

## Comparison of Biochemical Efficacy of Bilateral Orchidectomy and Medical Castration (Goserelin) in Patients with Advanced Prostate Cancer at Lagos State University Teaching Hospital, Lagos.

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### Abstract

**Background:** PCa is a leading cause of cancer –related deaths among men and it is the most commonly diagnosed cancer among Nigerian men. Most of the patients with PCa in Nigerian hospitals present with advanced disease and this requires ADT which can be in form of surgical or medical castration. This study was designed to determine which of the two options is more efficacious. **Aim:** The study compared the biochemical efficacy of medical castration (Goserelin) with bilateral orchidectomy in reducing serum testosterone and serum PSA in patients with advanced PCa. **Design and setting of the study:** A prospective, hospital based, non-randomized clinical study was conducted over one year period from November 2016 - October 2017. Each patient was followed up for six months. Patients who met the inclusion criteria were recruited consecutively into two groups; surgical and medical castration groups after obtaining written informed consent. Serum testosterone and PSA were measured before prostate biopsy was done using chemiluminescent immunoassay. Serum testosterone and PSA were repeated at 1, 3 and 6 months following commencement of treatment in the two groups. Data were analyzed using the Statistical Package for Social Sciences (SPSS IBM) version 20.0. **Results:** Fifty patients were studied, twenty-five patients in each group. The percentage drop in median serum testosterone at 1,3 and 6 months for the orchidectomy group was 85.40%, 91.30%, 91.90% respectively and the percentage drop in median serum testosterone for the medical castration(Goserelin) group at 1,3 and 6 months was 87.30%, 93.80%, 94.00% respectively. The percentage drop in median serum PSA at 1,3 and 6 months for orchidectomy treatment group was 69.40%, 97.50% and 99.20% respectively and for medical castration(Goserelin) group, the percentage drop in median serum PSA at 1,3 and 6 months was 68.40%, 96.80%, 98.20% respectively. Local complications associated with orchidectomy were scrotal hematoma (20%) and surgical site infection (28%). Injection site reaction (8%) was recorded in goserelin group. All patients in both groups had hot flushes, reduced libido and weak erection as systemic side-effects. **Conclusion:** Medical castration (Goserelin) and surgical castration(Orchidectomy) are both equally efficacious in the short term, in the treatment of advanced prostate cancer.

**Keywords:** Prostate Cancer, Medical castration, orchidectomy, PSA, testosterone.

### Introduction

Prostate cancer (PCa) is a leading cause of cancer-related deaths among men. It is the most commonly

diagnosed cancer among Nigerian men and the leading cancer among men of African descent in the USA, Caribbean, and SSA.<sup>2</sup> In the United States, PCa has been described to be more prevalent among the African-Americans with an incidence of 248.5 per 100,000 in contrast to 156.7 per 100,000 in white American men<sup>3</sup>. Men of African descent have the highest incidence and mortality rates of PCa worldwide.<sup>4</sup> A published data by Badmus et al<sup>3</sup> in Ile - Ife reported hospital prevalence rate of 182.5 per 100,000 male admission in the hospital. In a

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community study by Ikuerowo and colleagues<sup>5</sup> to determine the community burden of PCa in Lagos, the prevalence rate was 1046 per 100,000 in men of age  $\geq 40$  years. Most of the cases of PCa in Nigeria commonly present with advanced disease<sup>6</sup> and this might be as a result of poor health-seeking behavior of patients, low literacy level, poor access to health facilities, and lack of screening services. Advanced disease might be in form of locally advanced disease or metastatic disease.

When patients present with advanced PCa, hormonal therapy in form of Androgen deprivation therapy (ADT) remains the cornerstone of primary treatment. ADT can be in two forms; medical castration most commonly luteinizing hormone releasing hormone analogue (LHRH) e.g. goserelin acetate; or surgical castration (bilateral orchidectomy). Both methods aim at reducing serum testosterone concentrations to a castrate level which is currently defined as less than 50 ng/dl<sup>7</sup>. Suppression of testosterone production is effective in decreasing tumour burden and hence the serum PSA.<sup>8</sup> Therefore, Serum PSA and testosterone are laboratory tools used in monitoring patients with PCa treated with ADT.<sup>9</sup>

This study was designed to compare the biochemical efficacy of the two modalities of ADT in advanced PCa in order to advise patients on which of the two options is more efficacious and appropriate. In view of absence of direct similar studies in our environment, this study's eventual outcome will go a long way in adding to current knowledge in the management of patients with advanced PCa in our locality.

### Patients and Methods

**Aim:** To compare the biochemical efficacy of medical castration (goserelin) with bilateral orchidectomy in reducing serum testosterone and serum PSA in patients with advanced prostate cancer.

