Hormone replacement therapy is an issue of vital medical importance in the care of increasing of an ageing women, Who simultaneously balance professional and domestic commitment. Various formulation, combinations, route and duration of therapy exist for use. To date, oral therapy either continuously or cyclically has been the most common hormone treatment. However, The introduction of transdermal therapeutic system has allowed estradiol to be administered in low doses, improving quality, tolerability and compliance while maintaining efficacy.

The present study was conducted on 50 post menopausal patient to evaluate comparative efficacy of different type of HRT (Premarin, Evalon, E2 gel and Ovral-L). All patient were examined thoroughly for clinical manifestations, vaginal smear pattern, serum lipoproteins, liver function test. Reevaluation of all things was done 2 months and 6 months after therapy.

Lastly comparison of all four types of HRT done with placebo therapy whether hormone therapy is effective in real sense are just as placebo therapy.

Total 50 post menopausal patients were divided into 5 groups -
A. Premarin Group.
B. Evalon Group.
C. E2 Gel Group.
D. Ovral-L Group.
E. Control Group.

Each group has 10 patients.

A. **Premarin Group** :-

In this group 10 patients were treated with oral conjugated equine estrogen 0.625 mg per day for 3 weeks with one week off. Medroxy progesteron given 10 mg. for last 10 days per months.

B. **Evalon Group** :-

In this group 10 patients were treated with oral Estriol tablet 1 mg. per day for 3 week with 1 week off. Estriol is natural estrogen. Medroxy progesteron given 10 mg. for last 10 days per month.

C. **E2 Gel Group** :-

In this group 10 patients were treated with transdermal 17 beta Estrediol gel. 2.5 g gel applied over for arm and Shoulder, twice a week for 3 week with one week off. Medroxy progesteron given 10 mg. for last 10 days per months.

D. **Ovral-L Group** :-

In this group 10 patients were treated with oral a combination of ethinyl estrediol 0.03 mg. and leonorgestrel
0.15 mg., 1 tablets per day for 3 week per months with 1 week off.

**Effect of HRT on Serum Lipids -**

Studies have shown that serum lipids levels are significantly higher in post menopausal women. Effect of HRT on serum lipids are also significant than in age matched menopausal women which is not taken HRT (Aitken 1971, Gustofson and svanberg 1972, Punnonen and Rauromo 1976-80, patterson et al 1980, Notelviez et al 1983, PEPI trial group of writing 1995, Darling et al (1997).

In the present work serum lipid lipoproteins levels were estimated in women undergoing natural and surgical menopause.

**A. Premarin -** (Conjugated equine estrogen)
The mean basal level of serum cholesterol (STC), Triglyceride (STG), High Density lipoprotein (HDL) and Low Density lipoprotein (LDL) were, 216 mg/dl, 127 mg/dl, 41.1 mg/dl and 150.8 mg/dl respectively. There was significant changes in serum lipoprotein after 2 month and after 6 months, changes occurred highly significant of premarin therapy.
A ratio of basal sample to 2 month (A : B) and 6 month (A:C) and a ratio of after 2 month to 6 months (B: C) of therapy shown statistical significant (Table - IV).

A : B -

STC : $ t = 3.2 , P < 0.05 $ significant.
STG : $ t = 2.74 , P < 0.05 $ significant.
HDL : $ t = 2.44 , P < 0.05 $ significant.
LDL : $ t = 7.37 , P < 0.01 $ highly significant.

A : C -

STC : $ t = 5.83 , P < 0.01 $ highly significant.
STG : $ t = 5.36 , P < 0.01 $ highly significant.
HDL : $ t = 8.77 , P < 0.01 $ highly significant.
LDL : $ t = 10.70 , P < 0.01 $ highly significant.

B : C -

STC : $ t = 6.02 , P < 0.01 $ highly significant.
STG : $ t = 5.78 , P < 0.01 $ highly significant.
HDL : $ t = 10.00 , P < 0.01 $ highly significant.
LDL : $ t = 9.48 , P < 0.01 $ highly significant.

