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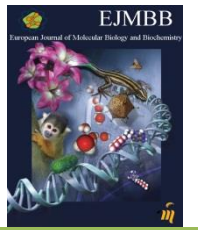

EVALUATION OF THE BIOCHEMICAL PARAMETERS AND TREATMENT OF ACUTE PROSTATIC HAEMATURIA WITH DUTASTERIDE

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ABSTRACT

After transurethral prostate excision, dutasteride has been demonstrated to minimise chronic prostatic haemorrhage when given 2-6 weeks before the surgery. Acute gross prostatic haematuria is being studied to see whether the medicine has any impact on it. Patients and Methods: Patients with repeated episodes of severe haemorrhage were included. All three tests were performed in order to rule out the possibility of haematuria being caused by medical, renal, or bladder issues. Those suspected of having prostatic haematuria were subsequently investigated utilising a blood PSA and a Prostate Scan. Prostate biopsy was performed on those who had a PSA level more than or equal to 10 ng/ml and a negative digital rectal examination (DRE). There were two groups of patients. Dutasteride was given to the second group, whereas the control group was given normal saline and broad-spectrum antibiotics. After the haematuria subsided, we kept note of how long it took and how much irrigation fluid we used. SPSS 20.0 was used for the statistical analysis. Prostatic haematuria was discovered in a total of 75 individuals. Sixty-five percent had BPH and thirty-six percent had cancer of the prostate. An additional oral dutaste-ride was given to 24 of the 49 BPH patients (49 percent), while usual saline irrigation and antibiotics were administered to 25 (51%). Most patients received saline drainage and antibiotics, but only a small percentage received dutasteride as an extra therapy. As compared to the control medication, dutasteride was able to eliminate haematuria more quickly and with less irrigation fluid than the former. Prostatic haematuria may be cured more quickly with the increment of 0.5 mg of orally dutasteride per day.

INTRODUCTION

BPH or prostate cancer account for 27% and 8%, respectively, of all instances of gross haematuria [1]. Even if they are viable choices, emergency prostatectomy [2] and its related problems are not specific. It would be a godsend to have an effective oral drug. [4] Dutasteride's chemical name (5, 17)-N 2,5 bis (trifluoromethyl) phenyl-3-OXO-4-azaandrost-1-ene-17-carboxamide belongs to a category of drugs known as 17 substituted 4-azasteroids.

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Competitively inhibits 5 reductase type 1 and 2 isoenzymes using this chemical. Slow dissociation with 5 reductase creates an insoluble compound, which inhibits enzymes from binding to testosterone [6]. Because dutasteride inhibits the 5 reductase enzyme, the active form of androgen is dihydrotestosterone (DHT). Dutasteride works by preventing the synthesis of DHT.

An anti-DHT agent, such as dutasteride, can be used to deprive prostates of DHT, which is the primary growth stimulator, without causing any injury to the prostate. In turn, this decreases the possibility of illness [7] and its consequences [8] developing as well as the symptoms that go along with it developing. DHT has been demonstrated to enhance prostatic angiogenesis in addition

to these effects. Prostatic blood flow and vascular density are reduced when DHT is removed by dutasteride or other 5-hydroxytryptamine reductase inhibitors [10].

For the treatment of chronic or lengthy prostatic bleeding, dutasteride and finasteride were shown to be very effective. These varied processes are assumed to be the reasons for this effectiveness. When it comes to transurethral resection of prostate, the medications have been administered for 2-6 weeks prior to surgery [11]. They considerably relieve lower urinary tract symptoms if administered for six months or longer [7].

There is no information on the usage of dutasteride for acute prostatic bleeds, despite the fact that it has been used to decrease long-term prostate bleeds. If oral dutasteride is effective in treating acute prostatic bleeding, it will lessen the need for emergency prostatectomy as a last resort for patients with refractory prostatic haemorrhage.

In order to find out whether or not dutasteride is effective in treating acute gross prostate gland haematuria caused by benign prostatic hypertrophy or prostate cancer, this study is being conducted.

Patients and Method

Participants in the study had to be admitted to the University of Port Harcourt Teaching Hospital during January 2011 and June 2014. After being properly informed of the treatment's benefits and possible downsides, all subjects agreed. The research covered all adult male patients with prostatic haematuria. There was a thorough evaluation of all of the applicant's medical history, as well as the physical examination, and appropriate tests. Those with abnormal liver and renal function tests were excluded from the study. Excluded from the study were patients who had had an orchiectomy and those on androgen blocking. In order to exclude out renal and bladder cancers, cytoscopy and intravenous urography were performed. As a last resort, patients suspected of having prostatic haematuria had their PSA and Prostate Scan results examined. Patients with PSA levels more so than or equal to 10 ng/ml or a problematic DRE result had their prostates biopsied. BPH patients were separated from CaP patients based on histological findings.

Each patient was given a three-way size 22 or 24 G Foley catheter while being evaluated for the underlying cause of their haematuria. Using a catheter tip bladder syringe, the urinary bladder was carefully flushed to eliminate any leftover blood clots. Continuous saline bladder irrigation was then started, with the pace being determined by the severity of the hemorrhagic symptoms. In order to prevent or treat an infection, broad-spectrum antibiotics were added.