**Design and setting of the study:** The study was a prospective, hospital based, non-randomized clinical study. The study was for one year period from November 2016 - October 2017 while each patient was followed up for six months. Sample size of 50 patients was calculated. Patients that met the inclusion criteria were recruited consecutively into with 25 patients in each group after obtaining written

informed consent. Serum testosterone and PSA were measured before prostate biopsy was done using chemiluminescent immunoassay. Both groups of patients were started on bicalutamide 50mg daily for only two weeks starting from the day treatment was commenced. This is necessary to prevent the tumour flare associated with LHRH analogue. Serum testosterone and PSA were repeated at 1, 3 and 6 months following commencement of treatment in the two groups. The data were analyzed using the Statistical Package for Social Sciences (SPSS IBM) version 20.0.

### Results

Fifty patients were studied, twenty-five patients in each group.

The ages of the patients were 60-80 years. The mean ages were  $71.72 \pm 7.3$  and  $68.3 \pm 7.3$  (years) for the bilateral orchidectomy and the goserelin groups respectively. There was no significant difference in the ages of the two groups, ( $P=0.409$  Table 1).

Figures 1 & 2 show changes in the serum testosterone and the serum PSA respectively in both treatment groups. The percentage drop in median serum testosterone at 1,3 and 6 months for the orchidectomy group was 85.40%, 91.30%, 91.90% respectively while the percentage drop in median serum testosterone for the goserelin group at 1,3 and 6 months was 87.30%, 93.80%, 94.00% respectively (Table 1).

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Variable	Bilateral orchidectomy	LHRH (Goserelin)	P-value
Frequency	25	25	
Age (Mean $\pm$ SD)	$71.72 \pm 7.3$	$68.3 \pm 7.3$	<b>0.409</b>
<b>Serum PSA</b>			
Pre-treatment	104.40 (%drop)	98.00 (% drop)	<b>0.371</b>
1-month	32.00 69.40%	31.00 68.40%	<b>0.712</b>
3-months	2.60 97.50%	6.10 96.8%	<b>0.165</b>
6-months	0.80 99.20%	1.80 98.2%	<b>0.364</b>
<b>P value</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	
<b>Serum Testosterone</b>			
Pre-treatment	322 (%drop)	401 (% drop)	<b>0.124</b>
1-month	47 85.40%	51 87.30%	<b>0.892</b>
3-months	28 91.30%	25 93.80%	<b>0.541</b>
6-months	24 91.90%	24 94.0 %	<b>0.932</b>
<b>P value</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	

**Table 2: Local and Systemic Side-Effects.**

	Bilateral orchidectomy	LHRH (Goserelin)	p-value
Wound infection	7(28%)		
scrotal hematoma	5(20%)		
injection site reaction		2(8%)	
Hot flushes	25(100%)	25(100%)	NA
Loss of libido	25(100%)	25(100%)	NA
Weak erection	25(100%)	25(100%)	NA

The percentage drop in median serum PSA at 1,3 and 6 months for orchidectomy treatment group was 69.40%, 97.50% and 99.20% respectively while for goserelin group, the percentage drop in median serum PSA at 1,3 and 6 months was 68.40%, 96.80%, 98.20% respectively (Table 1).

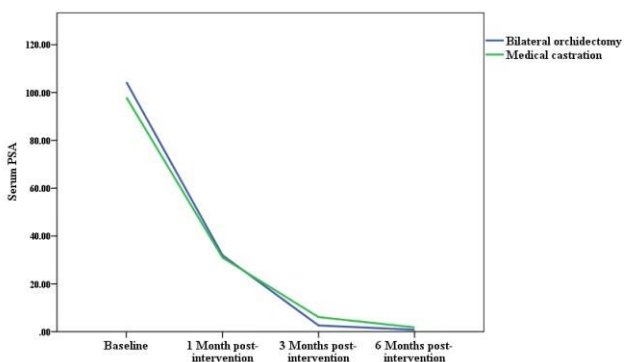
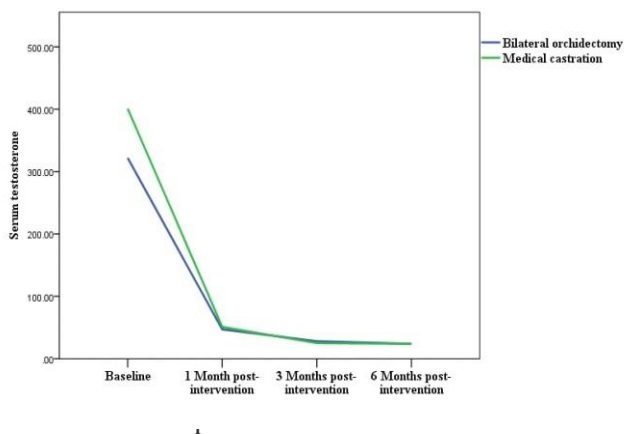
Table 2 shows the local and systemic side-effects following the two treatment modalities. Twenty percent, 28% of the total number that had bilateral orchidectomy developed scrotal hematoma, and surgical site infection respectively while 8% of those that had medical castration developed injection site reaction. All patients in both groups had hot flushes, reduced libido, weak erection as systemic side-effects following ADT.

### Discussion

The goal standard of management of advanced prostate cancer is androgen deprivation therapy. This can be achieved by medical or surgical approach. This study was set out to compare the biochemical efficacies of these two approaches.