Initially STC STG and HDL shown significant changed (P<0.05). After 2 month of therapy LDL shown highly significant changes (P<0.01).

B. Evalon - (Estriol)

The mean basal level of serum cholesterol (STC), Triglyceride (STG), High Density lipoprotein (HDL) and Low
Density lipoprotein (LDL) were, 205.5 mg/dl, 126 mg/dl, 38.1 mg/dl and 142.2 mg/dl respectively. There was significant changes in all above entities after two month and 6 month of evalon therapy.

A ratio of basal sample to 2 month (A : B) and 6 month (A:C) and a ratio of after 2 month to 6 months (B: C) of therapy shown statistical significant as below. (Table V)

**A : B -**

<table>
<thead>
<tr>
<th></th>
<th>t</th>
<th>P</th>
<th>Significant</th>
</tr>
</thead>
<tbody>
<tr>
<td>STC</td>
<td>2.74</td>
<td>&lt;0.05</td>
<td>significant.</td>
</tr>
<tr>
<td>STG</td>
<td>3.16</td>
<td>&lt;0.05</td>
<td>significant.</td>
</tr>
<tr>
<td>HDL</td>
<td>4.0</td>
<td>&lt;0.01</td>
<td>highly significant.</td>
</tr>
<tr>
<td>LDL</td>
<td>5.0</td>
<td>&lt;0.01</td>
<td>highly significant.</td>
</tr>
</tbody>
</table>

**A : C -**

<table>
<thead>
<tr>
<th></th>
<th>t</th>
<th>P</th>
<th>Significant</th>
</tr>
</thead>
<tbody>
<tr>
<td>STC</td>
<td>4.14</td>
<td>&lt;0.01</td>
<td>highly significant.</td>
</tr>
<tr>
<td>STG</td>
<td>8.76</td>
<td>&lt;0.01</td>
<td>highly significant.</td>
</tr>
<tr>
<td>HDL</td>
<td>14.3</td>
<td>&lt;0.01</td>
<td>highly significant.</td>
</tr>
<tr>
<td>LDL</td>
<td>12.97</td>
<td>&lt;0.01</td>
<td>highly significant.</td>
</tr>
</tbody>
</table>

**B : C -**

<table>
<thead>
<tr>
<th></th>
<th>t</th>
<th>P</th>
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</tr>
</thead>
<tbody>
<tr>
<td>STC</td>
<td>7.30</td>
<td>&lt;0.01</td>
<td>highly significant.</td>
</tr>
<tr>
<td>STG</td>
<td>14.72</td>
<td>&lt;0.01</td>
<td>highly significant.</td>
</tr>
<tr>
<td>HDL</td>
<td>8.80</td>
<td>&lt;0.01</td>
<td>highly significant.</td>
</tr>
<tr>
<td>LDL</td>
<td>15.0</td>
<td>&lt;0.01</td>
<td>highly significant.</td>
</tr>
</tbody>
</table>
Initially STC and STG shown slow changes but statistical significant (P<0.05). HDL and LDL shown highly significant (P<0.01) first 2 month of therapy.

C. **E2 Gel**  - (17 beta Oestradiol)

The mean basal value of (STC), (STG), (HDL) and (LDL) were, 211.4 mg/dl, 126 mg/dl, 39.8 mg/dl and 146.4 mg/dl respectively. There were significant changes shown after 2 months and 6 months of therapy.

A ratio of A : B , A:C and B: C shown statistical significant as below.(Table VI)

**A : B**

STC : t = 2.63 , P < 0.05 significant.
STG : t = 2.36 , P < 0.05 significant.
HDL : t = 2.87 , P < 0.05 significant.
LDL : t = 5.30 , P < 0.01 highly significant.

**A : C**

STC : t = 4.37 , P < 0.01 highly significant.
STG : t = 2.44 , P < 0.05 significant.
HDL : t = 6.58 , P < 0.01 highly significant.
LDL : t = 7.72 , P < 0.01 highly significant.

