Prolactin (PRL) is a single-chain peptide hormone secreted from lactotroph cells of the anterior pituitary gland. It mainly promotes milk secretion from mammary glands during postpartum period.

PROLACTIN SERUM ISOFORMS

Prolactin exists in three major circulating molecular isoforms: **Monomeric or little PRL** (molecular weight [MW] 23 kDa) - 80–95% of the total prolactin in healthy subjects and those with prolactinomas, **DimERIC or big PRL** (MW 45–60 kDa), **Multimeric / big-big PRL** or macroprolactin (MW > 150 kDa)

REGULATION OF PROLACTIN SECRETION

Prolactin is secreted in pulsatile manner following a circadian rhythm with the highest plasma concentration during sleep and the lowest in the morning about 2–3h after waking up. The predominant regulatory signal is the inhibition of prolactin secretion by the neurotransmitter, dopamine, from neurons in the hypothalamus.
Hyperprolactinemia is defined as the presence of abnormally high level of prolactin in the blood above normal levels of 10–28 ng/mL in women and 5–10 ng/mL in men. The prevalence ranges from 0.4% to as high as 9-17% in women with reproductive diseases.

**CLINICAL SIGNS AND SYMPTOMS**

- It is present in 10% to 25% women with secondary amenorrhea or oligomenorrhea, in 30% of women with galactorrhea or infertility, and in 75% of those with both amenorrhea and galactorrhea.
- Hyperprolactinemia causes hypogonadotropic hypogonadism (HH) which is due to suppression of pulsatile GnRH thus causing anovulation, hypoestrogenism and hence osteoporosis in perimenopausal women.
- When hyperprolactinemia is caused by a prolactinoma, additional pressure symptoms may include headaches, visual field defects and abnormal pituitary function.
- Hyperprolactinemia in men may result in decreased libido, impotence, decreased sperm production, infertility, weight gain and osteoporosis.

**ETIOLOGY**

Fig. 1. Regulation of prolactin secretion and causes of hyperprolactinemia

- Increased PRL production
  - Ovarian: poly cystic ovarian syndrome
  - Pituitary tumors: adenomas
  - Hypothalamic stalk interruption
  - Hypophysitis (inflammation)

- Abnormal molecules
  - Macroprolactinemia

- Reduced PRL elimination
  - Renal failure
  - Hepatic insufficiency

- Other causes, mechanism unclear

- Inhibitory signal
- Stimulatory signal
Potential causes of hyperprolactinemia.

- **Prolactinomas:** The most frequent cause of persistent hyperprolactinemia is the presence of a micro- (<10 mm diameter) or macro-prolactinoma (>10 mm). These pituitary tumours either may produce an excessive amount of prolactin or disrupt the normal delivery of dopamine from the hypothalamus to the pituitary. Raised prolactin levels can also be caused by pituitary adenomas co-secreting prolactin hormone.

- **Idiopathic hyperprolactinemia** accounts for 30–40% of cases where there is no obvious cause for the disorder and hypothalamic pituitary anatomy is normal.

- **Macroprolactinemia:** It is a condition where more than 60% of circulating PRL is made up of macroprolactin, which has low biologic activity instead of the normal 5–10%. Hyperprolactinemia due to macroprolactin is because of its lower renal clearance, longer half-life and its lower capability to activate hypothalamic dopaminergic tone, which negatively regulates the secretion of pituitary prolactin. These patients are usually asymptomatic and no medication or further tests are recommended.

### DIAGNOSIS

- Exclude physiological and pharmacological causes on history.
- Evaluate signs of hypothyroidism, hypogonadism, renal failure and visual field defects.
- **Measure Serum Prolactin. Also measure TSH, free T4, and creatinine levels** to rule out primary hypothyroidism and renal failure.
- PRL levels greater than 500ng/mL are commonly seen in macroprolactinoma. PRL levels > 250ng/mL usually indicate the presence of a prolactinoma, however, prolactinoma cannot be excluded in the presence of lower levels and PRL levels >100ng/mL are present in some patients with idiopathic hyperprolactinemia. Several drugs may cause PRL elevations above 200ng/mL.
- Hyperprolactinemia without an identified cause requires imaging of the hypothalamic-pituitary area. Although Computerized axial tomography (CAT) scan can be used, magnetic resonance image (MRI) with gadolinium enhancement provides the best visualization of the sellar area.

**Endocrine Society Clinical Practice Guidelines for Diagnosis.** See annexe 1 for level of evidence.

| To establish the diagnosis of hyperprolactinemia , a single measurement of fasting serum prolactin is recommended (2-3 hrs after waking up ) ; a level above the upper limit of normal confirms the diagnosis as long as the serum sample was obtained without excessive venipuncture stress. Dynamic testing of prolactin secretion for the diagnosis of hyperprolactinemia is not recommended | 1|⊕⊕⊕⊕ |
|---|---|
| In patients with asymptomatic hyperprolactinemia, the screening of macroprolactinemia is recommended by polyethylene glycol- (PEG-) precipitation method, and the confirmative and qualitative examinations include gel chromatography, protein A/G column and 125I-PRL binding studies | 2|⊕⊕⊕⊕ |
TREATMENT

Endocrine Society Clinical Practice Guideline for Management of drug-induced hyperprolactinemia

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Evidence Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>When there is a discrepancy between a very large pituitary tumor and a mildly elevated prolactin level, do serial dilution of serum samples to eliminate an artifact that can occur with some immune radiometric assays leading to a falsely low prolactin value (“hook effect”)</td>
<td>1</td>
</tr>
</tbody>
</table>
Dopamine agonists are the drug of choice.

