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ORIGINAL ARTICLE

Comparison of Neoadjuvant Chemo-Hormonal Therapy Versus Hormonal Therapy in Locally Advanced Prostate Cancer

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ABSTRACT

Background: Prostate cancer cells depend on testosterone to grow and spread. Hormone therapy aims to decrease testosterone levels, either by directly reducing testosterone production or by inhibiting the action of testosterone on cancer cells. It can be used alone or in combination with other treatments like radiotherapy, chemotherapy, immunotherapy and surgery. Chemotherapy uses drugs to destroy cancer cells. Hormone therapy is combined with chemotherapy to offer more effective control of prostate cancer in advanced cases. Early, aggressive treatment approaches such as neoadjuvant hormonal therapy has been explored as a way to improve long-term outcomes in locally advanced prostate cancer.

Objective: To compare the neoadjuvant chemohormonal therapy versus hormonal therapy in locally advanced prostate cancer.

Methodology: This comparative study was conducted at Urology Department, Jinnah Hospital Lahore from 1st July 2022 to 30th September 2023. A total of 200 patients were compared for the outcomes of locally advanced prostate cancer and each group comprised equal number of patients. Group A patients were treated with chemotherapeutic agent docetaxel, dosage 75mg/m2 IV over 1 hour every 3 weeks; prednisone 5mg orally 2 times a day and hormonal agent bicalutamide 50 mg once daily. Group B patients were treated only with hormonal agent bicalutamide 50 mg once daily. The mean therapy time was taken as 3.7 months. The diagnosis was based on the chest and abdomen computed tomography and pelvic magnetic resonance imaging as well as bone scanning. The clinical tumor and nodal staging was based on the magnetic resonance imaging or computed tomography and results were in accordance to the TNM staging classification. Male patients with a confirmed diagnosis of prostate cancer through biopsy, stage pT3b–pT4 disease, ISUP grade ≥4, or a post-prostatectomy prostate specific antigen level ≥0.2 ng/ml were also included. The exclusion criteria included histological subtypes of prostate cancer with small cell neuroendocrine or sarcomatous differentiation, history of prior treatment including prostate surgery, radiotherapy, chemotherapy, or immunotherapy, diagnosis of other malignancies or evidence of disease progression, cases with metastatic changes, hypersenstivity of drugs, immunocompromised, hepatic and renal impaired patients were excluded. The results of both therapies were compared in terms of primary and secondary outcomes.

Results: The mean age of both group patients was almost similar as 67.15±3.1 and 69.1±2.3 year. The mean PSA levels before any intervention was also reported to be insignificantly variant within both groups (52.2±20.5 and 56.5±21.0 ng/ml) respectively. The mean therapy time was taken as 3.7 months. However, within the comparison of pre-treated with post-treatment results, a highly significant improvement in T staging was observed in group A with a substantial decrease from pre-treatment, 50% T3b staging to 36% in post-treatment through neoadjuvant chemohormonal therapy. The post-treatment response presented a significant decrease in the mean testosterone level in group A compared to group B. Further post-treatment, the pathological response grade presented better improvement in group A as compared to group B. The pathological down staging of group A was presented as in 61% cases in comparison to only 35% in group B. The PSA complete response was observed in 67% of group A patients in comparison to 35% in group B. Moreover the comparison of the biochemical recurrence-free survival (bRFS) rate, this study presented a significant increase in survival rate with neoadjuvant chemohormonal therapy than hormonal therapy.

Conclusion: Neoadjuvant chemohormonal therapy is more efficient than hormonal treatment in terms of the biochemical recurrence-free survival rates, improved pathological downstaging outcomes and more substantial prostate specific antigen reduction in patients with locally advanced prostate cancer.