**B : C**

STC : t = 6.55 , P < 0.01 highly significant.
STG : t = 2.37 , P < 0.05 significant.
HDL : t = 9.72 , P < 0.01 highly significant.
LDL : t = 8.00 , P < 0.01 highly significant.
There were significant change shown STC, HDL and LDL but STG shown significant changes not exceed P<0.05.

**D. Ovral-L**

The mean basal value of (STC), (STG), (HDL) and (LDL) were, 205.8 mg/dl, 120 mg/dl, 40.5 mg/dl and 140.3 mg/dl respectively. There were significant changes shown after 2 months and 6 months of therapy.

A ratio of A : B , A : C and B : C shown statistical significant as below (Table VII)

**A : B**

STC : \( t = 3.09 \), \( P < 0.05 \) significant.

STG : \( t = 3.20 \), \( P < 0.05 \) significant.

HDL : \( t = 2.75 \), \( P < 0.05 \) significant.

LDL : \( t = 4.34 \), \( P < 0.01 \) highly significant.

**A : C**

STC : \( t = 5.26 \), \( P < 0.01 \) highly significant.

STG : \( t = 5.43 \), \( P < 0.01 \) highly significant.

HDL : \( t = 11.93 \), \( P < 0.01 \) highly significant.

LDL : \( t = 11.47 \), \( P < 0.01 \) highly significant.

**B : C**

STC : \( t = 6.44 \), \( P < 0.01 \) highly significant.

STG : \( t = 10.27 \), \( P < 0.01 \) highly significant.

HDL : \( t = 15.10 \), \( P < 0.01 \) highly significant.

LDL : \( t = 10.27 \), \( P < 0.01 \) highly significant.
Initially STC, STG, HDL showed statistical significant at (P<0.05) and LDL shown significant (P<0.01) after 2 months of therapy.

**E. Control Group** - (Placebo therapy)

The mean basal value of (STC), (STG), (HDL) and (LDL) were, 202 mg/dl, 122 mg/dl, 42.4 mg/dl and 130.4 mg/dl respectively. There were 50 ml significant changes shown after 6 months of therapy.

A ratio of basal to 2 months (A : B) and 6 months (A : C) and after 2 months to 6 months (B : C) observation on placebo therapy changes in serum lipoprotein shown as below (Table - VIII).

**A : B -**

<table>
<thead>
<tr>
<th></th>
<th>t</th>
<th>P</th>
<th>Significant</th>
</tr>
</thead>
<tbody>
<tr>
<td>STC</td>
<td>2.09</td>
<td>&gt; 0.05</td>
<td>not significant.</td>
</tr>
<tr>
<td>STG</td>
<td>1.00</td>
<td>&gt; 0.05</td>
<td>not significant.</td>
</tr>
<tr>
<td>HDL</td>
<td>1.97</td>
<td>&gt; 0.05</td>
<td>not significant.</td>
</tr>
<tr>
<td>LDL</td>
<td>2.20</td>
<td>&gt; 0.05</td>
<td>not significant.</td>
</tr>
</tbody>
</table>

**A : C -**

<table>
<thead>
<tr>
<th></th>
<th>t</th>
<th>P</th>
<th>Significant</th>
</tr>
</thead>
<tbody>
<tr>
<td>STC</td>
<td>2.29</td>
<td>&lt; 0.05</td>
<td>significant.</td>
</tr>
<tr>
<td>STG</td>
<td>1.25</td>
<td>&gt; 0.05</td>
<td>not significant.</td>
</tr>
<tr>
<td>HDL</td>
<td>3.2</td>
<td>&lt; 0.05</td>
<td>significant.</td>
</tr>
<tr>
<td>LDL</td>
<td>4.5</td>
<td>&lt; 0.01</td>
<td>highly significant.</td>
</tr>
</tbody>
</table>

**B : C -**

<table>
<thead>
<tr>
<th></th>
<th>t</th>
<th>P</th>
<th>Significant</th>
</tr>
</thead>
<tbody>
<tr>
<td>STC</td>
<td>2.97</td>
<td>&lt; 0.05</td>
<td>significant.</td>
</tr>
<tr>
<td>STG</td>
<td>2.17</td>
<td>&gt; 0.05</td>
<td>not significant.</td>
</tr>
</tbody>
</table>
HDL :  \( t = 2.07 \), \( P > 0.05 \) not significant.
LDL :  \( t = 3.20 \), \( P < 0.05 \) significant.

