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Tamsulosin 0.4mg in the Treatment of Symptomatic BPH: Assessment of Response in African Men.

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Abstract
Introduction: *To assess the presence and extent of response to Tamsulosin 0.4mg in African men with lower urinary tract symptoms (LUTS) due to Benign Prostatic Hyperplasia (BPH) over a short term.*
Materials and Methods : *A total of 106 men were enrolled in the study. After assessing the severity of their LUTS using the International Prostate Symptom Score (IPSS) and the Quality Of Life (QOL) Score, patients were assigned to 0.4mg Tamsulosin (Contiflo[R]). At 4 weeks the IPSS and QOL were re-assessed.*
Results : *Two patients (1.9%) were lost to follow up along the course of the study. Mean age of patients was 63.9years age while range was 41-90 years. Mean IPSS at baseline was 18.04, whereas mean QOL score was 5.15. There was statistically significant improvement in IPSS and QOL Score from baseline at 4 weeks. The pooled mean IPSS showed a 47.7 % (p<0.001) improvement while the QOL score showed a 38.9% (p=0.00) improvement at the end of the study.*
Conclusion: *Our study demonstrated that African men with LUTS due to BPH can expect significant improvement in their symptoms while using Tamsulosin 0.4 mg.*
Keywords: *Tamsulosin, BPH, Africans*

I. Introduction

The incidence of benign prostatic hyperplasia (BPH), as well as the presence of bothersome lower urinary tract symptoms (LUTS) increase with age, and become prevalent as early as the fourth decade [1]. Benign prostatic hyperplasia (BPH) is the commonest cause of bladder outlet obstruction in men older than 50 years[2-3]. Estimates of this disease in the West African sub- region give prevalence of BPH under 60 years as 21% and for men over 80 years as 53%[4]. Prevalence of symptoms of BPH by lower urinary tract symptoms (LUTS), International prostate symptom score (IPSS) and peak flow rate (PFR) in men aged 40 years is given as 14%, in 50 year olds 25%, in 60 year olds 43% and 50 % in 75 year olds[4].

The modalities of treatment of BPH vary depending on the severity of symptoms as measured by the IPSS score and on the presence or absence of complications e.g. acute or chronic urine retention and the size of the gland[5, 6]. These modalities include; watchful waiting, medical management, minimally invasive methods, Transurethral resection of the prostate (TURP) and open surgery.

Medical management of BPH is the first therapeutic option for many patients with BPH [3] and consists of, alpha – 1 antagonists e.g. prazosin, doxazosin and tamsulosin; 5-alpha reductase inhibitors e.g. Finasteride, combination of alpha-1-antagonist and 5-alpha-reductase inhibitors. Phytotherapy – the bark of saw palmetto (*serenoa repens*), and African star grass (*hypoxis rooperi*) among others, may also be used as medical therapy for patients with BPH.

Alpha blockers are the most universally prescribed medications in BPH treatment[7, 8] Tamsulosin 0.4 mg is the most widely used drug in the treatment of lower urinary tract symptoms associated with benign prostate hyperplasia .The drug has a relatively low propensity for side effects and this has been well established in randomized placebo-controlled clinical trials[9] .The mechanism for the selectivity of the drug for urinary tract-related symptoms was proposed to be associated with the a1-adrenoceptor selectivity profile of the drug [10].

Studies have demonstrated the benefits of Tamsulosin at doses of 0.2 to 0.8 mg daily[9]. These studies have mainly been in Asia, Europe and the Americas.

In Sub Saharan Africa, because paucity of local literature on the efficacy of the drugs used for medical management of BPH, the medical management of BPH has largely been overlooked, or at best viewed with cynicism.

In this study we set out to determine the response African patients with LUTS suggestive of BPH can expect when receiving Tamsulosin 0.4 mg daily. We also sought to determine what adverse effects they can anticipate.

II. Methods

This is an interventional single blind study that determined the response to Tamsulosin in patients with BPH seen at Jos University Teaching Hospital and Bingham University Teaching Hospital both in Jos, North-Central Nigeria. The study used the IPSS and Quality of Life (QOL) score as primary outcome measures. Men 40 years and older who had LUTS were invited to participate. Patients with urological malignancy, liver disease, renal disease, urinary tract infection were excluded. All patients provided informed consent.

All patients were evaluated by history taking, physical examination, IPSS and QOL questionnaire. All patients recruited had their International Prostate Symptom Score (IPSS) and Quality of Life (QOL) Score assessed at the onset of the study and at 4 four weeks after commencement of Tamsulosin 0.4mg (Contiflo^{R}). Side effects reported were graded as tolerable, or intolerable.