Keywords: Neoadjuvant chemohormonal therapy, Hormonal therapy, Locally advanced prostate cancer, Biochemical recurrence

INTRODUCTION

Radical prostatectomy (RP) and radiotherapy are standard treatment options for selected individuals diagnosed with high-risk, locally advanced prostate cancer. Despite therapeutic advances, these patients remain at a considerable risk of biochemical recurrence (BCR), metastatic disease, and prostate cancer-specific mortality.[1-5]

Although high-risk prostate cancer represents only about 20% of all localized prostate cancer cases, nearly half of these patients eventually experience BCR, and the 15 year cancer-specific mortality rate exceeds 30% following curative-intent treatment. One possible reason for this poor prognosis is the presence of micrometastasis at the time of diagnosis.[6]

Early, aggressive treatment approaches such as neoadjuvant chemohormonal therapy have been explored as a way to improve long-term outcomes in this group. Some studies have assessed the impact of administering chemohormonal therapy prior to RP. Clinical trials investigating neoadjuvant chemohormonal therapy (CHT) have shown benefits such as tumor downstaging, prostate volume reduction, and lower rates of positive surgical margins.[7] However, these benefits have not translated into improved outcomes in terms of biochemical recurrence-free survival (bRFS) or overall survival, leading current European Association of Urology (EAU) guidelines to advise against the routine use of neoadjuvant chemohormonal therapy before RP.[8,9]

While radiotherapy remains a valid treatment alternative for locally advanced disease, but not all patients are suitable candidates such as those with significant comorbidities like systemic scleroderma, systemic lupus erythematosus, patients aged 70 years or more, inflammatory bowel disease, pregnancy, or individuals with a history of pelvic radiation. Additionally, younger patients may derive greater benefit from early surgical intervention.[10] Consequently, there is a pressing need to optimize management strategies for patients for whom surgery is the preferred or only feasible treatment option.

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MATERIAL AND METHODS

This comparative study was conducted at Urology Department, Jinnah Hospital Lahore from 1st July 2022 to 30th September 2023. A total of 200 patients were compared for the outcomes of locally advances prostate cancer and each group comprised equal number of patients. Group A patients were treated with chemotherapeutic agent docetaxel, dosage 75mg/m^2 IV over 1 hour every 3 weeks; prednisone 5mg orally 2 times a day and hormonal agent bicalutamide 50 mg once daily. Group B patients were treated only with hormonal agent bicalutamide 50 mg once daily. The mean therapy time was taken as 3.7 months. Each patient was presented with a written informed consent to sign before their enrolment as a study participant. The sample size was calculated by using sample size calculator available through web. It applied 80% power of test, 95% CI and 5% margin of error. The inclusion criteria were based upon all those patients which were suffering from locally advanced prostate cancer and were screened and clinically diagnosed. The diagnosis was based on the chest and abdomen CT and pelvic MRI as well as bone scanning. The clinical tumor and nodal staging was based on the MRI or CT and results were in accordance to the TNM stagging classification. Male patients with a confirmed diagnosis of prostate cancer through biopsy, stage pT3b–pT4 disease, ISUP grade ≥ 4, or a post-prostatectomy PSA level ≥ 0.2 ng/ml were also included. The exclusion criteria included histological subtypes of prostate cancer with small cell neuroendocrine or sarcomatous differentiation, history of prior treatment including prostate surgery, radiotherapy, chemotherapy, or immunotherapy, diagnosis of other malignancies or evidence of disease progression, cases with metastatic changes, hypersenstivity of drugs, immunocompromised, hepatic and renal impaired patients were excluded. Each patient was completely briefed about the research. The results of both therapies were compared in terms of primary and secondary outcomes related with pathological downstaging of the disease, biochemical recurrence free survival, biochemical response rate, post-treatment prostate size and testosterone level. All the significant variable details including demographical characteristics were recorded. The data was interpreted and analyzed using SPSS version 26.0 where in independent t test was used for comparison between two variables. P value less than 0.05 was considered as significant

RESULTS

The mean age of patients in both groups was almost similar as 67.15±3.1 and 69.1±2.3 years. The mean PSA levels before any intervention was also reported to be insignificantly variant within both groups (52.2±20.5 and 56.5±21.0 ng/ml) respectively. The mean prostate volume before treatment in group A was 55.83ml and 49.20ml in group B. The mean therapy time was taken as 3.7 months (Table 1).