There were no changed in serum lipoprotein first 2 month of observation. Some slight statistical significant changed in countered after 6 months of observation. (STC, HDL and LDL shown statistical significant). STG was not shown any statistical significant changed after 6 month of observation.

There were significant changed shown is serum lipoprotein (STC, STG, HDL, LDL) by all four types of HRT which are contained estrogen in different form.

Serum Cholesterol decreased significantly in all four type of HRT after 2 months significant at \( (P<0.05) \) and after 6 months significant at \( (P<0.01) \).

STG increased significant in all four type of HRT but E2 gel shown significant only at \( P<0.05 \) after 2 months and after 6 months of therapy. Rest oral form of estrogen therapy shown increased STG gradually statistical significantly after 2 months \( P<0.05 \) and after 6 months \( P<0.01 \).

HDL increased significant with all four type of HRT, after 2 months \( (P<0.05) \) and after 6 months \( (P<0.01) \). But Evalon increased highly statistical significant changed after 2 month of therapy \( (P<0.01) \).
LDL declined highly statistically significant with all four type HRT after 2 months (P<0.01) and after 6 months (P<0.01) of therapy.

There was significant declined in LDL/HDL ratio after 2 months and after 6 months of therapy.

<table>
<thead>
<tr>
<th></th>
<th>Before therapy</th>
<th>After 2 months</th>
<th>After 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premarin</td>
<td>3.6 : 1</td>
<td>3.1 : 1</td>
<td>2.8 : 1</td>
</tr>
<tr>
<td>Evalon</td>
<td>3.7 : 1</td>
<td>3.5 : 1</td>
<td>3.0 : 1</td>
</tr>
<tr>
<td>E2 gel</td>
<td>3.6 : 1</td>
<td>3.4 : 1</td>
<td>2.9 : 1</td>
</tr>
<tr>
<td>Ovral-L</td>
<td>3.5 : 1</td>
<td>3.3 : 1</td>
<td>2.7 : 1</td>
</tr>
</tbody>
</table>

In Control group there were slightly changed in serum lipoprotein. STC increased slightly after 6 month of observations (t = 2.29 ; P<0.05). STG shown statistically in significant changed after 2 months and 6 months of observations. HDL not decreased significantly after 2 months but after 6 months of observations shown statistical significant changed (t = 3.20 ; P < 0.05). LDL increased gradually but not statistical significant after 2 months yet after 6 months of observations shown statistical significant changed (P<0.01).

Aitken (1971) showed that administration of 20-40 ug of mestronol daily in oopherectomised women was associated with significant fall in serum cholesterol and a significant rise in serum triglycerides.
Gustoson and Svanberg (1972) : an oestrogenic steroid was given for three weeks period to 6 oopherectomised women. There as significant rise in HDL and VLDI and decrease in LDL levels.

Punnonen and Rauramo (1976) showed that administration of 2 mg estradiol valerate in oopherectomised women showed significant rise in serum phospholipids but no significant effect on cholesterol and triglyceride levels.

Patterson et al (1980) showed that there was little alterations in the mean serum cholesterol concentration and triglycerides with cyclical oestrogen but sequential oestradiol valerate and norgestrel significantly reduced the mean serum cholesterol and significant rise in serum triglyceride in post menopausal women.

Punnonen and Rauramo (1980) showd that injections of both 10 mg of oestradiol valerate and 2.5 mg of estradiol benzoate plus 10 mg estradiol thinyl propionate caused significant rise in HDL cholesterol level in bilateral oopherectomised women.

