

POST-ORCHIECTOMY ANAEMIA IN PATIENTS WITH ADVANCED CARCINOMA OF THE PROSTATE

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ABSTRACT

Objective: To study postorchietomy anaemia in black Nigerian patients who had bilateral orchietomy for advanced carcinoma of the prostate. Anaemia has been observed in similar studies done on Caucasians and non-black patients in non-tropical environments

Materials And Methods: Consecutive patients with advanced carcinoma of the prostate who were managed by the authors over a four-year period, and who were treated with bilateral orchietomy were prospectively studied. They also satisfied the set criteria for inclusion in the study.

Result: Thirty-six patients were studied. The mean age was 71 years (SD=7.6). Preoperative white blood cell count with blood film examination, and serum urea and creatinine were within normal limits and remained so for the duration of the study. The mean value of the haemoglobin concentration dropped significantly from 11.9g/dl to 10.1g/dl at six months ($p<0.005$). The prostate specific antigen decreased from a mean preoperative value of 62.2ng/ml (SD=58.6) to a mean postoperative nadir of 2.9ng/ml (SD=1.3) after three months.

Conclusion: In Nigerians, there is a statistically significant decrease in the haemoglobin concentration after bilateral orchietomy. This should be closely monitored, and treated when indicated.

Keywords: Post-Orchietomy Anaemia; Advanced Carcinoma of Prostate (*Accepted 27 February 2007*)

INTRODUCTION

Bilateral orchietomy is a major therapeutic option in the management of patients with advanced carcinoma of the prostate and in our environment and centres, it is the main modality available¹. The current therapeutic strategy of newly diagnosed prostate cancer is however dependent on the stage of the disease. While most organ-confined diseases are subjected to radical prostatectomy or brachytherapy, the choice for advanced carcinoma of the prostate is based on androgen manipulation^{2,3}.

The effects of androgen on haematopoiesis have been studied extensively, and normocytic, normochromic anaemia has been found to be associated with androgen deprivation^{2, 4,5}. Various studies have also shown that haemoglobin levels declined in parallel with serum testosterone from normal levels, rising again on return of the serum testosterone to normal values. No associated changes were found in the levels of serum erythropoietin^{2, 5, 6}. In our practice, we observed that

anaemia developed in our patients after bilateral orchietomy for advanced carcinoma of the prostate, such anaemia sometimes being of sufficient severity to warrant blood transfusions. We also noted from the available literature that studies have been done on the anaemia associated with bilateral orchietomy^{4,5}. These studies were done on Caucasians and non-black races. Based on these earlier observations in other environments, clinical settings and racial groups, we decided to study systematically our patients with carcinoma of the prostate who were treated with bilateral orchietomy. This is a report of the observations made on the anaemia associated with bilateral orchietomy for advanced carcinoma of the prostate in tropical sub-Saharan Africa.

MATERIALS AND METHODS

All patients who presented to the authors with advanced carcinoma of the prostate and were treated with bilateral orchietomy were studied. The patients presented between July 1, 2000 and June 30, 2004 at the Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria, and the Macbenson Hospital,

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Onitsha, Nigeria. They were all of the Black African race. Criteria for inclusion in the study were as follows:-

1. Histologically proven carcinoma of the prostate
2. Normal pre-operative (baseline) haemoglobin concentration and white blood cell count including blood film.
3. Normal pre-operative renal function that also remained normal for the duration of the study.
4. Adequate post-operative follow up period of at least six months
5. Evidence of complete response to orchiectomy with no evidence of disease progression during the period of study
6. Absence of radiological evidence of skeletal metastasis
7. Absence of any other explanation for the anaemia e.g haematological disorders.

Thus, the baseline evaluation included a full blood count with a blood film examination, serum urea and creatinine, serum prostate specific antigen, chest x-ray, and x-ray of the lumbo-sacral spine and pelvis. For the purpose of this study, the evaluation of the full blood count was repeated postoperatively every month for three months, and then at six months. Serum urea and creatinine and serum PSA were repeated at least once within the duration of the study, usually between the third and the sixth month. Haemoglobin concentrations were estimated monthly within the preceding 3-6 months before operation. If it was found that the haemoglobin concentration had decreased through one or two succeeding assessments during the period, the patient was excluded from further evaluation for the purpose of this study. Haemoglobin concentration

value below which anaemia is suggested for the ordinary Nigerians is 11gm/dl⁷ and this value was applied in this study. Statistical analysis was done using simple descriptive statistics and the unpaired students 't'-test. Fisher's F-test of differences of variance was always applied before the use of the t-test, and the z-test used if it was significant. Accepted level of significance was p<0.05.

RESULT

Forty-four patients presented during the period, 34 of them at the Nnamdi Azikiwe University Teaching Hospital, and 10 at MacBenson Hospital. Of these only 36 patients satisfied the set criteria and were studied. The mean age of the patients studied was 71.1 (SD=7.6) years, with a median of 71 years, and a range of 56-83 years. The clinical stage of the prostate cancer included 20 patients with T3 (Stage C) and 16 patients with T4 (Stage D). There was no evidence of disease progression during the period of study.

Pre-operative values of the white blood cell count, serum urea and creatinine (Table I) were within the normal limits of 4-11000/mm³, 2-6mmol/litre, and 60-120umol/litre respectively, and they remained within these normal limits for the duration of the study. Blood film studies were normal. The mean prostate specific antigen value decreased from 62.2 (SD=58.6) ng/ml preoperatively to a mean nadir of 2.9(SD=1.3) ng/ml after 3 months. The preoperative range of values was 10.2-226ng/ml with a median of 50ng/ml, and the postoperative range was 1.4-6.7ng/ml with a median of 2.7ng/ml.