The pre-treatment T staging, N staging and surgical options were categorized within Group A and Group B. The T3b staging, NO staging, ISUP biopsy grade 5 and radical prostatectomy (RP) was considerably higher in Group B than Group A. However, within the comparison of pre-treated with post-treatment results, a highly significant improvement in T staging was observed in Group A with a substantial decrease from pre-treatment, 50% T3b staging to 36% in post-treatment through neoadjuvant chemotherapy (Fig.1).

The post-treatment response presented a significant decrease in the Mean Testosterone level in group A compared to Group B. The median change in prostate volume was also significantly improved in group A (35.20 ml) than group B (41.61 ml) [Table 2].

Further post-treatment, the pathological response grade presented better improvement in group A (52%) as compared to group B (42%). The pathological downstaging of group A was presented as in 61% cases in comparison to only 35% in group B. The PSA complete response was observed in 67% of the group A patients in comparison to 35%in group B patients (Fig. 2).

Moreover the comparison of the biochemical recurrence-free survival (bRFS) rate, this study presented a significant increase in survival rate with neoadjuvant chemohormonal therapy than classical hormonal therapy (Fig. 3).

Table 1: Comparative analysis of age, prostate specific antigen mean levels and volume within group before therapy

Features	Group A (n = 100)	Group B (n = 100)	P value
Age (years)	67.15±3.1	69.1±2.3	0.892
PSA (ng/mL)	52.2±20.5	56.5±21.0	0.857
Prostate (mL)	55.83±11.8	49.20±15.2	0.015
Median therapy time in months (IQR)	3.7 (3.4–4.5)	3.7 (3.4–4.2)	0.827

Table 2: Comparative outcomes of post treatment prostate level and volume

Post-treatment response	Group A (n = 100)	Group B (n = 100)	P value
Mean (IQR) Testosterone (ng/dL)	21.3 (4.51–29.90)	25.94 (13.3-42.9)	0.045
Median change in prostate volume (mL) (IQR)	35.20 (20.32–40.62)	41.61 (35.99–47.51)	< 0.001

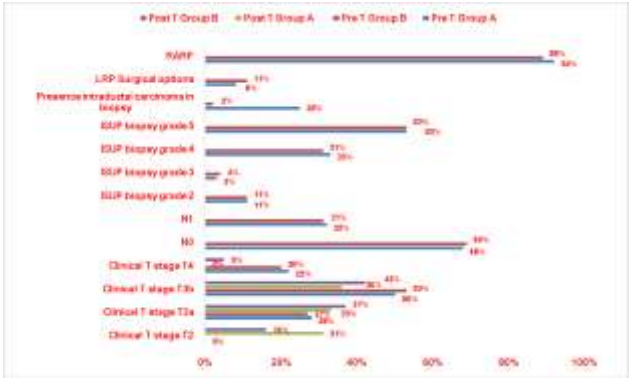

Fig. 1: Outcomes comparison between neoadjuvant and classical hormonal therapy among locally advance prostate cancer patients

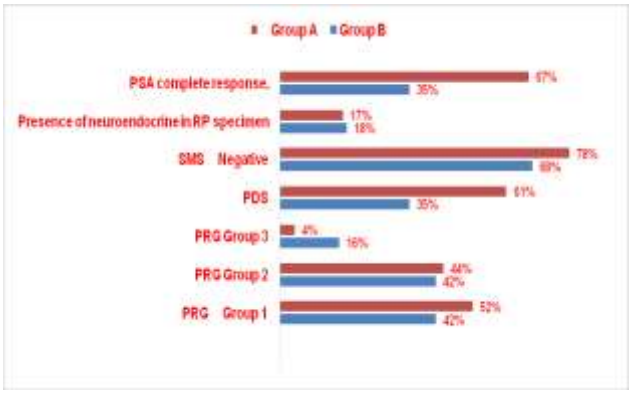

Fig. 2: Comparative outcomes of pathological response grade group, pathological down staging and surgical margin status of group A and B

