A comparative clinicocytological study of post-menopausal women using oral and transdermal routes of hormone replacement therapy

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Summary: **A total of 80 post-menopausal women with natural and artificial menopause of less than 2 years with one or the other climacteric symptoms were studied. It was found that maximum number of cases presented with urogenital complaints (65%) followed by psychological symptoms (37.5%) and symptoms of vasomotor instability in 32%. They were studied clinically and vaginal cytology was done at the time of presentation and again after 1 and 6 months of low dose oestrogen therapy in the form of transdermal or oral route. Relief of symptoms and improvement in maturation index was found to be better with transdermal group after 1 month i.e. early response was achieved. However, after 6 months there was no significant difference. Control group showed no improvement in symptoms and vaginal cytology.**

Introduction

With increasing life expectancy, menopause is a "growing problem". Oestrogen deficiency ravages the health and well being of the woman at and after menopause. Hormone replacement therapy can offer relief. It can be given in variety of routes - oral, transdermal, subcutaneous and vaginal. In the present study, a comparative clinicocytological evaluation of oral and transdermal routes of hormone replacement therapy was done.

Material and methods

The present study was conducted in the Department of Obstetrics and Gynaecology, S.N. Medical College, Agra. Total 80 post-menopausal cases with 6 months amenorrhoea or panhysterectomy at least one month back and with one or other climacteric symptoms were selected for study. Climacteric symptoms included:

1. Symptoms of vasomotor instability - hot flushes, night sweats, vertigo, palpitation and weakness.
2. Symptoms of urogenital atrophy - burning micturition, frequency, urgency, stress incontinence, vaginal symptoms such as pruritus vulvae, discharge, dyspareunia etc.
3. Psychosomatic changes - anxiety, irritability, depression, insomnia, diminished libido etc.
4. Late consequences such as bony pain and spontaneous fracture.

Patients with undiagnosed vaginal bleeding, genital neoplasia, breast neoplasia, history of cardiovascular disease and thromboembolic phenomenon were excluded from the study. Selected patients were divided into 3 groups:

a. Transdermal group
b. Oral group
c. Control group

Complete haemogram, liver function tests, renal function test, serum cholesterol, low density lipoprotein, high density lipoproteins, serum calcium and hormonal levels were done before therapy.

Therapy was given as follows

a. Transdermal group

Patients were treated with HRT in the form of transdermal

therapeutic system 50 (Estraderm TTS-50) twice weekly in cyclic manner for 6 months, which deliver estradiol at the rate of 0.05 mg/day; patch was applied to skin over the buttock of the patients.

b. Oral group

Oral estradiol 1 mg/day (Evalon) was given to patients in this group in cyclic manner (3 weeks on with one week off) For 6 months.

significant difference. Vasomotor instability showed complete abolition in 62.5% and in 87.5% after 1 and 6 months of transdermal therapy as compared to abolition in 37.5% and 75% in oral route (Table II).

As regards hot flushes total abolition of symptoms was seen in 62.5% cases with transdermal as against 37.5% with oral route (Table III). Improvement in vaginal cytology was also studied and comparison showed that

Table I

Distribution of cases according to clinical manifestation

S. No.	Clinical Symptoms	Transdermal Group		Oral Group		Control Group	
		No.	%	No.	%	No.	%
1.	Vasomotor instability	8	32	8	32	8	26.7
2.	Uro-genital syndrome	16	64	20	80	16	53.3
3.	Psychological symptoms	10	40	10	40	10	33.3
4.	Late consequences	4	16	6	24	6	20

c. Control group

Oral calcium or placebo patch were given to patients of this group.

All patients were examined clinically and vaginal cytology was done at the time of presentation.

Re-examination was done after 1 and 6 months of therapy.

Observations

According to the present study, genitourinary complaints are the main symptom of menopausal women in India (65% cases) followed by psychological symptoms (37.5%) and symptoms of vasomotor instability (32%) (Table I). On comparative studies on effect of various routes of therapy on various climacteric symptoms, it was found that transdermal route was better in early response i.e. after 1 month of therapy. After 6 months, there was no

with 1 month of therapy with transdermal route, normal pattern rose from 16% to 48% as against 20% to 40% in oral group. After 6 months, normal pattern was seen in 48% of transdermal group and in 44% in oral group (Table IV). Table V shows the number of parabasal cells reduced from 40 to 8 to 0 after 1 month and 6 months of therapy in transdermal group. While in oral group number of parabasal cells reduced from 52 to 20 to 0 after 1 month and 6 months of therapy respectively.

Side effects in both transdermal and oral groups were very minimal (Table VI).

