Comparison between rectal Bromocriptine and oral Cabergoline in treatment of hyperprolactinemia

A.Y.Rezk , A.A.Abd El Hameed , T.M.Assar , A.K.E.Abbas
Obstetrics and Gynecology, Dept., Faculty of Medicine, Benha Univ., Benha, Egypt
E-Mail:ahmed2356@gmail.com

Abstract
This study compared between oral cabergoline and rectal bromocriptine in the treatment of female patients suffering from hyperprolactinemia. This study was conducted on 220 female patients suffering from hyperprolactinemia with whose serum prolactin level above 25 ng/ml. A detailed history taking, clinical examination and serum prolactin level were done to all participants. The patients were divided into two groups in a randomized pattern; group (a), included 110 patients were treated with 2.5 mg bromocriptine rectally daily once up to 3 months.; group (b), included 110 patients were treated with oral cabergoline.1/2 tablet twice a week up to 3 months. Prolactin level was assayed before treatment then after 4 weeks and 4 months respectively, comparing prolactin level pre- and post-treatment, there was significant decrease in prolactin level after treatment in Bromocriptine group (mean prolactin=16.5 versus 40, p<0.001); as well as in Cabergoline group (mean prolactin= 11.3 versus 41, p<0.001). Cabergoline group after treatment had significantly lower prolactin level when compared to Bromocriptine group (p<0.001). Change in prolactin level after treatment compared to baseline level was calculated, Cabergoline group showed significantly higher percentage change in prolactin level when compared to Bromocriptine group (mean percentage change=64.9% versus 55%, p<0.001). Stratifying cases into recurrent and non-recurrent hyperprolactinemia, revealed that those with non-recurrent hyperprolactinemia, cabergoline group had significantly lower level when compared to bromocriptine group (11.3 versus 13.5, p<0.001). While those with recurrent hyperprolactinemia, cabergoline and bromocriptine groups had non-significant difference in prolactin level at 4 months after treatment (p>0.05). Treatment with Cabergoline had significantly lower prolactin level when compared to Bromocriptine group at 4 weeks and 4 months.

Keywords: Hyperprolactinemia, cabergoline, Bromocriptine.

1.Introduction
Hyperprolactinemia is a frequent cause of reproductive problems encountered in clinical practice; variety of pathophysiological conditions can lead to hyperprolactinemia (Vander et al., 2018).

In women, a high blood level of prolactin often causes hypoestrogenism with anovulatory infertility and a decrease in menstruation. In some women, menstruation may disappear altogether amenorrhea. In others, menstruation may become irregular or menstrual flow may change. Women who are not pregnant or nursing may begin producing breast milk (Rebar et al., 2016)

Bromocriptine is derivative of lysergic acid substituted with bromine that binds to dopamine-D2-receptors. The dopamine agonist, bromocriptine mesylate, is often the initial drug of choice and may require high doses to achieve clinical improvement and shrinkage of prolactinomas. It can lower the prolactin level in 70-100% of patients it is a useful tool in the treatment of hyperprolactinemia (Majrashi et al., 2017). Bromocriptine is available in the market as oral tablets and capsules, only 28–30% of the oral dose is absorbed. The oral bioavailability is only 4.5-6% because of extensive pre-systemic metabolism by the liver. In addition to adverse side effects, commonly being postural hypotension, nausea, vomiting, fatigue, headaches, dizziness and faintness in 50% to 70% of women, causing about 10% discontinue therapy (Sita et al., 2017). Cabergoline is an ergot derivative which is long-acting dopamine agonist that is very effective and well tolerated in patients with pathological hyperprolactinemia (Malik et al 2014). Cabergoline stimulates centrally-located dopaminergic receptors resulting in a number of pharmacologic effects. Cabergoline can treat symptoms associated with irregular menstruation, unwanted breast milk production, infertility, bone loss, and sexual problems. As with bromocriptine therapy, nausea and dizziness are possible side effects but may be avoided if treatment is started slowly (Montejo et al 2017).

The aim of the Work was to compare the clinical effectiveness, side effects and tolerability of rectal Bromocriptine as compared to oral Cabergoline tablets for treating hyperprolactinemia.

