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Efficacy of Tibolone and Isoflavones in the Management of Postmenopausal Symptoms

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Abstract:

Background: After the recent publication of results from two large prospective studies, Women's Health Initiativeand Heart and Estrogen/ Progestin Replacement Therapy (HERS) indicating increased risk with hormone replacement therapy (HRT) for menopausal symptoms, HRT is no longer recommended for asymptomatic postmenopausal women. Tibolone has emerged as an attractive alternative for treatment of perimenopausal women. Interest in the use of Isoflavones, the most common from of phytoestrogens for treatment of menopausal symptoms has been encouraged by observation of lower prevalence of menopausal symptoms.The present study attempts to evaluate the efficacy and side effects of tibolone and isoflavone in the treatment of menopausal symptoms.

Methods: This prospective comparative study assessed the usefulness of tibolone and isoflavone for the management of menopausal symptoms among 80 postmenopausal symptoms .The patients were asked about symptomatic improvements ; detailed physical examination were carried out ; TVS and lipid profile were done initially and at 1 , 6 and 12 months.

Result : Improvement in vasomotor , genitourinary symptoms and joint pain were significantly higher in tibolone group in comparison to isoflavone in most of the follow up visits and after the completion of treatment.Blood pressure records did not show any change with the use of both the drugs over 12 months. Incidence of breakthrough bleeding was nil in isoflavone and nominal in tibolone group . No significant adverse effect on lipid profile was found in both the groups .

Conclusion: Efficacy of tibolone was found to be significantly better than the isoflavones in management of postmenopausal symptoms.

Keywords : Tibolone , Isoflavone , Postmenopausal symptoms

I. INTRODUCTION

The world population is not only growing but also graying. So maintenance of peri and postmenopausal health is of paramount importance to minimize the economic impact on our society . Due to fear and dislike of adverse effects, as well as possible long term risk of HRT, there is increasing interest in effective & safe alternatives to HRT for menopausal problems. Tibolone, a synthetic steroid, represents an advance in hormone replacement therapy, offering an attractive option for treatment of menopausal women. On the other hand, plant derived substances structurally related to estrogens that have been shown to bind to estrogen receptors, commonly termed phytoestrogens are currently used by many women as alternatives to HRT . Of this isoflavones, the most common from of phytoestrogens, primarily found in soy beans and their by products are most widely used and studied class. The specific objectives of the stud**y** are to evaluate the efficacy of tibolone and isoflavones in the management of postmenopausal symptoms, in relation to alleviation of symptoms and side effects

II. MATERIALS AND METHODS

A total of 80 postmenopausal women seeking help for relief of menopausal symptoms were recruited for this prospective comparative study between tibolone (2.5 mg) and isoflavones (100 mg) in the department of Obstetrics and Gynecology, National medical college and hospital, Kolkata, between June 2009 to September 2010. Ten women from tibolone and 7 women from isoflavone group were lost during follow up and foregoing description and analysis pertains to 30 and 33 women from the respective groups. Patient were advised to come for follow up at 1 month, 6 month and 12 months after initiation of therapy. Patient were enquired about symptomatic improvement

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(vasomotor symptoms, urinary symptoms, vaginal symptoms and joint pain) ; a detailed physical examination was performed in each visit. Fasting lipid profile and transvaginal sonography were performed initially and after six month and twelve month. Statisrical analysis was performed using SPSS for windows, Student t test and chi squere test were used wherever appropriate. A p value of < 0.05 was taken as statistically significant.

III. RESULT AND ANALYSIS

Table1. *Effect of Treatment on Vasomotor Symptoms*

	Response	after 1 month		Response	after 6 months		Response	after 12 months		Response	
	Complete	Partial	Nil	Complete	Partial	Nil	Complete	Partial	Nil	Overall improvement	Nil
Tibolone (N=26)	10(38.46 %)	13(50 %)	3(11.54 %)	16(61.54 %)	9(34.64 %)	1(3.85 %)	17(65.38 %)	8(30%)	1(3.85 %)	25(95%)	1(3.85%)
Isoflavones (N=25)	0	10(40 %)	15(60%)	0(0%)	15(50%)	10(40%)	2(8%)	15(60%)	8(28%)	17(68%)	8(28%)
Statistical analysis							X^2(Yates corrected) =15.55 , p=.00007 89	Significa nt		X^2(Yates corrected) =5.15, p=0.0232 degree of freedom=1	Significa nt