Discussion

In our study mean age of patient was 44.2 years which was comparable to 44.35 years studied by Anklesaria (1995). In Western studies, it is around 50.8 years. In

Table II

Effect of therapy on clinical symptoms

Clinical Symptoms	Before therapy	After one month						After six months					
		Complete abolition		Significant reduction		Reduction to some extent		Complete abolition		Significant reduction		Reduction to some extent	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
A. Transdermal Group													
Vasomotor Instability	8	5	62.5	2	25	1	12.5	7	87.5	1	12.5	-	-
Urogenital Symptoms	16	9	56.25	4	25	3	18.75	12	75	2	12.5	2	12.5
Psychological Symptoms	10	5	50	3	28.5	2	20	6	60	2	20	2	20
Late Consequence	4	2	50	-	13.3	1	25	3	75	1	25	-	-
B. Oral Group													
Vasomotor Instability	8	3	37.5	4	50	1	12.5	6	75	1	12.5	1	12.5
Urogenital Symptoms	20	13	52	6	30	1	18	15	75	4	20	1	5
Psychological Symptoms	10	2	20	4	25.7	2	30.8	7	70	2	20	1	10
Late Consequence	6	3	50	1	16.7	2	33.3	4	66.7	-	-	2	33.3
C. Control group													
Vasomotor Instability	8	-	-	-	-	3	37.5	-	-	-	-	3	37.5
Urogenital Symptoms	16	-	-	-	-	2	12.5	-	-	-	-	4	25
Psychological Symptoms	10	-	-	-	-	4	40	-	-	-	-	4	40
Late Consequence	6	-	-	3	50	-	-	-	-	3	50	-	-

Table III

Effect of therapy on hot flushes after one month

S. No.	No. of hot flushes (/24 hours)	Transdermal Group		Oral Group		Control Group	
		Before therapy	After one month	Before therapy	After one month	Before therapy	After one month
1.	No Hot Flush	-	62.5%	-	37.5%	-	-
2.	1-4/24 hrs	12.5%	25.0%	20%	50.0%	25.0%	37.5%
3.	5-8/24 hrs	25.0%	12.5%	40%	12.5%	25.0%	37.5%
4.	9-12/24 hrs	50.0%	-	30%	-	50.0%	25.0%
5.	>12/24 hrs	12.5%	-	10%	-	-	-

Table IV

Effect of therapy on vaginal cytology

S.No.	Transdermal Group			Oral Group			Control Group		
	Before therapy	After one month	After six months	Before therapy	After one month	After six months	Before therapy	After one month	After six months
1. Normal pattern	16	48	48	20	40	44	20.7	20.7	3.3
2. Early menopausal pattern	40	32	44	28	40	40	36.7	43.3	53.3
3. Intermediate pattern	36	20	12	48	40	40	40.0	40.0	40.0
4. Atrophic pattern	8	-	-	4	-	-	3.33	3.3	3.3

Table V

Changes in vaginal cytology and maturation index before and after therapy

S.No.	Groups	Before therapy	After one month	After six months
1.	Transdermal	40:48:12	8:62:30	0:64:36
2.	Oral Group	52:40:8	20:62:18	0:78:22
3.	Control Group	28:50:22	28:58:14	32:60:8

Table VI

Comparative evaluation of side effects of oral and transdermal groups

S. No.	Side Effects	Transdermal Group		Oral Group	
		No.	%	No.	%
1.	Local				
	Itching/rashes	5	20.0	-	-
2.	Systemic				
	Headache/migraine	2	8.0	4	16.0
	Increase in weight	2	8.0	-	-
	Nausea and vomiting	-	-	-	-
	Break through bleeding	1	4.00	-	-
	Vaginal discharge				

this study, genitourinary symptoms were the main complaints in 65% as against 74% in the study by Anklesaria (1995). Vasomotor instability was found only in 30% in our study, as against 75% in the study of Studd and Barber (1992).

After one month of therapy, significant reduction (87.5%) occurred in acute symptoms of vasomotor instability by both routes but for complete abolition of symptoms, transdermal route was found to be more effective (62.5%) as against oral route (37.5%). After 6 months, both routes were found to be equally effective.

Our results are comparable to those of other workers, Judd (1987) found that 50µg/24 hours patch relieved hot flushes in 60% of the cases within 1 month and 80-90% of cases within 3 months of therapy.

Whitehead (1990) described a progressive decline in hot flushes with each month of cyclical estradiol therapy - 60% improvement after 1 month, 80% after 2 months and 90% after 3 months of cyclical treatment with transdermal route.

Vaginal cytology

Normal pattern was seen in 16% cases. After 1 month of therapy, this rose up to 48% with transdermal route as against from 20% to 40% with oral route. No significant change was seen with placebo. As regards maturation index, after 1 and 6 months of therapy - the parabasal cells showed reduction in number from 40 to 08 to 0 with transdermal route as against 2 to 20 to 0 with oral route. Number of intermediate cells rose from 48 to 62 to 64 in transdermal route as against 3 to 18 to 22 in oral route. Number of superficial cells rose from 40 to 62 to 78 after transdermal route as compared to 8 to 18 to 22 after one and six month of therapy with oral route. Control group showed no improvement and rather deterioration in percentage of superficial cells.

Results

Thus on comparative study beneficial effects of both routes of hormonal replacement therapy were found to be equally effective but transdermal route therapy showed better early response.

References

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