2.Patients and Methods
A comparative study conducted on two hundreded and twenty females gathered from the Gynecology and obstetrics outpatient's clinics at Benha University Hospital, during the period between April 2018 till January 2020. The inclusion criteria of the study group were cases Patients in child bearing period (18-38) years old with symptoms suggesting hyperprolactinemia: galactorrhea, menstrual
disturbances and patient’s seeking for fertility primary or secondary and patients who did not take any prolactin normalizing drug. While women with other causes of infertility as male factor or tubal factor, women with other as thyroid dysfunction, liver cell failure, renal failure and women who were lactating were excluded from the work. Approval of the Research Ethical Committee was granted before starting the study.

The participant women had been randomized according to computer generated random numeric table. The random allocation sequence was concealed in sealed dark envelope then patients have been assigned randomly into Group1: 110 patients who received 2.5 mg bromocriptine rectally daily once for 3 months. Group2: 110 patients who received oral cabergoline 1/2 tablet twice a week for 3 months. Prolactin level was assayed before treatment then after 4 weeks and 4 months respectively.

3.Statistical analysis

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25. Armonk, NY: IBM Corp.). The results were shown in tables & figures, collected data was statistically represented in terms of range, mean, standard deviation (+\- SD) and percentage.

4.Results

A randomized controlled comparative clinical trial was conducted to evaluate and compare the efficacy of two different modalities in the treatment of hyperprolactinemia, 242 cases of hyperprolactinemia were assessed for illegibility; 22 were excluded because they didn’t fulfill the inclusion criteria. All 220 participants were enrolled in the study; patients were divided into two groups in a randomized pattern; group (a), included 110 patients were treated with 2.5 mg bromocriptine rectally daily once up to 3 months.; group (b), included 110 patients were treated with oral cabergoline.1/2 tablet twice a week up to 3 months. Prolactin level was assayed before treatment then after 4 weeks and 4 months respectively.

Baseline data of all studied groups

![Fig 1. Study flow chart.](image-url)
The present study was conducted on 220 patients with symptoms suggesting hyperprolactinemia. Their mean age was 27.8 years. Their mean BMI was 24.9 kg/m². No significant differences were found between bromocriptine and cabergoline groups regarding age (mean=28.3, 27.4 years respectively, p>0.05); BMI (mean=15.2, 24.6 respectively; p>0.05).

Table 2. Comparison of complaint between all studied groups.

Most of studied cases complained of infertility (primary in 33.2%, secondary in 20.5%), milk suppression in 19.1%, galactorrhea in 15%, amenorrhea in 6.8%, mastalgia in 5% and irregular menses in 0.5%. No significant differences were present between both groups who received bromocriptine or cabergoline (p>0.05).

Table 3. Comparison of Prolactin level among studied groups.

Comparing prolactin level pre and post treatment, there was significant decrease in prolactin level after treatment in Bromocriptine group (mean prolactin= 16.5 versus 40, p<0.001).
p<0.001); as well as in Cabergoline group (mean prolactin= 11.3 versus 41, p<0.001).

Cabergoline group after treatment had significantly lower prolactin level when compared to Bromocriptine group (p<0.001).

**Table 4.** Comparison of percentage change in prolactin level among the studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Bromocriptine group</th>
<th>Cabergoline group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=110</td>
<td>N=110</td>
<td></td>
</tr>
<tr>
<td></td>
<td>mean ±SD</td>
<td>mean ±SD</td>
<td></td>
</tr>
<tr>
<td>Change in prolactin level (%)</td>
<td>55 ±15.3</td>
<td>64.9 ±13.3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Fig 3.** Percentage change in prolactin level among the studied groups.

Change in prolactin level after treatment comparing to baseline level was calculated, Cabergoline group showed significantly higher percentage change in prolactin level when compared to Bromocriptine group (mean percentage change=64.9% versus 55%, p<0.001).

**Table 5.** Comparison of recurrence of hyperprolactinemia among the studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Bromocriptine group</th>
<th>Cabergoline group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=103</td>
<td>N=104</td>
<td></td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Recurrence</td>
<td>13</td>
<td>12.6%</td>
<td>13</td>
</tr>
</tbody>
</table>

**Fig 4.** Recurrence of hyperprolactinemia among the studied groups.

After 4 months, prolactin level was assayed, no significant difference was found regarding recurrence of hyperprolactinemia among the studied groups (12.6% versus 12.5%, p>0.05).