Notelovitz et al (1983) : different types and doses of oestrogen was administered in bilateral oopherectomised women. After 3 months serum cholesterol levels were unaffected by 1 and 2 mg of micronized 17 beta oestradiol or 0.625 and 1.25 mg of conjugated equine oestrogen.
Triglyceride levels were significantly elevated with conjugated oestrogen administration. A trend towards higher relative protein of high density lipoprotein and lower relative proportion of low density lipoproteins was observed in all.

The writing group for PEPI Trial (1995) It was demonstrated that there is a decreased in total cholesterol, an increasing in HDL level by about 10%, and decreased in LDL level also by about 10% on unopposed oestrogen for HRT.

Darling et al (1997) When HRT in pharma of continuous conjugated equine estrogen with medroxyprogesteron acetate 5 Mg was compare with simvastatin, both caused a similar degree increase in HDL level.

**Age Incidence of Menopause**

In our present study 16 case of surgical menopause (with or without oopherectomy) and 34 natural menopausal woemn.

The mean age of menopause was 44 years in the present study which includes both surgical and natural menopause. The mean age of natural menopause was 46 years in our study, which was comparable to those of Anklesaria (1995), according to that study, it was 44.35 years. But in west it is around 50.8 years.

Age of menopause is affected by type of menopause due to increased incidence of panhystrectomy at an early age incidence of menopause comes down.
Studies in India conducted by Wyon et al (1966), Randhawa et al (1987), and Kaws et al (1994), consistently showed a lower age at menopause among Indian women as compared to those in west. Most Indian studies locate the mean age at menopause as 48 years, while those from the west reveals the same to be about 51 years (WHO Scientific group 1981). It appears to be unaffected by socio-economic status, parity, height and weight of female.

**Duration of menopause:**

At the time of presentation, in most of the cases average duration of menopause was 2-3 years. This finding can be explained by low socio-economic status, more of illiteracy among Indian females and ignorance about menopausal symptoms. Only when atrophic symptoms interfere with their day to day life, then they seek medical advice. In most of the cases, it was seen that duration of menopause was affected by type of menopause whether it was surgically induced or natural. In cases of surgical menopause, most of the patients presented within 2 months with symptoms of vasomotor instability. It might be due to sudden hormonal withdrawal from removal of ovary.

**Menopausal Symptoms:**

On pre-treatment counseling of post-menopausal females hot flushes and night sweats were seen in 25 patients (50%). Genito-utinary complaints were found in 25 patients (50%).
Psychological symptoms were seen in 46 patients (92%) and patients with late consequence of menopause were 3 patients (6%).

Mostly patients represented with 2 or 3 group of symptoms like:

- Vasomotor/Urogenital = 5 (10%)
- Vasomotor/Psychological = 20 (40%)
- Urogenital/Psychological = 15 (30%)
- Late consequence/Psychological = 3 (6%)
- Vaso/Uro/Psychological = 8 (16%)

-------------
50 100%
(Table No. 9)

Relative frequency of post-menopausal symptoms by various workers.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Symptoms</th>
<th>Western studd &amp; Barber 1992</th>
<th>Indian Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Hot flushes &amp; Night sweat</td>
<td>78 %</td>
<td>33 %</td>
</tr>
<tr>
<td>2.</td>
<td>Urinary complaints</td>
<td>20 %</td>
<td>35 %</td>
</tr>
<tr>
<td>3.</td>
<td>Psychological symptoms</td>
<td>92 %</td>
<td>20 %</td>
</tr>
<tr>
<td>4.</td>
<td>Bony pains</td>
<td>48 %</td>
<td>25 %</td>
</tr>
</tbody>
</table>

From the above table, it is clear that our results are comparable to these workers in different, in different entities.
Vasomotor and psychological symptoms comparable nearly to studd (1992). Urogenital and Late consequence symptoms comparable near by Anklesaria (1995). Wide variation of our study may explained by Lack of awareness of symptoms and due to iliteracy, those patients in which have symptom of late consequence like bone pain not come to gynaecologist frequently because of those thing it may orthopaedic in origin. Vasomotor and urogenital atrophy symptoms mostly associated with phycological problem also because of disturbance in daily routine life and night sleep disturbances.