Table2. *Effect of Treatment on Genital Symptoms*

	Respon se	after 1 month		Respons e	after 6 month		Respo nse	after 12 month		Response	
	Comple te	Partial	Nil	Complet e	Partial	Nil	Compl ete	Partial	Nil	Overall improvement	Nil
Tibolone (N=26)	I (7.14%)	7(50%)	6(42.86%)	6(42.86 %)	6(42.86 %)	2(14.2 9%)	8(57.1 4)	4(28.57)	2(14.29)	12(85.71%)	2(14.29%)
Isoflavo nes (N=25)	0	2(14.29 %)	12(85.71 %)	0	3(21.43 %)	11(78. 67%)	0	3(21.43 %)	11(78.6 7%)	3(21.43%)	11(78%)
Statistica l analysis					Significa nt		Signifi cant			X^2=9.19, p=.00243 Degree of freedom=1	Significant

Table3. *Effect of Treatment on Urinary Symptoms*

	Response	after 1 month		Respons e	after 6 month		Response	after 12 month		Response	
	Complet e	Partial	Nil	Complet e	Partial	Nil	Complet e	Partial	Nil	Overall improvement	Nil
Tibolone (N=26)	1(12.5%)	3(37.5%)	4(50%)	2(25%)	4(50%)	2(25%)	3(37.5%)	3(37.5%)	2(25 %)	6(75%)	2(25%)
Isoflavone s (N=25)	0	2(16.66%)	10(83.33%)	0	3(25%)	9(75%)	0	3(25%)	9(75 %)	3(25%)	9(75%)
Statistical analysis		Significant			Significan t			Significan t		x^2(Yates corrected) = 3.04, p=.081 Degree of freedom=1	Significa nt

Table4. *Effect of Treatment on Joint Pain*

	Response	after 1 month		Response	after 6 month		Response	after 12 month		Response	
	Complete	Partial	Nil	Complete	Partial	Nil	Complete	Partial	Nil	Overall improvement	Nil
Tibolone (N=26)	0	2(25%)	6(75%)	2(25%)	3(37.5%)	3(37.5%)	4(50%)	3(37.5%)	1(12.5%)	7(87.5%)	1(12.5%)
Isoflavones (N=25)	0	0	8(100%)	0	2(25%)	6(75%)	0	2(25%)	6(75%)	2(25%)	6(75%)
Statistical analysis										X^2(Yates corrected) =4.06, p=.0438 degree of freedom=1	Significant

Table5. *Side Effects of Tibolone and Isoflavone*

Complaints	Tibolone (N=30)	Isoflavone(N=33)
Gastrointestinal upset	4(13.3%)	6(18.18%)
Weight gain	2(6.66%)	Nil
Breast complaints	Nil	Nil
Vaginal bleeding(after 12 month)	2(14.3%)	Nil

Table6. *effect on BP after 12 month of treatment*

	Response	Tibolone	Isoflavone
Systolic BP	Pre treatment	123.26±12.11	124.72±11.7
	Post treatment	124.2±11.13	125.45±10.35
	Statistical difference	t =0.31[DF=58], p=0.75 Non significant	t= 0.78 [DF= 64], t=0.27 Non significant
Diastolic BP	Pre treatment	78.46±10.09	80.06±9.23
	Post treatment	79.6±10.1	80.55±7.60
	statistical difference	t= 1.39[DF= 88], p=0.17 Non significant	t= 0.24[DF=64], p=0.82 Non significant

Table7. *Incidence of Breakthrough Bleeding*

Duration of treatment	Tibolone (N=14)	Isoflavone (N=16)
1 month	7(50%)	2(12.5%)
6 month	3(21%)	0
12 month	2(14.3%)	0

Table8. *Change in Endometrial Thickness (Mm)*

Duration of treatment	Tibolone (N=14)	Isoflavone (N=16)
At recruitment	3.25±.89	3.16±.73
After one year	3.4±.49	3.11±.53
Statistical difference	t=0.55[DF=26], p=0.55 Non significant	t= 0.22[DF=30], p= 0.83 Non significant

Table9. *Alteration in Lipid Parameters*

Lipid parameters	Tibolone		Isoflavones	
	Baseline	After 12 month	Baseline	After 12 month
Total cholesterol	169.63±26.12	149±23.01	147.12±21.53	146.12±18.84
	t= 3.25 [DF=58], p= 0.002 Significant change		t=0.20 [DF 64], p= 0.84 Non significant change	
HDL cholesterol	51.53±11.25	35.86±6.52	50.3±6.96	52.12±5.63
	t= 6.60 [DF= 9.58], p= 0.004 significant change		t= 1.17 [DF= 64], p= 0.2 Non significant change	
LDL cholesterol	88.03±21.03	88.5±21.18	91.69±11.42	88.39±12.79
	t= 0.09 [DF= 58], p=0.9 Non significant change		t=1.11 [DF=64], p=0.273 Non significant change	
Triglycerides	148.73±24.54	115.71±21.62	147.12±21.53	146.29±18.84
	p= < .001 Significant change		t= 0.17 [DF= 64], p=0.8 Non significant change	