**Table (6).** Comparison of prolactin level 4 months after treatment in all, non-recurrent and recurrent cases.
After 4 months, prolactin level was assayed, cabergoline group had significantly lower level when compared to bromocriptine group (11.5 versus 14, \( p=0.002 \)).

Stratifying cases into recurrent and non-recurrent hyperprolactinemia, revealed that those with non-recurrent hyperprolactinemia, cabergoline group had significantly lower level when compared to bromocriptine group (11.3 versus 13.5, \( p<0.001 \)). While those with recurrent hyperprolactinemia, bromocriptine and cabergoline groups had non-significant difference in prolactin level at 4 months after treatment (\( p>0.05 \)).

**Table 7.** Comparison of prolactin level 4 weeks and 4 months after treatment among the studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Bromocriptine group</th>
<th>Cabergoline group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ( \pm SD )</td>
<td>Mean ( \pm SD )</td>
</tr>
<tr>
<td>All cases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non recurrent</td>
<td>14 ( \pm 13.5 )</td>
<td>11.5 ( \pm 15.3 )</td>
</tr>
<tr>
<td>Recurrent</td>
<td>46.8 ( \pm 14.8 )</td>
<td>53.4 ( \pm 13.7 )</td>
</tr>
</tbody>
</table>

**Table 8.** Comparison of duration of treatment between studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Bromocriptine group</th>
<th>Cabergoline group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ( \pm SD )</td>
<td>Mean ( \pm SD )</td>
</tr>
<tr>
<td>Duration of treatment (weeks)</td>
<td>4.8 ( \pm 1.4 )</td>
<td>4.7 ( \pm 1.5 )</td>
</tr>
</tbody>
</table>

Fig 5. Change in prolactin level in studied groups throughout the study.

Stratifying cases according to recurrence in each treatment group, and comparing prolactin level 4 weeks and 4 months post treatment revealed that prolactin level decreased significantly in non-recurrent cases in both groups (\( p<0.001 \), \( =0.003 \) respectively).

On the other hand, prolactin level increased significantly in recurrent cases in both groups (\( p=0.001 \) for each group).

**Table 8.** Comparison of duration of treatment between studied groups.

|                      | Bromocriptine group | Cabergoline group | \( p \)    |
|----------------------|---------------------|------------------|           |
| Duration of treatment (weeks) |               |                  |           |
| Mean treatment duration in bromocriptine and cabergoline groups was about one month, with no significant difference between both groups (\( p>0.05 \)).

**Table 9.** Comparison of prolactin level normalization after treatment between studied groups.
Both groups showed non-significant differences for duration of prolactin level to be normalized. Although those received cabergoline had non significantly higher frequency of normalized females after 4 weeks when compared to Bromocriptine group (p>0.05).

### Outcome of studied groups

#### Table 10. Comparison of side effects between all studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Bromocriptine group</th>
<th>Cabergoline group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=110</td>
<td>N=110</td>
<td></td>
</tr>
<tr>
<td>All side effects</td>
<td>37</td>
<td>36</td>
<td>0.886</td>
</tr>
<tr>
<td>Constipation</td>
<td>15</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rectal irritation</td>
<td>18</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Abdominal cramps</td>
<td>11</td>
<td>0</td>
<td>0.001</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2</td>
<td>0</td>
<td>0.498</td>
</tr>
<tr>
<td>Headache</td>
<td>1</td>
<td>9</td>
<td>0.010</td>
</tr>
<tr>
<td>Dizziness and fainting</td>
<td>0</td>
<td>9</td>
<td>0.003</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>0</td>
<td>6</td>
<td>0.029</td>
</tr>
<tr>
<td>Hypotension</td>
<td>0</td>
<td>2</td>
<td>0.498</td>
</tr>
<tr>
<td>Bloating</td>
<td>0</td>
<td>11</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Fig 6. Side effects in all studied groups**

Bromocriptine group was significantly associated with constipation, rectal irritation, abdominal cramps (p<0.001, <0.001, =0.001 respectively).

