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Research Paper

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Medical Management of Post Menopausal Stress Urinary Incontinence

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ABSTRACT

Objectives: To compare the efficacy of pelvic exercises, vaginal estrogen and Duloxetine in the management of post menopausal stress incontinence.

Methods: The study was conducted on 160 post menopausal patients with confirmed stress incontinence who were randomly divided into 4 groups of 40 patients each. Group A served as control, B treated with pelvic exercises, C with estrogen and exercises and D with Duloxetine. These groups were compared using appropriate statistical tools in regard to subjective and objective assessment for improvement of symptoms.

Results: Pelvic exercises did not result in subjective improvement (p=0.15) but objective improvement was significant (p=0.0001). Pelvic exercises with estrogen produced both subjective and objective improvement (p=0.0001). Duloxetine produced highly significant subjective and objective improvement (p=0.0001).

Study conducted at: Department of Obstetrics and Gynecology, Artemis Health Institute, Gurgaon, Haryana, India from June 2010 to December 2011.

CONCLUSION: Pelvic exercises and Duloxetine produced statistically significant improvement in stress incontinence while estrogen did not.

INTRODUCTION:-

The International Continence Society has defined urinary incontinence as "the complaint of any involuntary leakage of urine"[1]. If the leakage is distressing to the patient, evaluation and treatment should be offered. Incontinence can almost always be improved and frequently can be cured, often using relatively simple, nonsurgical interventions. Stress urinary incontinence occurs during period of increased intra-abdominal pressure for example sneezing, coughing or exercise, when the intra-vesical pressure rises above the urethral closure pressure. Stress urinary incontinence is the most common form of urinary incontinence in women[2]. It occurs essentially due to pelvic floor muscle weakness. Physical changes resulting from pregnancy, childbirth & menopause often cause stress incontinence[3].

The pelvic floor muscles wrap around the underside of the bladder and rectum and help in urinary continence. **Strengthening the pelvic floor muscles is a good (painless and free) first step treatment for stress incontinence[4].**

5-HT receptor blockers and 5-HT reuptake inhibitors are important compounds in the pharmacologic treatment of detrusor hyperactivity and urinary incontinence[5]. Duloxetine has been demonstrated to modulate bladder function through selective inhibition of both 5-HT and norepinephrine receptor sites[6].

The bladder trigone, urethra and pelvic floor muscles display estrogen receptors similar to vaginal tissue. Urethral pressure profilometry shows increased maximum urethral pressures and symptomatic improvement when conjugated estrogens are given. Based on the biological rationale, it was thought that estrogen could effectively treat urinary incontinence given the presence of estrogen receptors in the bladder, urethra and levator ani.

This study was conducted to determine and compare the efficacy of pelvic floor muscle exercises, vaginal estrogen and that of Duloxetine in the management of post menopausal stress urinary incontinence.

METHODS:-

The study was conducted on the patients attending outdoor clinic in the Department of Obstetrics and Gynecology, Artemis Health Institute from June 2010 to December 2011. All those postmenopausal women, who complained of stress incontinence, were evaluated in detail regarding their symptoms, precipitating factors (coughing, straining), stress test and detailed voiding diary which they were explained and asked to maintain for 3 days. As such, 160 patients with confirmed stress urinary incontinence were selected for the study. These patients were randomly divided into 4 groups of 40 patients each.

Group A:- 40 patients served as control in our study as they were given placebo treatment in the form of calcium tablet 1twice daily.

Group B:- 40 patients were taught the pelvic floor muscle exercises and were asked to perform 20-25 such contractions 5-6 times a day.

Group C:- 40 patients of group C were asked to apply vaginal estrogen cream at bed time in addition to the pelvic floor muscle exercises as in the group B.

Group D:- 40 patients of group D were treated with Tab Duloxitine 40 mg 1 twice daily.

The patients were followed up regularly and results were observed. They were called for follow up after 3 months. At that time, they were compared regarding the satisfaction and subjective perception of improvement in their problem, objective improvement in their problem by comparing their pre- and post-treatment voiding diaries, drop- out rates as well as the side effects experienced by them.

