresión linear múltiple.

Conclusiones: El dutasteride no tuvo un impacto significativo en las variables estudiadas en este pequeño estudio no aleatorizado.

Introduction

Finasteride is a 5-α-reductase inhibitor (5ARI) that blocks conversion of testosterone into dihydrotestosterone (DHT) and is indicated for the treatment of benign prostatic hyperplasia (BPH).[1] Its effect in the treatment of hematuria of a prostatic origin has been studied.[2-4] The effect of finasteride to decrease perioperative bleeding during transurethral resection of the prostate (TURP) has also been investigated. This effect has had good results even when the drug was given for different time periods.[1,5,6] Dutasteride is a new dual 5ARI. Dutasteride differs from finasteride in that it inhibits both isoenzymes of 5-α-reductase, resulting in an almost complete suppression of serum DHT.[7] The effect of dutasteride on bleeding reduction during TURP has been given little attention in the literature.

Materials and methods

Patients

From April 2007 to July 2008, patients with severe (>20) lower urinary tract symptoms (LUTS) according to the International Prostate Symptom Score (IPSS) or urinary retention and an indwelling catheter were consecutively invited to participate in this study. The study was submitted to and approved by the ethics committee of our institution. All patients were provided with an informed consent sheet before enrolment. Patients receiving finasteride or dutasteride with renal damage (defined as serum creatinine levels >2 mg/mL), prostate volume <30 cm^3, and age <50 were excluded from this study. Patients with abnormal prostate-specific antigen (PSA) levels (>4 ng/dL) and/or abnormal digital rectal examination during physical examination had a biopsy and, if the histopathological result was negative and they agreed to participate, they were enrolled into the study. Forty patients were recruited into this study. Prostate volume was measured before treatment by transrectal ultrasound (TRUS) using a high definition GE 2007 X pro device with a 7.5 mHz transducer (General Electric Company®, USA). Patient characteristics are shown in table 1.

Treatment

Patients were divided into two groups, Group 1 included 24 consecutive patients who agreed to receive dutasteride (Avodart®, GlaxoSmithKline) 0.5 mg/day for 30 days before TURP. Group 2 consisted of 16 consecutive patients with no additional treatment as control group. The IPSS score was not measured after treatment because it was not part of the study objectives.

TURP

TURP was performed using a continuous flow 24 Fr resectoscope (ACMI Corporation, USA Elite System™) with patients under general, epidural, or spinal anesthesia. During TURP, 1.5% glycine (Glisuret®, Laboratorios PiSA) was used as irrigation solution. Hemoglobin (Hb) values before and immediately after TURP and weight of resected tissue in

Table 1 – Patient characteristics

Variable	Group 1 (dutasteride) Mean (SD)	Group 2 (control) Mean (SD)	p value
Age	71 (5.6)	73 (8.7)	0.52[a]
Total PSA in ng/dL	5.72 (4.4)	6.9 (5)	0.86[b]
Prostate volume in cm^3	66.8 (26.9)	57 (20.4)	0.25[a]

SD: Standard deviation.
[a]Student's t test.
[b]Mann-Whitney's U test.

grams (WRT) were recorded. Surgeon was blinded. Aspirin intake was discontinued 7 days before the procedure.

Statistical analysis

Statistical analysis was performed using MedCalc software version 11.1.1 (http://www.medcalc.be). When data were normally distributed, differences were analyzed using a Student's t test. Otherwise, a nonparametric Mann-Whitney test was preferred. A multiple linear regression analysis was done to identify significant effects in a bleeding model. The dependent variable in the model was the difference in Hb levels before and after TURP between both groups. This was calculated by separately subtracting in each group the Hb value before TURP from the post-TURP value. The difference found in group 2 was then subtracted from that found in group 1 to obtain the difference in Hb level between the groups. Independent variables included groups, prostate volume, and WRT. Requirements for use of linear regression were met.