Cabergoline group was significantly associated with headache, dizziness, fainting, nausea, vomiting, bloating (p=0.01, 0.003, 0.029, 0.001 respectively).

Diarrrhea, hypotension and noncompliance did not differ between both groups (p>0.05).

### Mean onset of side effects of bromocriptine and cabergoline groups was about one month, with no significant difference between both groups (p>0.05).

#### Table 11. Comparison of onset of side effects between studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Bromocriptine group</th>
<th>Cabergoline group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=110</td>
<td>N=110</td>
<td></td>
</tr>
<tr>
<td>Onset of side effects (weeks)</td>
<td>4.2 ±1.3</td>
<td>3.4 ±1.1</td>
<td>0.094</td>
</tr>
</tbody>
</table>

No significant differences were found between both groups regarding onset of side effects.

#### Table 12. Comparison of tolerability of the patients between all studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Bromocriptine group</th>
<th>Cabergoline group</th>
<th>p</th>
</tr>
</thead>
</table>

During the whole period of the study, some cases dropped out, 7 cases were dropped out from Bromocriptine group and 6 cases were dropped out from Cabergoline group.

No significant differences were found between both groups regarding tolerability of the patients (p>0.05).

Table 13. Comparison of reproductive outcome among the studied groups

<table>
<thead>
<tr>
<th></th>
<th>Bromocriptine group</th>
<th>Cabergoline group</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=110</td>
<td>N=110</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>pregnancy</td>
<td>23</td>
<td>20.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig 7. Reproductive outcome among the studied groups.

Among those received Bromocriptine, 20.9% get pregnancy, while among those received Cabergoline, 15.5% get pregnancy, with no significant differences between both groups (p>0.05).

5. Discussion

Prolactin is a polypeptide hormone that is synthesized in the anterior pituitary gland and secreted in a pulsatile manner. It plays central role in a variety of reproductive functions and lactation. Prolactin release in humans depends on physiological state and varies in response to different stimuli (12).

Hyperprolactinemia is a common endocrinological disorder; it could be physiological, pathological or idiopathic in origin. The predominant physiological consequence of hyperprolactinemia is suppression of pulsatile GnRH. The clinical manifestations of conditions vary significantly depending on the age and the sex of the patient. In women, it frequently leads to gonadal dysfunction including ovulatory disorder, menstrual disturbances, galactorrhea and infertility (5).

Bromocriptine methylate, as a dopamine agonist, is being used for treatment of hyperprolactinemia since a long time. It is proved to be effective in causing dramatic decline of serum prolactin after its oral use. However, it frequently causes adverse side effects if given orally like nausea, vomiting, fatigue, headaches, dizziness, and faintness in 50-70% of women (19). Non-oral approach may eliminate most of these symptoms (12).

The non-oral routes of administration of drugs avoid destruction or inactivation by the pH or enzymatic activity of the stomach or intestine, eliminate stomach irritation, and omit drug destruction by portal circulation by first pass through the liver. Moreover, these routes are convenient for patients who may be unable or unwilling to swallow medication and it is an effective route in the treatment of patients with vomiting episodes. For systemic effects, the mucous membranes of the rectum permit the absorption of many soluble drugs (14).

Cabergoline is an agonist specific to the D2 dopamine receptor and possesses a long half-life, allowing its weekly administration (7). Based on these characteristics and on several comparative studies, cabergoline has been considered superior to bromocriptine for the treatment of hyperprolactinemia and effective in many patients’ resistant to bromocriptine (4). To prove this hypothesis, we have designed a comparative study that evaluated rectal bromocriptine versus carbergoline in the treatment of hyperprolactinemia.
This study was conducted on 220 hyperprolactinemic patients suffering from gonadal dysfunction, galactorrhea, menstrual irregularities, mastalgia and infertility, this study was done at Benha university hospital outpatient clinics at the period from April 2018 to January 2020.

All the patients had serum prolactin level above 25 ng/dl at time of treatment & divided randomly (computerized) into two groups the first group received bromocriptine 2.5mg rectally daily up to 3 months. The second group received 0.5 mg of oral cabergoline each 3 days up to 3 months. serum prolactin was assayed after 4 weeks and 4 months from the beginning of the treatment the patients were observed for the success of the treatment as regard the normalization of serum prolactin level, restoration of gonadal function, milk suppression, pregnancy and tolerability.