Results:-

Table 1 shows the treatment satisfaction and subjective perception of improvement in the different groups.

Table 2 shows the objective improvement in the patients' voiding diaries.

Table 3 shows the frequency of side effects in the different groups.

Table 4 shows the statistical differences in different groups.

Table 5 shows the results of logistic regression analysis and

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odds ratio in favor of improvement in different groups as compared to control group.

Discussion:-

The study was conducted to evaluate the relative efficacies of different medical modalities of treatment for post menopausal stress urinary incontinence.

In spite of regular contact, in first follow up visit after 3 months, 25% patients in the Group A (control group) failed to report, the group that had maximum drop-out rate. This appears to be because of inability to gain any benefit from the treatment that was offered to them. Drop-out rate was also 20% in the Duloxetine treated group which was chiefly because of the high cost of treatment as was reported by the patients.

When these patients were asked about the subjective perception of improvement in their problem of incontinence and treatment satisfaction, maximum response was noted in the Duloxetine treated group (62.5%). The satisfaction in the patients treated with pelvic floor exercises alone was only 6.7% which was not significantly different from the control group (p= 0.15). However, addition of vaginal estradiol to the pelvic floor exercises resulted in significant improvement in the patients perception of problem as compared to pelvic exercises alone(p= 0.0126).

However, when the patients' outcome was objectively compared using their pre- and post-treatment voiding diaries, it was found that although all the groups had significant improvement as compared to placebo, addition of vaginal estrogen to the pelvic floor muscle exercises did not result in any significant improvement over pelvic floor exercise group alone, p value being 1. This signifies that although addition of estrogen to the PFME group significantly increases the amount of satisfaction in the patients, this difference is not reflected in their true improvement of problem in the form of number of incontinent episodes in their voiding diary. Similar result was found in the study of Jackson et al[7]. In fact, sometimes oral hormone administration increased rates of urinary incontinence and transdermal or vaginal estrogen results in inconsistent improvement of urinary incontinence as was found in the studies of Shamiliyan et al[8].

Our study showed that Duloxetine resulted in extremely significant improvement in patients symptoms and voiding diary as compared to placebo (p=0.0001). Also, there was high rate of satisfaction and subjective improvement of problem among users of Duloxetine. Norton PA et al[9] also found similar results.

The most important finding was that pelvic floor exercises are a very effective mode of treatment in patients with post menopausal stress urinary incontinence with 57.6% patients showing improved voiding diary. However, patients' satisfaction rates are found to be lower, which may be because the patients usually give more importance to the pharmacological modality of treatment rather that simple life style modifications and exercises. But if these patients are counselled in detail regarding the utility and importance of pelvic floor exercises and explained exactly how and how often to perform it, it may prove to be a priceless and highly effective first line therapy for stress incontinence.

During the follow up of these patients, we also studied the side effects experienced by them. Two patients in the group treated by pelvic floor muscle exercises reported that they felt extreme weakness and fatigue, and found it difficult to perform exercises at correct frequency. Among the patients treated with vaginal estradiol, 9 patients reported adverse effects (25.7%), 7 of them experienced irregular vaginal bleeding and 2 patient experienced hot flushes like symptom. In the fourth group, where patients were treated with Duloxetine, side effects were most frequent. Eleven patients out of 32 (34.3%) reported adverse effects most commonly nausea, dry mouth, fatigue and somnolence.

It is thus concluded that pelvic floor exercises alone did not result in statistically significant improvement in patients' subjective problem (p=0.15) but objective improvement was extremely significant as compared to control (p=0.0001). These findings correspond with the findings of Choi H et al[10]. When pelvic floor exercises were combined with estrogen, both subjective (p=0.0001) and objective (p=0.0001) improvement in patients' problem was extremely significant. Duloxetine also resulted in extremely significant improvement both subjectively and objectively (p=0.0001). Addition of estrogen to pelvic floor exercises resulted in significant subjective improvement in patients' symptoms (p=0.01) although the objective difference was statistically not significant (p=1). This was in accordance with the study of Hendrix SL et al[11]. Subjective improvement in Duloxetine treated group was very significant as compared to pelvic floor exercises group (p=0.01), while objective improvement was not statistically significant (p=0.30). Difference between Duloxetine and combined exercise and estrogen group was not significant both subjectively (p=0.46) as well as objectively (p=0.31).