Variables were analysed using SPSS version 16. In all tests p-value of 0.05 were considered statistically significant.

III. Results

One hundred and six patients were recruited for this study, having met the inclusion criteria and given their consent. Their ages ranged from 41-90 years with a mean age of 63.9±9.4 years. Two patients (1.9%) dropped out during the course of the study.

At the onset of study 37 patients (34.9%) had severe LUTS, 65(61.3%) had moderate LUTS and 4(3.8%) had mild LUTS. (Figure 1).

Mean IPSS at onset of study was18.04±5.06 (Figure 2).At the end of the study 2 patients (1.9%) had severe LUTS , 55 patients (51.9%) had moderate LUTS and 49 patients (46.2%) had mild LUTS, (Figure 3). Mean IPSS at four weeks was 9.44±3.98. (Figure 2).Mean baseline QOL score was 5.15±0.89 while mean QOL score at four weeks was 3.09±1.01. (Figure 4). Sixteen patients (15.1%) had side effects while on the drug and in all of them side effects were tolerable. (Table 1)

Pooled mean improvement in IPSS after four weeks of therapy was 47.7%. The pooled mean improvement in QOL score over the same period was 39.8%. Using the paired t-test there was statistically significant improvement in pooled IPSS and QOL score with
$p<0.001$ and $p<0.05$ respectively.

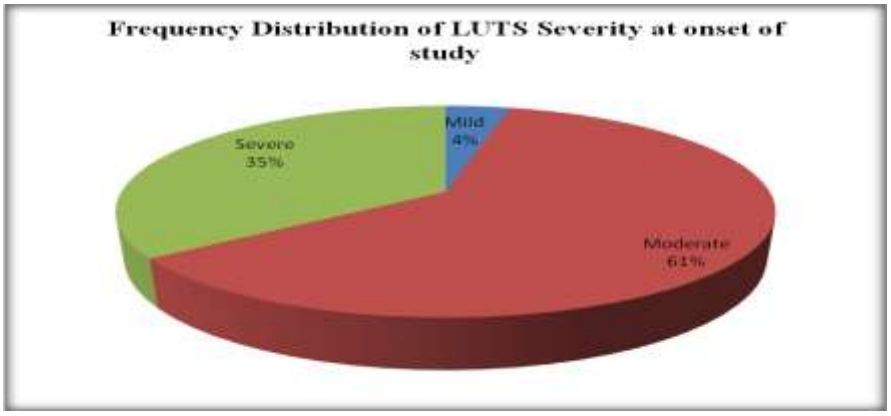
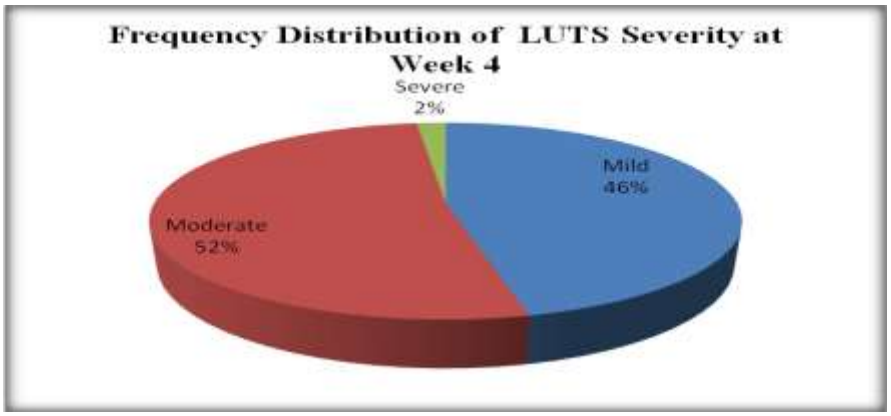