This study is considered one of the first studies to assess rectal bromocriptine versus cabergoline in the treatment of hyperprolactinemia which renders comparison between its results and other researches difficult. However, many other researchers investigated the role oral bromocriptine versus oral cabergoline in the treatment of hyperprolactinemia.

The efficacy of bromocriptine has been evaluated in previous studies which demonstrated the benefit of bromocriptine in lowering serum prolactin level and restoring regular menstrual bleeding and relieving galactorrhea in the majority of patients, (19), which are in agreement with the results of this study. The percentage of reduction of serum prolactin level obtained in the present study in bromocriptine group (82.2%) that was better than (12) (69.2 %) and close to the value of 83% reported by (15).

The PRL normalization rate according to (12) where the success rates were 59%, and 67.7 %, respectively. Regarding CAB, the current results are in agreement with several other studies demonstrating the efficacy of CAB treatment in hyperprolactinemia. Our percentage of success (87.4 %) in attaining normal PRL levels in the CAB group falls within the margins of 82–93 % success of other studies. When we compared the CAB and BRC groups, we detected a significantly higher success rate on recovery of hyperprolactinemia in the CAB-treated group, which was in accordance with previous results (6). These findings clearly indicate that CAB is superior to BRC in normalizing PRL levels.

In our study among those who received Bromocriptine, 20.9% get pregnancy, while among those received Cabergoline, 15.5% get pregnancy, with no significant differences between both groups (p>0.05).

(14) found that Treatment with a DA restores ovulation in over 90% of women with prolactinoma and anovulatory infertility and their study confirms that DA use during the first five weeks of pregnancy is safe and not associated with an increase in the number of miscarriages, congenital malformations or other adverse neonatal and pregnancy outcomes beyond population normal ranges.

(10) found that Both bromocriptine and cabergoline, the two most commonly prescribed dopaminergic agents, share many characteristics and adverse effects. Cabergoline is, however, preferred, particularly in patients with prolactinoma, due to a greater therapeutic efficiency, a better tolerance and consequently, greater adherence to treatment and, finally, because of a more convenient administration regimen. cabergoline is administered once or twice weekly, while bromocriptine requires dosing every 8–24 hr. Compared with bromocriptine, cabergoline has a lower affinity for D1 receptors and stimulates 5HT2B receptors stronger. in our study we needed to administer bromocriptine rectally once only per day & this had improved the tolerability to bromocriptine.

(2) showed that CAB was more effective in controlling symptoms associated with prolactin hormone excess, normalizing serum PRL levels (87.4 vs. 41.4 %, p = 0.029), compared to BRC in a similar duration of treatment.

In our study Treatment with CAB had significantly lower PRL level when compared to BRC group at 4 weeks and 4 months. group (mean percentage change=64.9% versus 55%, p<0.001).

According to duration of treatment both groups showed non-significant differences for duration of prolactin level to be normalized. In comparing the ability of BRC and CAB to treat symptoms related to hyperprolactinemia, we found that CAB and BRC are equally efficacious in restoring regular menses, relieving galactorrhea, relieving mastalgia and improve the fertility. After 4 months, prolactin level was assayed, cabergoline group had significantly lower level when compared to bromocriptine group (11.5 versus 14, p=0.002).

Stratifying cases into recurrent and non-recurrent hyperprolactinemia, revealed that those with non-recurrent hyperprolactinemia, cabergoline group had significantly lower level
when compared to bromocriptine group (11.3 versus 13.5, p<0.001). While those with recurrent hyperprolactinemia, bromocriptine and cabergoline groups had non-significant difference in prolactin level at 4 months after treatment (p>0.05).

(18) found a low percentage (35.2%) of withdrawal of DA therapy in subjects with prolactinoma. Females, microprolactinomas, patients with lower initial serum PRL levels and with longer therapy duration all had a higher probability of seeing their therapy discontinued. Remission rates with bromocriptine range from 7 to 44%, whereas remission rates with cabergoline vary from 17 to 46%, or even 69% if only microprolactinomas are taken into account.

