Can Subepididymal Orchiectomy Re-emerge as the Treatment of Choice in Patients with Advanced Prostatic Carcinoma?

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Abstract To study the effectiveness of bilateral subepididymal orchiectomy compared to bilateral simple and subcapsular orchiectomy in terms of androgen ablation, control of disease progression and esthetic superiority. 114 patients of advanced prostatic carcinoma (T3, T4, M1) were randomized to 3 groups- Group A: bilateral simple orchiectomy (38 patients), Group B: bilateral subcapsular orchiectomy (38 patients), & Group C: bilateral subepididymal orchiectomy (38 patients). Serum PSA and serum testosterone values were checked pre-operatively and at 3 months follow-up. Patients' esthetic satisfaction was scored on a quality of life scale of 1–5. In Groups A, B and C, at 3 months the post-operative mean serum testosterone values were 34.7, 38.1 and 36.7 ng/dl ($p=0.0524$); and mean serum PSA values were 4.2, 3.9 and 3.4 ng/ml ($p=0.09$) respectively, the differences not being statistically significant. On esthetic satisfaction scale the average scores were 1.8, 2.7 and 4.0 respectively, the difference being highly significant ($p<0.0001$). Subepididymal orchiectomy maintains esthetic appearance of scrotum and provides superior patient satisfaction as compared to standard total and subcapsular orchiectomy, while achieving equal efficacy. Bilateral sub-epididymal orchiectomy may thus be considered procedure of choice to achieve androgen ablation in advanced prostatic carcinoma.

Keywords Epididymis · Orchiectomy · Prostatic neoplasms · Testis

Introduction

Castration has been the treatment of choice for androgen ablation in advanced prostate cancer since Huggins and Hodges published their Nobel Prize winning article in 1941 [1, 2]. However, in recent years LHRH analogues have come into widespread use because of patients' fear of surgery and negative psychological impact associated with bilateral orchiectomy, and possibly also due to the marketing drive of pharmaceutical companies [3].

Sub-epididymal orchiectomy is an option of surgical castration, which is as effective as total orchiectomy and sub-capsular orchiectomy in terms of androgen ablation and control of disease progression in patients with advanced prostatic carcinoma, while simultaneously maintaining the cosmetic appearance of the scrotum. In the present study, we have compared sub-epididymal orchiectomy with total orchiectomy and sub-capsular orchiectomy in terms of degree of androgen ablation (serum testosterone), control of disease progression (serum PSA) and esthetic superiority (patient satisfaction).

Materials and Methods

This prospective randomized study included advanced prostatic carcinoma (T3, T4 or any T with bony metastases). From June 2000 to May 2010, 114 patients were randomized into three groups: group A: bilateral simple (total) orchiectomy (38 patients), group B: bilateral sub-capsular orchiectomy (38 patients) and group C: bilateral sub-epididymal orchiectomy with epididymoplasty (38 patients)

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(Fig. 1). The study was conducted after obtaining the institute review board approval, and randomization was done using a systematic sampling technique. The methodology followed was as per the CONSORT statement.

Pre-operative estimation of serum PSA and serum testosterone were done in each patient. All procedures were done on out-patient basis using local anesthesia in the form of spermatic cord block with 2 % lignocaine, under perioperative antibiotic cover. Analgesia in the form of oral diclofenac was given as and when required. At 3 months follow-up, the values of serum PSA and serum testosterone were re-estimated. Each patient was also asked to rate his esthetic satisfaction score on a scale of 1–5. (1 – very unsatisfied, 2 – unsatisfied, 3 – no difference, 4 – satisfied, 5 – happy)

The pre-operative and post-operative values of serum testosterone and serum PSA among the three groups were compared using the ANOVA parametric method. Kruskal Wallis and Dunn's multiple comparison tests were applied to compare the patient satisfaction score. The software used for statistical analysis was InStat 3 (Graph Pad Software Inc., San Diego).

Results

The mean age of patients in groups A, B and C was 73.3, 76.4 and 72.2 years, respectively. The mean pre-operative serum testosterone values were 688.3 ± 50 , 710.2 ± 43.5 and

Fig. 1 Sub-epididymal orchidectomy—operative steps

701.8±48.9 ng/dl, respectively. The mean pre-operative serum PSA values were 25.4±6.5, 27.5±5.9 and 28.4±5.7 ng/ml, respectively. The mean operative time in groups A, B and C was 45, 56 and 51 min, respectively. No statistically significant difference among the three groups was found in any of these parameters ($p>0.05$).

There was no significant difference in post-operative analgesia requirements ($p>0.05$). There were no significant immediate or delayed complications in any of the patients.

In follow-up, the mean post-operative serum testosterone values at 3 months in each group was in the castrate range (<50 ng/dl) and were comparable to each other (Fig. 2). The mean serum PSA values at 3 months in all three groups were comparable (Fig. 3) with no significant difference ($p=0.09$). Thus, there was no statistically significant difference among the three groups in terms of androgen ablation and control of disease progression.

Figure 4 presents the patient satisfaction score in each group. The mean score for group C was the highest (4.0), followed by group B (2.7), and was the least for group A (1.8) (Kruskal Wallis test, $p<0.0001$). With Dunn's multiple comparison test, the following p values were obtained: group A vs. group B, $p<0.05$; group A vs. group C, $p<0.001$; group B vs. group C, $p<0.001$. Thus, the difference among the three groups is highly significant.