Figure 1



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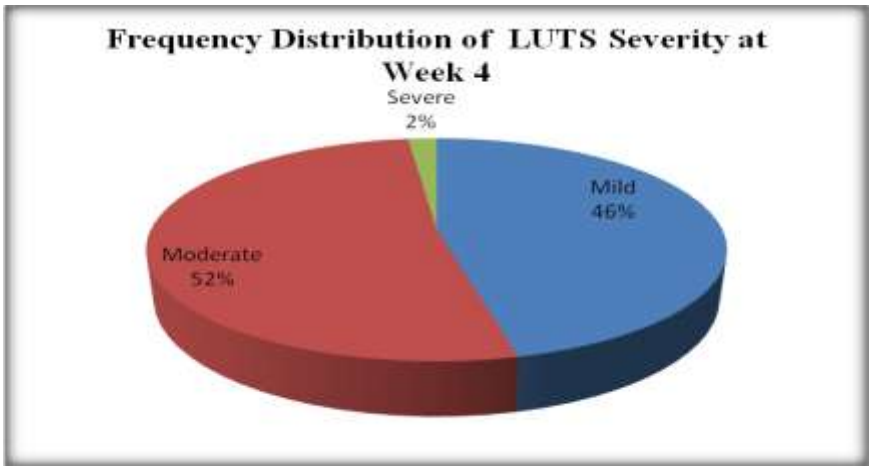

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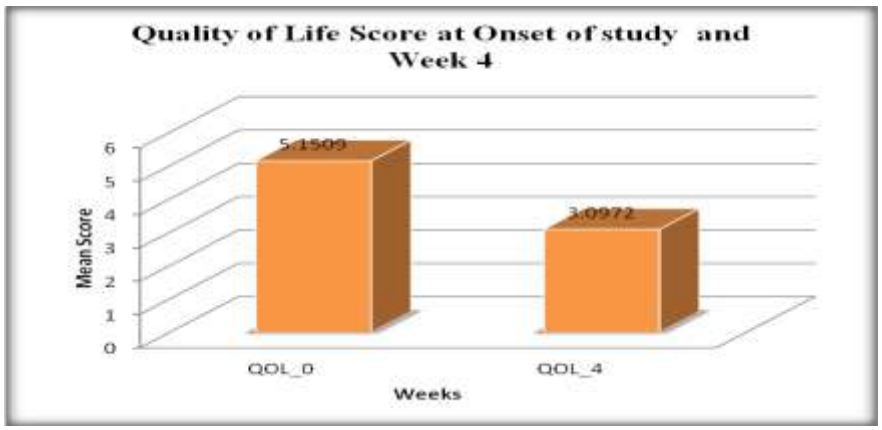

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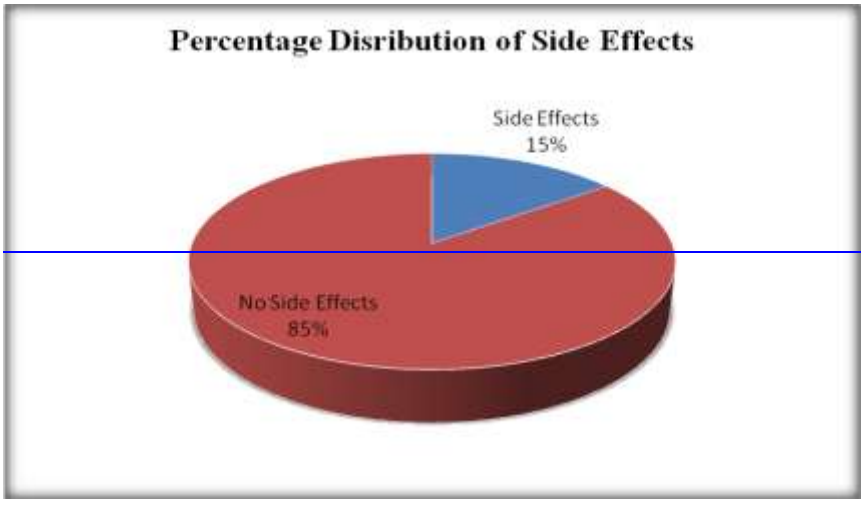

Figure 5

Table 1 : Side effect profile of Tamsulosin 0.4mg

Side Effect	**Number**	**Percentage (%)**
Headache	**5**	**31.25**
Retrograde Ejaculation	**2**	**12.5**
Weakness	**3**	**18.75**
Nausea	**1**	**6.25**

GIT upset	**4**	**25**
Bitter taste	**1**	**6.25**
Total	**16**	**100**

IV. Discussion

Tamsulosin is a selective alpha-1 adrenergic receptor antagonist and its efficacy and safety has been demonstrated in various studies in other regions of the world [11]. Normally 4 weeks of treatment with Tamsulosin has been shown to be enough to improve symptoms[12]. This study set out to assess the response over a short period of time to Tamsulosin 0.4mg in Africans with symptomatic BPH.

There was statistically significant improvement in pooled mean IPSS (47.7%), over the course of this study with p value <0.001.This is portrayed by the finding that at the onset of the study 4% of patients had mild LUTS, 35% had moderate LUTS and 61% had severe LUTS whereas at the end of the study, 46% had mild LUTS, 52% had moderate LUTS and only 2% had severe LUTS.