However, (9) found different results, suggesting that under the premise of maintaining normoprolactinemia, patients with reduced cabergoline intake to the lowest dose before withdrawal had a lower recurrence rate than patients taking higher cabergoline doses at the time of withdrawal.

(3) showed that in management of mastalgia carried on 140 women with premenstrual mastalgia were enrolled in the study the positive response rates to treatment were similar (BRC 66.6% and CAB 68.4%). The pain reduction rates for each month were also similar. Moreover, the pain reduction rate was maximum in the second month of treatment for both groups.

In our study 11 women & 8 women with mastalgia treated by BRC & CAB showed improvement within 4 weeks with minimal adverse side effects. There was no correlation between the baseline breast pain score and prolactin level but post-treatment pain reduction was well correlated with prolactin level.

The number of patients suffering from adverse effect in the present study was lower in the cabergoline group (32.7%) compared with the bromocriptine group (33.6%). There were no lower gastro intestinal symptoms in the cabergoline group compared with the bromocriptine group. But central & upper gastrointestinal symptoms were higher in CAB group. Our results are similar to those obtained in the previous studies that showed also fewer adverse effects with cabergoline and higher incidence with bromocriptine (4).

(2) showed that twenty-four (5.3 %) patients in the CAB group and 14 (29.1 %) in the BRC group reported side effects (p < 0.001). Eight out of 450 patients in the CAB group experienced constipation, nine headache, and seven dizziness. Headache was reported in four patients, stomach discomfort in four, dizziness in five, and sleepiness in one out of 48 patients in the BRC group which are less common than our study.

In our study BRC group was significantly associated with constipation, rectal irritation, abdominal cramps (p<0.001, <0.001, <0.001 respectively). While CAB group was significantly associated with headache, dizziness, fainting, nausea, vomiting, bloating (p=0.01, 0.003, 0.029, 0.001 respectively). Diarrhea, hypotension and noncompliance did not differ between both groups (p>0.05).

(9) reported adverse events or intolerance on CAB therapy. Mild and short-lasting adverse effects including postural hypotension, sleepiness and dizziness were reported in two patients, which spontaneously disappeared in the second week of treatment. No heart valve damage or valvular regurgitation was found in all patients. There was one patient who showed a reduction in left ventricular relaxation by ultrasound before CAB treatment, and his cardiac function was normal during the whole CAB treatment. Mean onset of side effects of BRC and CAB groups was about one month, with no significant difference between both groups (p>0.05).

(7) published that BRC and CAB can be administered intravaginally or rectally, which may lessen gastrointestinal symptoms by avoiding hepatic first pass effect, but this route of administration does not appear to reduce centrally mediated side effects in controversy to our study that rectal BRC route had diminished central side effects.

During the whole period of the study, some cases dropped out, 7 cases were dropped out from BRC group and 6 cases were dropped out from CAB group. No significant differences were found between both groups regarding tolerability of the patients (p>0.05). But (16) found that CAB is more tolerable than BRC in patients with hyperprolactinemia with less discontinuation’s episodes 1.2% vs 6%.

This study is the one of the first studies to compare Rectal BRC & oral CAB in management of female patients with hyperprolactinemia with no preference of any of both over the other & our results accepting changes and criticism and documentation for their efficacy, tolerability & side effects.

6. Conclusion

Bromocriptine & cabergoline are both effective in the treatment of hyperprolactinemia with restoration of gonadal function, fertility relieving of mastalgia & milk suppression. Use of rectal bromocriptine
decrease significantly the central & upper gastrointestinal adverse effect & tolerability in comparison to oral Bromocriptine. Cabergoline has superior effect in decreasing prolactin level than rectal bromocriptine. No significant difference was found regarding recurrence of hyperprolactinemia after treatment. Bromocriptine group was significantly associated with constipation, rectal irritation, abdominal cramps. Cabergoline group was significantly associated with headache, dizziness, fainting, nausea, vomiting, bloating. No significant differences were found between both groups regarding tolerability of the patients, reproductive outcome.

7. References


Endocrine Practice; vol. 20(6), pp. 608-616, 2014.