<table>
<thead>
<tr>
<th>Dopamine receptor target sites</th>
<th>Bromocriptine</th>
<th>Cabergoline</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1 and D2</td>
<td>D1 (low affinity) and D2 (high affinity)</td>
<td></td>
</tr>
<tr>
<td>Duration of action</td>
<td>8–12 h</td>
<td>7–14 days</td>
</tr>
<tr>
<td>Half-life (h)</td>
<td>3.3</td>
<td>65</td>
</tr>
<tr>
<td>Available doses</td>
<td>1.0 and 2.5 mg scored tablets; 5 and 10 mg capsules</td>
<td>0.5 mg scored tablets</td>
</tr>
<tr>
<td>Typical dose</td>
<td>2.5 mg/day in divided doses</td>
<td>0.5 mg/week or twice-weekly</td>
</tr>
<tr>
<td>Dosing regimens, starter packs, dosage</td>
<td>Start on 1.25–2.5 mg/day at bedtime. Gradually increase to a median of 5.0–7.5 mg/day and a maximum of 15–20 mg/day</td>
<td>Start at 0.25–0.5 mg twice-weekly. Adjust by every 2–4 months according to serum prolactin levels</td>
</tr>
<tr>
<td>Advantages</td>
<td>Long history of use; does not appear to be teratogenic; inexpensive</td>
<td>Good efficacy; low frequency of adverse events; may be useful in bromocriptine-resistant patients; weekly or twice-weekly dose</td>
</tr>
<tr>
<td>Disadvantages</td>
<td>Tolerance; recurrence; resistance; multiple daily dosing</td>
<td>Not yet indicated for use during pregnancy</td>
</tr>
<tr>
<td>Common side effects</td>
<td>Nausea, headache, dizziness, abdominal pain, syncope, orthostatic hypotension, fatigue</td>
<td>Milder and less frequent compared with bromocriptine</td>
</tr>
</tbody>
</table>

Table 1. Comparison between Bromocriptine and Carbergoline in the treatment of hyperprolactinemia.
### Endocrine Society Clinical Practice Guideline for Management of Prolactinoma

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use dopamine agonist therapy to lower prolactin levels, decrease tumor size,</td>
<td>1</td>
</tr>
<tr>
<td>and restore gonadal function for patients harbouring symptomatic prolactin-</td>
<td></td>
</tr>
<tr>
<td>secreting microadenomas or macroadenomas</td>
<td></td>
</tr>
<tr>
<td>Cabergoline is preferred to other dopamine agonists because it has higher</td>
<td>1</td>
</tr>
<tr>
<td>efficacy in normalizing prolactin levels, as well as a higher frequency of</td>
<td></td>
</tr>
<tr>
<td>pituitary tumor shrinkage</td>
<td></td>
</tr>
<tr>
<td>Do not treat asymptomatic patients harbouring microprolactinomas with dopamine</td>
<td>2</td>
</tr>
<tr>
<td>agonists</td>
<td></td>
</tr>
<tr>
<td>Treat with dopamine agonist or oral contraceptive in patients with amenorrhea</td>
<td>2</td>
</tr>
<tr>
<td>caused by a microadenoma</td>
<td></td>
</tr>
<tr>
<td>With careful clinical and biochemical follow-up, therapy may be tapered and</td>
<td>2</td>
</tr>
<tr>
<td>perhaps discontinued in patients who have been treated with dopamine agonists</td>
<td></td>
</tr>
<tr>
<td>for at least 2 years, who no longer have elevated serum prolactin, and who</td>
<td></td>
</tr>
<tr>
<td>have no visible tumor remnant on MRI</td>
<td></td>
</tr>
</tbody>
</table>

### Endocrine Society Clinical Practice Guideline for Management of Resistant and Malignant Prolactinoma

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Level of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>For symptomatic patients who do not achieve normal prolactin levels or show</td>
<td>1</td>
</tr>
<tr>
<td>significant reduction in tumor size on standard doses of a dopamine agonist,</td>
<td></td>
</tr>
<tr>
<td>increase the dose to maximal tolerable doses before referring the patient for</td>
<td></td>
</tr>
<tr>
<td>surgery</td>
<td></td>
</tr>
<tr>
<td>Patients resistant to bromocriptine be switched to cabergoline</td>
<td>1</td>
</tr>
<tr>
<td>Trans-sphenoidal surgical resection of the prolactinoma remains the main</td>
<td>2</td>
</tr>
<tr>
<td>option for patients who may refuse or do not respond to long-term</td>
<td></td>
</tr>
<tr>
<td>pharmacological therapy</td>
<td></td>
</tr>
<tr>
<td>Radiotherapy and/or estrogens are also reasonable choices if surgery fails.</td>
<td>2</td>
</tr>
<tr>
<td>Chemotherapy with temozolamide is limited to resistant and malignant</td>
<td>2</td>
</tr>
<tr>
<td>prolactinomas</td>
<td></td>
</tr>
</tbody>
</table>
Fig. 2 - Management of Hyperprolactinemia