The patients recruited into the study for both treatment groups; surgical castration and medical castration had mean age of  $71.72 \pm 7.3$  (years) and  $68.3 \pm 7.3$  (years) respectively. The age group most represented in the study is 60-69 years for both treatment groups. This finding confirmed the disease as of the aging and elderly patients. There is no significant difference in the age groups of patients that had both forms of treatment.

There was significant reduction in serum testosterone for orchidectomy and Goserelin groups within the first one month of treatment (85.4% and 87.30% respectively) and the levels remained progressively reduced below castrate levels in both groups by three and six months following treatment. The median serum levels of testosterone were reduced to 47ng/dl and 51ng/dl at week 4 in the orchidectomy and medical castration groups respectively and remained suppressed in castrate levels over the twenty-six weeks study period. This is similar to the results obtained by Parmar et al<sup>10</sup>, Soloway et al<sup>11</sup> and Vogelzang and colleagues<sup>12</sup> where median serum levels of testosterone were reduced to castrate levels (<50ng/dl) at week 4 in both orchidectomy and Goserelin groups. Serum testosterone remained suppressed for sixty weeks and four years in the studies carried out by Soloway et al<sup>11</sup> and Vogelzang et al<sup>12</sup> respectively. Fontana et al<sup>13</sup> also obtained similar result where he observed that the mean testosterone concentrations were suppressed to the castration range ( $\leq 2$  nmol/l) after 4 weeks of



**Figure 2: Decrease in Serum Psa in Both Treatment Groups.**

treatment with 3-month formulation of Goserelin injection for treatment of advanced PCa and remained suppressed throughout the study period, 108 weeks. In this index study, all patients in both groups attained castrate levels in one month and serum testosterone was monitored over six months period.

Sustenance of castrate levels of testosterone during the study period may possibly be due to short term period of monitoring, patients may develop castrate resistance during long term monitoring period. A fraction of patients may also develop castrate resistance in a short term following ADT as been reported by Oefelin and colleagues<sup>14</sup> where a small but potentially important subgroup of men on three-month depot of LH-RH agonist therapy (Zoladex<sup>®</sup> 10.8mg) for the treatment of advanced PCa failed to achieve a castrate level of testosterone after three months. Possible reason adduced to this was supposed inadequacy of the standard dose of LHRH agonist in these men considering their body-built.

From this study, the percentage rate of drop in serum testosterone was rapid within the first month of treatment and remained sustained till six months in both treatment groups. The rate of drop in serum testosterone is statistically significant in both treatment groups, P value < 0.001 (Table 1) which showed that advanced PCa were hormonal sensitive.

The suppression of gonadal testosterone is the mainstay of treatment of metastatic prostate cancer and is effective in decreasing tumour burden and the serum prostate specific antigen (PSA)<sup>15</sup>. This fact was confirmed in this study where the percentage drop in median serum PSA for orchidectomy and Goserelin groups at 1, 3 and 6 months were 69.4%, 97.5%, 99.2% and 68.4%, 96.8%, 98.2% respectively indicating significant drop in serum PSA. The rate of drop in serum PSA in both groups were statistically significant, P value < 0.001. (Table 1). The obtained result from this study is similar to the one reported by D. Fontana et al<sup>13</sup>, where goserelin acetate 10.8-mg depot was administered every 12 weeks and it provided reliable suppression of testosterone levels and produced a PSA response in the majority (86%) of patients. Mean PSA significantly reduced from 180ng/ml to about 60ng/ml (66% reduction) within 4 weeks and to about 20ng/ml in 3 months (88% reduction) then 10ng/ml in 6 months (94% reduction). Hot flushes, reduced libido and weak erection are the most well recognized systemic adverse effects from ADT and were recorded in all patients in both groups. Scrotal hematoma (20%) and surgical site infection (28%) were recorded in surgical castration and injection site abscess (8%) in medical castration groups.

Kaisary et al<sup>16</sup> reported similar findings: hot flushes, reduced libido and weak erection were 96%, 73%, 84% and 94%, 79%, 85% in medical and surgical castration groups respectively. The percentages of hot flushes reported by Karling et al<sup>17</sup> and Debruyne et al<sup>18</sup> were smaller, 68% and 70% respectively. Possible reason for higher percentages in the index study may be due to small sample size. Therefore, both forms of ADT are efficacious but are associated with systemic and local complication.<sup>19</sup>

## Conclusion

Medical castration (Goserelin) and surgical castration (orchidectomy) are both efficacious in the short term, in the treatment of advanced Pca.

Primary therapy with LHRH analogues (Goserelin) or bilateral orchidectomy led to suppression of serum levels of testosterone to castrate levels within the first month of therapy and also caused significant reduction in serum PSA and this suppression was maintained throughout the six months period of study.

## List of Abbreviations:

**PSA** Prostate Specific Antigen

**Pca** Prostate Cancer

**ADT** Androgen Deprivation Therapy

**LHRH** Luteinising Hormone Releasing Hormone

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