Overall improvement in vasomotor symptoms was significantly higher in tibolone group in all follow up visits and after the completion of treatment. Also complete relief of vasomotor symptoms was significantly higher number in tibolone group compared to isoflavones group. Tibolone was a better drug to relieve the genitourinary symptoms compared to isoflavones. But continued and sustained use of tibolone was required to achieve symptomatic relief. Effect of isoflavones was very mild in genitourinary symptoms and no women had complete relief of symptoms. Very few patients had symptomatic improvement in joint pain after 1month in tibolone group. But with continued and sustained use, a significant proportion of patient reported relief of symptoms. In isoflavones group, effect was very mild. Only 2 patient reported partial improvement in joint pain.

Blood pressure records did not show any changes with the use of any of the drug(s) over 12 month. 2 patients had vaginal spotting with in 1 month of initiation of therapy. No Women on isoflavones had lesser incidence of breakthrough bleeding. Only recurrence of bleeding was noticed in those 2 women and endometrial thickness also was <5mm. On the other hand incidence of breakthrough bleeding was higher in tibolone group (50% in first month, 21% in 6 month and 14.3% in 12 month). But on continued use incidence became less and very few recurrence of bleeding was found. No patient had endometrial thickness >5mm with breakthrough bleeding in tibolone group.No significant difference was found in endometrial thickness after 12 month from the initial thickness in both groups. Women using tibolone showed significant decrease in triglyceride (22.44± 3.9% from baseline) and total cholesterol (11.28±4.81% from the baseline) and decrease in HDL cholesterol (30.67± 5.25%). But no significant change was found in LDL cholesterol in tibolone group. In isoflavones group, no significant change in lipid profile was found.

IV. CONCLUSION

In the present comparative study, efficacy of tibolone was found to be significantly better than the isoflavones in alleviation of postmenopausal symptoms. Tibolone can be considered as an effective alternative to conventional hormone replacement therapy. On the other hand iso flavones have modest effect on vasomotor symptoms and very minimal effect on other postmenopausal symptoms.

REFERENCES

[1] Hammer M, Christau S, Nathorst-Boos J, Rud T, Garre K, A double blinded, randomized trial comparing the effects of tibolone and continuous combined hormone replacement therapy in postmenopausal women with menopausal symptoms, Br J Obstet Gynecol 105:904,1998.

[2] AL-Azzawi F, Wahab M, Habiba M, Akkad A, Mason T, Continuous combined hormone replacement therapy compared with tibolone, Obstet Gynecol 93:258, 1999.

[3] Laan E, Van Lunsen RHW, Everaerd W, The effects of tibolone on vaginal blood flow, sexual desire and arousability in postmenopausal women, Climacteric 4:28, 2001.

[4] Botsis D, Kassanos D, Kalogirous D, Antonious G, Vitoratos N, Karakitsos P, Vaginal ultrasound of the endometrium in postmenopausal women with symptoms of postmenopausal urogenital atrophy on low dose estrogen or tibolone treatment: a comparison, Maturitus 26:57, 1997.

[5] Castelo –Branco C, Vicente JJ, Figueras F, Sanjuan A, Martinez de Osaba MJ, Casals E, Pons F, Balasch J, Vanrell JA, Comparetive effects of estrogens and tibolone on bone, lipid pattern and sexuality in postmenopausal women, Maturitus 34:161,2000.

[6] Egarter C, Topcuolu AM, Vogl S, Sator M, Hormone replacement therapy with tibolone: effects of sexual functioning in postmenopausal women, Acta Obstet Gynecol Scand 81:649, 2002.

[7] Genazzani AR, Benedek Jaszmann L, Hart DM, Andolsek L, Kicovic PM, Tax L,Org OD14 and the endometrium, Maturitus 13:243, 1991.

[8] Ginsburg J, Prelevic G, Butler D, Okolo S, Clinical experience with tibolone (livial) over 8years, Maturitus 21:71, 1995.

[9] Geusens J, Dequeker J, Gielen J, and Schot LPC, Nonlinear increase in vertebral density induced by a synthetic steroid (Org OD14)in women with established osteoporosis, Maturitus 1991;13:155-162.

[10] Rymer J, Effects of 8years of treatment with tibolone 2.5mg daily on postmenopausal bone loss, Osteoporos Int 12:478, 2001.

[11] Trevoux R, Dieulangard P, Blum A, Efficacy and safety of org 0D 14 in the treatment of climacteric complaints, Maturitus 5:89,1983.