Tamsulosin used for this study is more effective in improving LUTS as assessed by IPSS than the older generation alpha -1 antagonists. Using Prazosin, Ogbonna et al[13] in Jos, North-Central Nigeria found an improvement in IPSS of 33% when they studied 31 patients awaiting prostatectomy. Their finding is lower than the 47.7% improvement in the IPPS found in this study. The difference may be because their study population already had indications for prostatectomy and so were at onset not the best category of patients to benefit from alpha-1 antagonist therapy. Furthermore, prazosin has less affinity for alpha-1_a receptors compared to Tamsulosin. This relative poor selectivity and (by extension) efficacy of the older generation alpha-1 antagonists can be seen in results reported by Vallencin et al[14], where only a 33.4% improvement in IPSS was seen when alfuzosin was used in 689 patients over a 3 year period.

Some studies seem to suggest Tamsulosin does not cause further improvement of LUTS with prolonged use. A previous study in 116 Asian patients over 16 weeks demonstrated a statistically significant improvement in LUTS when using Tamsulosin 0.4mg in the first 8 weeks of the study[15]. The improvement over the second 8 weeks was not statistically significant. Likewise, Michel et al [16] found that Tamsulosin treatment lowered the IPSS in 1784 Caucasians with the majority of the symptom reduction occurring in the first 8 weeks of treatment (with less significant reduction in symptoms over the remaining of the study) despite the continuous use of the drug for 24 weeks. These results seem to suggest that for patients on Tamsulosin 0.4mg any improvement in IPSS seen over short term is not likely to markedly increase even with long term therapy. There may be need for further investigations in this regard.

The improvement in pooled mean QOL score in our study was 40%, this was statistically significant. Ogbonna et al[13] reported an improvement in quality of life in 35% of patients the outcome measure being safe removal of catheter. A QOL score questionnaire was not administered in that study. Likewise Roehrborn[17] in reviewing the efficacy of and safety of alfuzosin noted that "the patients' quality of life was also significantly improved" but did not mention the parameter used to assess the quality of life. Chung et al showed a statistically significant improvement in QOL score (0.3+/- 0.8) while studying the effect of 0.4mg Tamsulosin[15]. In our study, the significant improvement in QOL score (40%) is an important outcome measure of the response to alpha-1 antagonists. This is because the bothersome symptoms of BPH adversely affect the sense of well being of these patients and more often than not is the driving force for seeking medical help. The degree of discomfort experienced by the patient is what is subjectively assessed by the QOL score. Thus improvement in their QOL score which implies a decrease in the degree of discomfort make alpha -1 antagonists a good first line therapy for patients' .

Sixteen patients (15.1%) had side effects while on the drug and in all of them side effects were tolerable. Headache was the most common side effect in this study (6.6%) unlike the findings of Vallencin et al[14] where dizziness was the most common side effect (4.5%). It is not clear if both side effects are due to impact on the cardiovascular system or otherwise.

Ejaculatory disorders (1.9%) were relatively rare in this study though higher than that found by Vallencin et al[14] (0.4%).This may be due to the difference in sample size i.e. 689 compared to 106 in this study. Nevertheless, one expected a higher incidence of ejaculatory disorders since a "uro-selective " a-1 antagonist was used and this class of drugs are associated with a high incidence of the side effect . We propose that given the mean age of these patients (63.9±9.4 years) the frequency of sexual intercourse would have greatly reduced and so the apparent rarity of ejaculatory disorders. Embarrassment in reporting this side effect in a conservative society such as ours may also be another reason.

A limitation in this study was the inability to assess severity of LUTS using urodynamics which was unavailable in our centre during the period of this study. The low level of literacy of these patients also caused the authors on many occasions to have to read and interpret the IPSS questionnaire to the patients. As a result

valuable information would have been lost since some of the symptoms or their severities are not easily interpreted in the patients' vernacular.

The findings in this study lend credence to previous reports of good response to Tamsulosin and to its relative safety in managing LUTS resulting from BPH. Our findings suggest African men with BPH can expect a significant improvement in their LUTS and QOL when using Tamsulosin 0.4mg.

There is room for further evaluation of the response to Tamsulosin using the peak flow rate and /or post void residual urine volume as primary outcome measures.

V. Conclusion

In African men with LUTS resulting from BPH who meet the criteria Tamsulosin offers significant improvement in IPSS and QOL score.

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