Regardless of their diagnosis, every patient had a different course of treatment. 0.5mg oral dutasteride was added to the bladder irrigation and broad-spectrum antibiotics given to the other group. As a way to compare treatment effects across both diagnoses, we collected data on how long it took for haematuria to clear up and how much irrigation fluid was necessary in each group. SPSS 20.0 was used for the statistical analysis.

The mean irrigation fluid volume utilised in the two treatment types was compared using a two-sample student t-test. To see whether there were any variations in the amount of time it took for the haematuria to clear up between the two treatment options, researchers performed Kaplan Meier Survival Analysis. Comparing the two groups' haematuria time-to-resolution rates was done in order to evaluate whether the observed differences were due to random chance. The Log Rank, Breslow, and Tarone-Ware tests were used to determine the relative relevance of the two treatment groups. To determine statistical significance, a P value of less than 0.05 (p 0.05) was employed.

RESULT

It was found that 75 men had prostatic haematuria. There were 49 (65.3 percent) men with prostate cancer, and 26 (34.7 percent) of the men had prostate cancer. The mean age of the whole population was 68.8 9.5 years. Patients with BPH were an average of 67.0 years old, but those with prostate cancer were an average of 71.4 years old, according to a new study. Prostate cancer patients' PSA levels were on average 47.9 ng/ml, compared to 14.8 ng/ml in men with benign prostatic hyperplasia (BPH).

One-fifth of the 49 BPH patients were given this extra medication in addition to the conventional regimen, including saline irrigation, antibiotics, and 0.5mg oral dutasteride. Saline irrigation was used in 14 of the 26 prostate cancer patients who got 0.5mg of oral dutasteride in combination (46.2 percent of the patients).There were no more haematuria in the 24 (100%) BPH patients receiving dutasteride 0.5 mg or the 25 (96%), who were in the control group. Four percent of patients required an open prostatectomy to end their haemorrhage.

Patients with prostate cancer who received dutasteride had a complete cessation of haematuria, whereas only 85.7% of those in the control group did. Before the haematuria went away in 2 of the prostate cancer patients, they underwent a bi-lateral sub capsular orchidectomy. Dutasteride improved haematuria in all 36 patients, but only in 36 (92.3 percent) of the 39 patients in the control group. Surgery was required in 3 of the 707 patients (7.7%) in the control group before the haematuria cleared up. To end haematuria, the normal saline control group needed anything from 6 to 55 litres of irrigation fluid, while the dutasteride group needed an average of 10.4 litres (Table 1). The quantity of irrigation fluid used by those using dutasteride was significantly different (t=-2.886, p=0.009) (Table 2). Those on dutasteride required an average volume of 17.3+9,6 litres of irrigation fluid to relieve their hemorrhagic symptoms, whereas those on the control arm needed between 4 and 48 litres (Table 1). According to the results of a student t-test, this group utilised much more irrigation fluid than the control group (Table 2).

Table 1. Every kind of diagnostic and therapy has its own haematuria length (in days) and volume of irrigation fluid used (in litres).

Diagnosis	TT	N	Min DUR	Max DUR	MD+SD	Min Vol	Max Vol	MV+SD
BPH	N/S+DUT	24	2	15	4.9±2.9	4	20	10.4± 5.2
	N/S only	25	3	38	8.0±6.8	6	55	2.0±11.9
CaP	N/S+DUT	12	1	8	4.7±1.9	3	20	8.3 ± 4.6
	N/S only	14	3	10	6.9±2.3	4	48	17.3 ±9.6

BPH = Benign prostatic hyperplasia, CaP = Prostate cancer, TT = Treatment type, N/S = Normal saline, DUT = Dutasteride, N = No of patients, Min = Minimum, Max = Maximum, DUR = Duration, MD = Mean Duration, MV = Mean Volume, SD = Standard deviation.

Table 2. Mean volume of irrigation fluid used before haematuria was resolved, as well as two sample student t-tests and p values, are displayed in this cross-tabulation of diagnosis and treatment.

Diagnosis	N/S and DUT	N/S only	t-test	t-test
	Mean ± SD	Mean ± SD		
BPH	10.4 ± 5.3	21. 1 ± 12.0	−2.886	0.009
CaP	8.4 ± 4.7	17.5 ± 9.8	−4.156	0.001

N/S = Normal saline, DUT = Dutasteride, BPH = Benign prostatic hyperplasia, CaP = Prostate cancer.

Both groups had haematuria for an average of three to 38 days in the control group, with a mean of eight to six days, while those on dutasteride had haematuria for an average of just over two to 15 days. Prostate cancer patients in the control group had hemorrhagic symptoms for an average of 6.92.3 days, while those in the treatment group experienced symptoms for one to eight days (Table 1).

Table 3. Survival time means and medians (time to resolution of haematuria).