Results

In group 1, 8 patients called our department to say that their LUTS had improved and they did not want to undergo TRUP. Thus, 32 patients underwent the procedure when scheduled. When the difference in post-TURP Hb levels was obtained, 2 patients (one in each group) were considered as outliers, and were therefore withdrawn from final analysis in order to meet the requirements of linear regression. No complications were reported. Mean difference between groups 1 and 2 in Hb values before and after TURP was 0.11 g/dL (95% CI –0.55; 0.77, p=0.88). Mean WRT was 17.6 (SD 7.53) vs 18 g (SD 5.92) in group 1 vs group 2 respectively, as shown in table 2. No patient required repeat surgery. No statistically significant differences were found in variables evaluated in the multiple linear regression model, as shown in table 3.

Discussion

Human studies with finasteride have shown a reduction in blood flow and vascular density.[8] Bleeding is expected during TURP, and it has been reported that approximately 4% of untreated patients may require blood transfusion after the procedure.[9] However, this may be decreased to a value close to 0% if patients have previously received finasteride.[1,5] The effect of dutasteride in this regard has been paid little attention in literature.

5ARIs have been shown to decrease prostate volume by 20%-27%, LUTS, and risk of urinary retention.[7,10,11] In our study, 33% of patients showed an improvement in LUTS after one month of treatment with dutasteride. The value of this observation is controversial because LUTS were not assessed in a comparative control group given placebo.

Donohue et al reported that a daily dose of finasteride given for 2 weeks before TURP decreased bleeding.[1] These findings led urologists to use finasteride, but with less consistent results. In a multicenter, double-blind, randomized, placebo-controlled study, Hahn et al[12] found no statistically significant differences between the dutasteride and placebo arms after 2 and 4 weeks of treatment. Tuncel et al[13] reported similar results in a clinical trial on a smaller sample. While our study was not randomized and had a small sample size, the same results were seen, and no statistically significant differences were found. However, our study may be difficult to interpret because Hb levels were not measured in the irrigation solution, the number of variables in the model was small, and outliers had to be removed to meet the requirements of multiple linear regression.

The scientific basis underlying dutasteride action in reduction of hematuria of a prostatic origin is inhibition

Table 2 – Results

Variable	Group 1 (dutasteride) Mean (SD)	Group 2 (control) Mean (SD)	p value
Resection time in min	67 (16.6)	64 (17.1)	0.68[a]
Resected tissue weight in g	17.6 (7.53)	18 (5.9)	0.87[a]
Hb decrease in g/dL	1.42 (0.85)	1.53 (0.91)	0.73[a]

[a]Student's t test.

Table 3 – Multiple linear regression R^2=0.054, F-ratio=0.4847, p=0.69

Independent variables	Coefficient	Standard error	t	p value
(Constant)	0.8530			
Resected tissue weight in g	0.01644	0.02556	0.643	0.5261
Groups	–0.1622	0.3427	–0.473	0.6401
Prostate volume in cm^3	0.00679	0.007193	0.944	0.3542

of angiogenic growth factors, thus decreasing prostate gland vascularization. This was shown by Donahue et al after 2 weeks of finasteride treatment.[14] In a recent study, Kravchick et al showed, using ultrasound, that prostate gland vascularization was reduced after 6 weeks of dutasteride treatment.[15] Methodology was limited, however, and these results should be confirmed by other studies. There has been research on the potential chemopreventive effect of long-term treatment with these drugs in prostate cancer.[16,17] However, such observations are beyond the scope of this article. Apart from this, if both treatments have been shown to have similar action mechanisms as regards vascularization, why has dutasteride not shown good results in reduction of perioperative bleeding during TURP in clinical trials? Hahn et al did not see the expression of endothelial growth factor in suburethral tissue reported in finasteride studies due to technical difficulties. Thus, the answer to this question may lie in a more thorough examination of prostate tissue.

Conclusions

No statistically significant differences were seen in bleeding during TURP after dutasteride administration, regardless of the methodological limitations of this study. This agrees with previous literature reports. Further studies are needed to find the reason for the lack of efficacy of dutasteride as compared to finasteride in this regard.

Conflict of interest

The authors declare no conflict of interest.

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