1. **Premarin**

   After 2 months of therapy 50% represented some extent in symptoms relief and 50% represented significant relief in symptoms. After 6 months of therapy 90% showed compelte abolition in symptom in 10% significant relief in symptoms.

2. **Evalon**

   After 2 months of therapy 50% represent some extent of relief in symptoms and 50% represent significant relief in symptoms. After 6 months of therapy 90% showed complete abolition in symptom in 10% significant relief in symptoms.

3. **E2 Gel**

   After 2 months of therapy 40% shown some extent of relief in symptoms and 60% represent significant relief in
symptoms. After 6 months of therapy 100% showed complete abolition in symptom.

4. **Ovral-L**

After 2 months of therapy 90% represented some extent of relief in symptoms and 10% shown significant relief in symptoms. After 6 months of therapy 80% showed complete abolition in symptom and 20% shown significant relief in symptoms.

5. **Control group - (Placebo therapy)**

After 2 months of placebo therapy 30% represented shown extent of relief in symptoms in 70% shown no change. After 6 months of placebo therapy 40% shown some extent in symptom relief and 60% shown no change in symptoms.

**Vasomotor Symptoms -**

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

According to Steingold and Laufer (1985), oral and transdermal estradiol are equally effective in the treatment of hot flushes.

In study by Kerzel (1987) in 112 patients hot flushes were completely abolished in 64% of patients and the frequency and intensity were markedly reduced in the remainders.

According to Nachtigall (1988), Randall (1988), efficacy can be maintained in long term study, where vasomotor symptoms were either greatly improved or abolished in majority of patients.

Superiority of transdermal route over placebo therepay has been confirmed in relieving symptoms of vasomotor instability placebo therapy is effective in only 40% cases. This observation is supported by Laufer et al (1983) and Steingold et al (1985).

This result can be compared with study by Steingold and Laufer (1985), oral estrogen and transdermal estradiol both are equally effective in the treatment of hot flushes.

**Urogenital Symptoms**

According to Grall (1990) after 6 months of transdermal therapy, dyspareunia and urinary disorder were completely abolished in 86% and 90% of patients, respectively.
According to Janaud (1990), Erkkola et al (1991), transdermal therapy relieved urogenital problem in up to 90% of the patients and 45-63% reduction in these symptoms in the first month of treatment with transdermal estradiol.

Khan et al (1990) reported beneficial effect of treatment with estriol therapy on urogenital symptoms.

**Psychological Symptoms**

Rabe et al (1990) reviewed the effect of two months of transdermal therapy on 15,194 patients and found 50% reduction in symptoms such as insomnia, irritability and depression.

Grall (1990) 75% of 2141 evaluable patients complained of insomnia before therapy; his was reduced to 25% after 6 months of treatment with transdermal estradiol. Schleusker (1988) noted an improvement in nervousness and insomnia in 120 patients after only 2 weeks of treatment.

**Let Consequence Symptoms:**

Estrogen replacement therapy appears to have a direct effect on osteoblast function (Emans SI, Grace E, Haffer FA; Hoffer FA woods ER (1990).

A four years randomized study from the university of taxes showed for the first time on the additive effect of
intermittent cyclical etidronate and HRT on the bone mineral density in both vertebral and the hip (Jha U.P. 1997).

**Vaginal Cytology:**

Vaginal cytology was done routinely in every patient with post-menopausal symptom and effect of hormone replacement therapy was seen after 2 month and 6 month of therapy. In all for group - Premarin, Evalon, E2 gel, Ovral-L and control group vaginal cytology pattern shown as below.

**Normal pattern** -

- 20% in Premarin
- 30% in Evalon
- 20% in E2 gel
- 20% in Ovral-L
- 20% in Control group.

**Intermediate Pattern** -

- 40% in Premarin
- 30% in Evalon
- 30% in E2 gel
- 20% in Ovral-L
- 20% in Control group.