Treatment	Mean				Median			
			95% Confidence Interval				95% Confidence Interval	
	Estimate	Std Error	Lower Bound	Upper Bound	Estimate	Std Error	Lower Bound	Upper Bound
N/S and DUT	7.492	1.819	5.885	9.098	6.000	1.458	5.102	6.898
N/S Irrigation Only	12.039	3.512	7.116	16.962	9.000	1.596	7.832	10.168
Overall	9.779	2.390	7.005	12.503	8.000	1.628	6.770	9.230

There was a statistically significant difference between the two therapy groups when it came to the time it took for haematuria to go away, according to this study's Kaplan Meier Survival Analysis (Figure 1). According to the results of this study, it is possible to infer that dutasteride may be more effective than saline irrigation in relieving symptoms of irritable bowel syndrome (IBS). For patients using dutasteride, haematuria was resolved more quickly than in those taking placebo (p = 0.009), showing that the observed survival curve variation was not attributable to chance Table 3.

DISCUSSION:

Gross prostatic haematuria has no particular therapy. When bleeding is severe, the first course of action may include observation, irrigation with antibiotics, or even emergency surgery. Bladder irrigation is mostly used to prevent blood clots from forming in the first place, rather than as a therapy in and of itself. As urokinase (a serine proteolytic enzyme) is washed away during bladder irrigation, some researchers believe that the length of

haemorrhagic symptoms may be reduced [12]. Retention and infection may paradoxically enhance bleeding as a result of clot formation [13] [14]. In this research, since bladder irrigation was performed in both therapy groups, whatever impact it had would have been wiped out.. This suggests that differences in irrigation fluid volume and duration are indicative of dutasteride's action.

Dutasteride-treated patients had haematuria cleared in fewer than five days, but patients with prostate cancer and BPH had haematuria resolved in less than seven and eight days, respectively, without dutasteride. Kaplan-Meier curve (Figure 1) shows that when the permissible exceed is provided; the time of haematuria is reduced. There is a high possibility that a patient on a specific therapy will receive relief at any point on the survival curve.. A lower curve indicates sooner alleviation for people who received dutasteride compared to those who received saline irrigation alone. Patients with haematuria who have not yet been alleviated of their symptoms are referred to as the percentile. As an example, 75% of patients were still experiencing haematuria after they reached the 75th %. This suggests that a quarter of the participants were free of

haematuria at the time of testing. 4 days for those who received du-tasteride and 6 days for those who received simply irrigation.

Findings that haematuria went away in less than five days while on dutasteride challenges the idea that apoptoisis and prostate shrinkage were primary mechanisms of action of 5- reductase inhibitors (ARIs) [15]. The prostate starts to shrink after around six months of 5ARIs treatment [5] [16]. This quick res-olution of haematuria may not be explained by another mechanism of action that 5ARIs are claimed to have, angiogenesis suppression, because angiogenesis is predicted to occur between 5 and 7 days. It's possible that dutasteride works on something deeper than just the symptoms of hemorrhagic cystitis, as its ability to diminish haematuria so swiftly suggests. This illness's root cause has been shown to be inflammation [17]. Neovascularization, edoema, and increased fragility and bleeding there in veins are all caused by an increase in vascular permeability. Dutasteride is able to reverse these effects because of its capacity to inhibit the growth of vegf. Peripheral vascular oedema is minimised as a result. By reducing oedema in the extracellular environment, which lowers intravascular pressure and prevents the loss of fragile new arteries, haematuria may be decreased.

Dutasteride was shown to be beneficial to prostate cancer patients who had not previously had androgen restriction therapy before developing gross prostatic haematuria. The primary emphasis of research in men with BPH has been on the impact of 5ARIs on prostatic haematuria. Finasteride is a type 1 5-reductase inhibitor, and Dahala et al. [18] warn against using it to treat prostatic haematuria in males with prostate cancer. Dutasteride may reduce prostate cancer-related prostatic haematuria even if androgen ablation has not been done, according to this study.

Both BPH and CaP patients had hemoptysis lasting 4.7 to 1.9 days, but there was no statistically significant difference in the duration of haematuria between the two groups. Because of the increased vascular density and neovascularization in BPH, the average duration of haematuria should have been much longer [9] [19]. This difference may be caused by a wide range of sample sizes (12 for CaP and 24 for BPH).

In this study, bilateral orchidectomy was shown to be an effective treatment for hematuria. Irrigation for more over 30 days failed to stop two CaP patients from bleeding in the control group. Both patients' haematuria ended after 24 hours following orchidectomy, which was performed on both of them using a bilateral complete orchidectomy. Furthermore, androgens have a significant role in the aetiology and pathophysiology of prostatic bleeding. After an orchidectomy, testosterone and DHT levels fall by more than 90% in the bloodstream [21]. This means that the effects of DHT and the inflammation it causes may be eliminated by having an orchidectomy.

CONCLUSION:

Oral 5ARIs may help reduce bleeding in situations of acute prostatic haematuria while awaiting final therapy either to benign prostatic hyperplasia or precastration prostate cancer. A bigger sample size is required to corroborate this.

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