In addition, logistic regression analysis has also been performed with assessment, both subjective and objective as response variable and different groups as indicator variables. Odds ratio has been calculated. It is found that pelvic floor exercises alone result in at least 4 times improvement in patients' symptoms as compared to control when objective assessment was made, but improvement when subjective assessment was made was statistically not significant. Addition of estrogen to exercises results in same 4 times improvement in patients' symptoms when assessed objectively, as is also found in the studies of Steinuer JE et al[12] but its addition also resulted in 3 times improvement in patients' subjective assessment as well. Duloxetine treatment produces at least 4 times improvement in problem when assessed subjectively and 8 times improvement in problem when assessed objectively. These findings correspond to the findings of Cardozo et al[13].

Conclusion:-

Important conclusion of our study are that pelvic floor exercises result in improvement in patients' subjective perception of problem but statistical significance could not be established, which is likely to be due to inadequate counselling of patients, but when this is assessed objectively, pelvic exercises result in highly significant improvement. Addition of estrogen does not give any added benefit in stress incontinence when assessed objectively. Duloxetine results in highly significant improvement when assessed both objectively as well as subjectively.

Table 1

Patient satisfaction and subjective perception of improvement in their problem as compared to control group

Group	Total patients	Subjective improvement in the problem	Percentage	Significance of difference as compared with control "p"
A	30	2	6.7%	-
B	33	7	21.2%	0.15N.S.
C	35	18	51.4%	0.0001 **
D	32	20	62.5%	0.0001 **

**highly significant

Table 2

Outcome of patients on the basis of their pre- and post-treatment voiding diary as compared to control group

Group	Total no of patients	>50% improvement in voiding diary	Perceatage	Significance of difference as compared with control "p"
A	30	1	3.3%	-
B	33	19	57.6%	0.0001**
C	35	20	57.1%	0.0001**
D	32	23	71.8%	0.0001**

**highly significant

Table 3

Side-effects experienced in different groups

Group	Total no of patients	No of patients experiencing noticeable side effects							Percentage
		nausea	Fatigue	Bleeding per vaginum	Hot flushes	Dry mouth	somnolence	Total	
A	30	1	-	-	-	-	-	1	3.3%
B	33	-	2	-	-	-	-	2	6.1%
C	35	-	-	7	2	-	-	9	25.7%
D	32	4	1	-	-	3	3	11	34.3%

Table 4

Table 4

Statistical analysis of differences in various groups

Groups compared	Significance of difference in subjective improvement "p"	Significance of difference in objective improvement "p"
PFME vs Control	0.15 N.S.	0.0001**
PFME+Estrogen vs Control	0.0001**	0.0001**
Duloxetine vs Control	0.0001**	0.0001**
PFME vs PFME+Estrogen	0.01*	1.00 N.S.
PFME vs Duloxetine	0.001**	0.30 N.S.
PFME+Estrogen vs Duloxetine	0.46 N.S.	0.31 N.S.

*significant

Table 5

Logistic regression analysis to compare improvement in various groups as compared to control (placebo)

Groups	Subjective improvement			Objective improvement		
	Odds ratio	Significance "p"	95% C.I.	Odds ratio	Significance "p"	95% C.I.
PFME	3.77	0.15N.S.	-	40.00	0.0001	4.78-333.3
PFME + Estrogen	14.93	0.0001	3.05-71.43	38.46	0.0001	4.72-333.3
Duloxetine	23.26	0.0001	4.69-111.11	76.92	0.0001	8.77-500

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