Discussion

In advanced prostatic carcinoma, palliative hormone therapy in the form of androgen ablation is the best treatment option. Surgical castration in the form of bilateral orchiectomy is a time-tested way to provide palliation to patients with advanced prostatic carcinoma. However, in recent years there has been a trend to shift away from this procedure because of compromised esthetics and negative psychological effects of an 'empty scrotum'.

Fig. 2 Serum testosterone values (ng/dl)

Fig. 3 Serum PSA values (ng/ml)

The choice of medical castration has shifted over a period of time from estrogens to anti-androgens and now to LHRH analogues. In recent years, LHRH analogues have become the most popular choice; with estimates that 70 % would choose the medical option in patient preference studies [4]. It is obvious that cosmetic expectation has a major role in influencing patient choice.

However, the biggest drawback of the use of LHRH analogues is the high cost along with the long duration of treatment. These drugs amount to 40 % of annual revenues of community urology practice in United States [3]. It has been found that on life-time basis estimates, treatment with LHRH analogues is 13–20 times costlier than the one-time surgical orchiectomy procedure. For an individual patient, the cost of LHRH agonist treatment surpasses the cost of surgery at less than 4.2 to 5.3 months and for combined androgen blockade at less than 2.7 to 3.4 months [5]. In 1995, Medicare was billed \$480 million for LHRH agonists [6].

Besides hot flushes and sexual dysfunction, a higher incidence of breast swelling with LHRH analogues compared to orchiectomy has also been reported (24.9 % vs. 9.7 %) [7]. In addition, contrary to popular belief, LHRH agonist therapy significantly decreases the testicular weight. Issa et al. have shown that the mean weight of the testis was 7 g in patients receiving LHRH agonists compared to 15 g in patients who

Fig. 4 Satisfaction score (scale of 1–5)

did not receive LHRH agonists [8]. Issa et al. have also reported that LHRH agonist therapy failed to achieve castrate levels of testosterone in 28 % patients [9]. Finally, treatment with LHRH agonists has a significant psychological impact on the patients as it is a regular reminder of the disease.

The option of surgical castration has been exercised mostly in form of bilateral simple orchiectomy. This one-time procedure, in objective terms, may be superior to any medical therapy in terms of cost, efficacy, compliance and side effects. In 1942, Riba pioneered sub-capsular orchiectomy, a procedure that involved the removal of testicular parenchyma and the simple closure of the tunica albuginea [10]. Controversy began when cells similar to Leydig cells were found in tunica albuginea after sub-capsular orchiectomy [11]. Though several studies have shown that the fear of incomplete removal of testicular tissue and reactivation of eventually remaining Leydig cells after sub-capsular orchiectomy is ill-founded [12, 13], the sub-capsular technique has somehow not found much favor with majority of urologists. The procedure also suffers from the disadvantage of reduced testicular size from the patient's point of view.

Autologous tunica vaginalis grafts with sub-capsular orchiectomy [14] have been tried to give good volume to the testis but have been tedious to perform and associated with poor patient satisfaction. Among the other modifications used are intracapsular fibrofatty tissue grafts, polytetrafluoroethylene paste or testicular prosthesis to simulate the appearance of normal testis [15–17]. For the most part, these modifications are cumbersome and have not gained sufficient popularity and acceptance in the urological community.

The technique of sub-epididymal orchiectomy with epididymoplasty was introduced for good esthetics of the scrotum and higher patient satisfaction [18]. It was found to be a simple and safe procedure easily done as an out-patient procedure under local spermatic block without any significant morbidity. As would be expected, it provides satisfactory androgen ablation comparable to total orchiectomy [9].

In our study, we have found that sub-epididymal orchiectomy with epididymoplasty is as effective as total orchiectomy and sub-capsular orchiectomy in terms of reducing the serum testosterone values to pre-pubertal values (<50 ng/dl). The post-operative values of serum PSA are also comparable among the three groups, as would be expected, thus effectively controlling the disease.

On the front of patient satisfaction, sub-epididymal orchiectomy with epididymoplasty clearly outscored the other techniques with a mean satisfaction score of 4.0 vs. 2.7 for bilateral sub-capsular orchiectomy and 1.8 for bilateral total orchiectomy. This procedure overcomes the main objection to total orchiectomy, i.e. negative psychological impact of 'empty scrotum', which has led the trend away from orchiectomy. Thus, it has the potential to re-emerge as a one-time surgical

alternative to hormone therapy as the first choice of treatment in advanced carcinoma prostate.

Conclusion

With this prospective randomized study, we conclude that bilateral sub-epididymal orchiectomy is as effective as its total and sub-capsular counterparts in terms of achieving castration. It clearly stands out in terms of the highest patient satisfaction score by avoiding the negative psychological impact of empty scrotum.

Thus, it seems timely that urologists should reconsider the one-time procedure of orchiectomy as the gold standard for androgen deprivation therapy, using bilateral sub-epididymal orchiectomy to achieve androgen ablation in advanced prostatic carcinoma.

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