**Atrophic Pattern** -

- 40% in Premarin
- 40% in Evalon
- 50% in E2 gel
60% in Ovral-L
60% in Control group.
(Table -11)

These types of pattern vaginal cytology are comparable to duration of menopause. Most of the postmenopausal female showed early menopausal and intermediate pattern. This can be explained by the fact that most of the patient of our study group were between 0-5 years of duration of menopause and during this short period of menopause vaginal epithelium does not showed marked atrophic changes because there are other showeds of estrogen production in female body. Beside this , there is also and another factor that most of women were sexually active during early menopause.

According to Leibium et al 1983 women who lead an active and satisfying sexual life after menopause, appears to be less likely to develop, post menopausal atrophy than the women whose sexual life is inactive.

**Effect of Hormone replacement therapy on vaginal cytology**

Normal → Intermediate → atrophic pattern vaginal cytology showed gradual deprivation of estrogen in circulation. estrogen therapy changed gradually atrophic → intermediate → normal pattern. In present study all four drugs showed significant effect on vaginal cytology after 2 months and after 6 months of theapy (Table 14).
After giving hormone replacement therapy, there was marked increased in maturation of vaginal epithelium. After 2 month of therapy intermediate to normal pattern changed in premarin 30% in evalon 20% in E2 gel 20% and overal-L 10%. After 6 months of therapy changed from intermediate to normal pattern. In premarin 60%, in Evalon 60%, E2 gel 50%, overal-L 40% and atrophic pattern to intermediate pattern after 6 months in premarin 100%, in Evalon 100%, in E2 gel 100%, Overal-L 100%.

In control group vaginal cytology showed changes apparently from normal to intermediate to atrophic after 6 months of observation. (Table - XIV)


According to Padwick et al (1985) mean percentage of basal cell fall from 40 to 0, mean percentage of intermediate and superficial cells rose from 54 to 74 and 6 to 26, respectively (P<0.05).

Laufer et al (1983) observed that the percentage of superficial cells and parabasal cells in post menopausal women treated with trnasdermal route were comparable to those in premenopausal women.
In our present study in prémarin mean percentage of parabasal cell fall from 23 to 9 after 2 months of therapy and 9 to 0 after 2-6 months of therapy. In Evalon parabasal cell fall 12 to 4 after 2 months of therapy and 4-0 after 2-6 months. In E2 gel parabasal cell for 11 to 4 after 2 months of therapy and 4 to 0 from 2 to 6 months of therapy. In ovral-L parabasal cell for 15 to 5 after 2 months of therapy and 5 to 0 from 2 to 6 months of therapy.

**Side Effect of HRT in various group**

Transdermal estrogen form (E2 gel) was found to be responsible for skin reaction at site of application, in form of etching and rashes in 20% cases after 2 to 3 application but it was not very severe. This problem was solved by changing the site of application. Other side effects were.

Weight gain 10%, Break through bleeding 10%, vaginal discharge 10% (Table-15).

According to Sitrukware (1990), Utiani (1988), Youngkins (1990), skin irritation at the site of application is most common adverse effect experienced when using the transdermal therapy.
Nachtegall (1988) reported skin irritation 14% of 133 patients receiving transdermal estradiol. There is no question of skin irritation with oral therapy.

In oral group of HRT found some GI and systemic side effect.

Premarin Group - Headache in 10%
                   Weight gain in 10%
                   Nausea/vomitting in 10%
                   Vaginal discharge in 10%

Evalon Group - Headache in 10%
                Vaginal discharge in 20%

Ovral-LGroup - Headache in 10%
               Break through bleeding 10%
               Vaginal discharge in 10%

There was no major side effect in all four group which need to discontinuation of therapy. All four drugs content low dose of estrogen which is minimized the side effect.

Transdermal estradiol therapy therapy has been shown to be at least as effective against post-menopausal symptoms as oral in all clinical trials, Furthermore it increase compliance and avoids some of the metabolic adverse effects associated with oral administration (Balfour & Heel, Bayour & Tavish 1992, Chetowski et al 1986, Utian 1988).