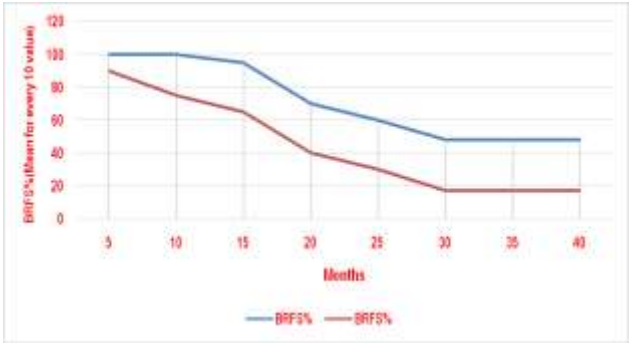

Fig. 3: Comparison of the biochemical recurrence-free survival (bRFS) rate of group A an group B

DISCUSSION

Androgen deprivation therapy (ADT) reduces the production or effects of testosterone which fuel prostate cancer cell growth. First, it is very effective in reducing cancer growth but cancer cells develop resistance. Hormonal therapy does not significantly improve biochemical recurrence-free survival (bRFS) or overall survival in patients with localized or locally advanced prostate cancer.[11] One possible explanation is that residual testosterone continues to activate the androgen receptor (AR) signalling pathway, as traditional hormonal therapies have relatively low binding affinity for the AR. In contrast, newer hormonal agents have been shown to bind the AR with greater affinity.[12] Multiple clinical trials have reported improved pathological outcomes with novel hormonal therapy combined with neoadjuvant chemotherapy.[13,14] Additionally, comparative analysis have shown that neoadjuvant therapy provides greater benefits in terms of biochemical recurrence (BCR) and metastasis-free survival compared to radical prostatectomy (RP) alone.[15]

Notably, these earlier studies used either neoadjuvant androgen deprivation therapy or radical prostatectomy alone as control groups, without including a neoadjuvant CHT group. In contrast, our study used neoadjuvant chemohormonal therapy focusing on pathological response as the primary endpoint. In this study, results showed decrease in pathology and TNM staging in patients, which is lower than what has been observed in previous reports.[16-18] Nonetheless, our findings indicate that the PSA complete response rate was higher in the neoadjuvant chemohormonal therapy group compared to the classic hormonal therapy group. These results suggest that neoadjuvant chemohormonal therapy may yield more favourable pathological outcomes in patients with locally advanced prostate cancer.[19]

The baseline prostate volume was larger in the neoadjuvant chemohormonal therapy group than in the classical hormonal therapy group. This likely reflects a clinical tendency to prefer chemohormonal for patients with larger prostate glands. The post-treatment response presented a significant decrease in the mean testosterone level and the median change in prostate volume was also significantly higher in neoadjuvant chemohormonal group than hormonal group (ADT). In earlier studies, neoadjuvant chemohormonal was associated with greater pathological downstaging, a more substantial reduction in prostate volume, and a deeper decline in PSA levels.[15,20] While we hypothesize that the greater PSA reduction seen with neoadjuvant chemohormonal therapy could be linked to improved biochemical recurrence-free survival.[20]

CONCLUSION

Neoadjuvant chemohormonal therapy is more efficient than hormonal therapy in terms of the biochemical recurrence-free survival rates, improved pathological downstaging outcomes and more substantial prostate specific antigen reduction in patients with locally advanced prostate cancer.

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