Table II shows the postorchiectomy haemoglobin concentrations. From a mean preoperative value of

Table 1: Preoperative White Blood Cell Count, Urea, Creatinine, And PSA Levels In 36 Patients With Advanced Carcinoma of The Prostate.

ESTIMATIONS	PSA		WBC		UREA		CREATININE		
	ng/ml		mm ³		mmol/l		µmol		
	Prp	3mt	Prp	>3mt	Prp	>3mt	Prp	>3mt	
MEAN VALUE	62.18	2.93	6410	6320	4.81	4.60	102.33	98.4	
STANDARD DEVIATION	54.58	1.26	2190	1820	0.92	0.83	13.51	9.8	
MEDIAN	50.00	2.70	5800	6100	4.95	4.72	107	103.2	
RANGE	10.20	1.40	4100-	4200	3.3	2.6	55	73	
	-226	-6.70	10800	-10600	-	6.2	-5.3	118	-110

KEY:

PSA = Prostate Specific Antigen, WBC = White Blood Cell Count, Prp = Preoperative, mt = Month
> = More than

11.9g/dl, the concentration fell to 11.3g/dl at 1 month, 10.9g/dl at 2 months, 10.6g/dl at 3 months and 10.1g/dl at 6 months. The preoperative mean haemoglobin concentration was compared with the under our pre-operative care. postoperative values as shown in Table III.

The preoperative value of the haemoglobin concentration was statistically significantly different from the mean values at each month of evaluation ($P < 0.005$). The mean drop of haemoglobin from the baseline to the end of the study at six months postoperatively was 1.8g/dl.

However, in 21(58.3%) patients, the haemoglobin concentration fell below 11.0gm/dl at some point during the postorchietomy period. In 4 patients, either because of the severity of the anaemia alone (< 7 g/dl) or because of the development of anaemic symptoms (fatigue, dyspnoea, dizziness, loss of appetite inability to concentrate), blood transfusions had to be given during the later course of the study. In all our studied patients, the levels of the haemoglobin concentrations estimated at monthly intervals preoperatively were either stable, or were improved under our pre-operative care.

Table II: Postorchietomy Haemoglobin Concentrations

MONTHS POST-OP	NO OF PATIENTS	MEAN HB (g/dl)	STANDARD DEVIATION	MEDIAN	RANGE
0(Pre-op)	36	11.9	1.3	11.7	11.1-14.7
1	36	11.3	1.1	11.3	9-13.7
2	36	10.9	1.2	10.9	7.6-13.7
3	34	10.6	1.1	10.7	7.9-13.2
6	32	10.1	0.9	10.6	9.2-12.6

Table III: Comparison of Preoperative And Postoperative Haemoglobin Concentrations

COMPARED GROUPS	MEAN DIFFERENCE IN HB CONC. (g/dl)	"t"	p value (P<0.05)
Preoperative vs .1 st month	0.6	2.17	<0.005
Preoperative vs .2 nd month	1.0	3.32	<0.0005
Preoperative vs .3 rd month	1.3	4.85	<0.0005
Preoperative vs .6 rd month	1.8	4.07	<0.0005

DISCUSSION

This study indicates that in our environment, and probably in the Black (Negro) race too, there is a statistically significant decrease in haemoglobin concentration in the patients after bilateral orchietomy for advanced carcinoma of the prostate. In our centres, bilateral orchietomy is the main modality available for the treatment of advanced carcinoma of the prostate.

Potential confounding factors for anaemia in advanced carcinoma of the prostate include bone marrow involvement and the anaemia caused by the burden of chronic diseases. It is to limit these confounders that the patients with evidence of skeletal metastasis were excluded within the facilities available to us. We also ensured that the peripheral blood films were not suggestive of any bone marrow depressing or replacing process, and

that there was response to the orchietomy with no evidence of disease progression during the period of study. In all the cases, the PSA dropped to a nadir by three months and remained so during the period of the study. Renal failure that could be a source of anaemia in such urological patients was excluded in all the patients by the estimation of the serum urea and creatinine levels. We tried to exclude anaemia of chronic diseases and other factors that may cause a coincidental drop in haemoglobin concentration by ensuring a normal preoperative haemoglobin concentration and also proposing exclusion for patients whose monthly preoperative haemoglobin concentrations were observed to have had a decline whatever the cause. However, none of our patients was so excluded.

Our study provides no pathophysiological explanation for the decrease in haemoglobin

concentration but we believe, as has been shown by other studies, that it was due to the androgen deprivation from the bilateral orchiectomy^{2,4,5}. Such anaemia is usually normocytic and normochromic and this was our finding in this study. Similar normocytic and normochromic anaemia have also been demonstrated using monotherapy with LHRH analogues, which achieve similar mode of androgen deprivation as bilateral orchiectomy. Anaemia has however not been found in patients treated with antiandrogen monotherapy, which has a different mode of androgen deprivation¹⁰.

Though we have not evaluated the treatment of such orchiectomy-induced anaemia in our study, we however ensured that before and during the study, all the patients were on iron supplementation therapy. This was to ensure adequate iron stores in the patients, a habit we had developed earlier in our pre-study postorchiectomy patients on observing anaemia in them.

CONCLUSION

The anaemia observed in the patients with advanced carcinoma of the prostate after bilateral orchiectomy in our environment is real and similar to that observed in other races and environments. We advise that patients who have had bilateral orchiectomy should be closely monitored for anaemia. Prompt treatment should be initiated in the patients who develop severe or symptomatic anaemia because of the effects of anaemia on the quality of life

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