1. Prolactin level
   - Macroprolactinemia
   - Repeat measurement
   - Rule out secondary causes

2. Pathological hyperprolactinemia
   - MRI of pituitary
     - Normal pituitary
     - Micro lesion (<10 mm)
     - Macro lesion (≥10 mm)

3. Micro lesion (<10 mm)
   - Asymptomatic
     - Follow-up prolactin measurement once yearly
   - Symptomatic
     - Treatment (see Fig. 3)

4. Macro lesion (≥10 mm)
   - Correct underlying cause: replace thyroid hormone, remove/substitute potentially offending medication
TREATMENT OF PROLACTINOMAS

During normal pregnancy, serum prolactin rises progressively to around 200-500 ng/mL. The Endocrine Society clinical guidelines for the diagnosis and treatment of hyperprolactinemia during pregnancy

| Women with prolactinomas be instructed to discontinue dopamine agonist therapy as soon as they discover that they are pregnant | 1|
| In selected patients with macroadenomas who became pregnant on dopaminergic therapy and who have not had prior surgical or radiation therapy, it may be prudent to continue dopaminergic therapy throughout the pregnancy, especially if the tumor is invasive or is abutting the optic chiasma | 1|
| In pregnant patients with prolactinomas, do not perform serum prolactin measurements during pregnancy | 1|
| Pituitary MRI during pregnancy in patients with microadenomas or intrasellar macroadenomas is not recommended unless there is clinical evidence of tumor growth such as visual field compromise | 1|
| Women with macroprolactinomas who do not experience pituitary tumor shrinkage during dopamine agonist therapy or who cannot tolerate bromocriptine or cabergoline be counseled regarding potential benefits of surgical resection before attempting pregnancy | 1|
| Visual field assessment followed by MRI without gadolinium in pregnant women with prolactinomas is recommended who experience severe headaches and/or visual field changes | 1|
| Bromocriptine therapy is recommended in patients who experience symptomatic growth of a prolactinoma during pregnancy | 1|

CONCLUSIONS

- Hyperprolactinemia is a common pituitary hormone disorder usually found in both sexes with abnormal sexual and/or reproductive function or with galactorrhea.
- Asymptomatic patients with microprolactinemia do not require any treatment.
- Cabergoline is the drug of choice, however in pregnancy Bromocriptine is preferred.
- Persistent Hyperprolactinemia without an identified cause requires imaging of the hypothalamic-pituitary area.
- Giant or aggressive prolactinomas may require multiple approach involving surgery, radiotherapy or both.
Table 2 - Grade Classification of Guideline Recommendations

<table>
<thead>
<tr>
<th>QUALITY OF EVIDENCE</th>
<th>High Quality</th>
<th>Moderate Quality</th>
<th>Low Quality</th>
<th>Very Low Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description of Evidence</td>
<td>• Well-performed RCTs  • Very strong evidence from unbiased observational studies</td>
<td>• RCTs with some limitations  • Strong evidence from unbiased observational studies</td>
<td>• RCTs with serious flaws  • Some evidence from observational studies</td>
<td>• Unsystematic clinical observations  • Very indirect evidence observational studies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>STRENGTH OF RECOMMENDATION</th>
<th>Strong (1): “We recommend...” Benefits clearly outweigh harms and burdens, or vice versa</th>
<th>Conditional (2): “We suggest...” Benefits closely balanced with harms and burdens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

References

IFS SECRETARIAT
302, 3rd Floor, Kailash Building
Kasturba Gandhi Marg, C.P, New Delhi-110001
Contact No. 9899308083 Email Address - indianfertilitysocietydelhi@gmail.com Web - indianfertilitysociety.org
Welcome to FERTIVISION 2019

Dear Friends,

On behalf of the Indian Fertility Society (IFS), we are extremely pleased to announce and cordially invite you to the much awaited academic event – the 15th National Annual Conference - Fertivision 2019, to be held on 6th, 7th & 8th December 2019 at Hotel The Leela Ambience, Gurugram, New Delhi / NCR, India.

This conference is aimed to provide the most comprehensive academic platform in the field of Infertility and Assisted Reproductive Technology (ART)” befitting the theme of the meeting “Beyond Tomorrow”

Renowned and leading expert faculty from around the world would gather and deliver talks in our cutting edge scientific program which will not only enrich your current knowledge and clear all doubts faced in day-to-day clinical practice, but will also enlighten you about the latest innovations and ongoing research.

A large number of renowned international faculties have already confirmed their participations till date. The pre-congress workshops on 6th December are specially designed for informal in-depth training with hands on sessions on simulators and live, where ever feasible. There will be 4 simultaneous running streams on 7th & 8th December covering a wide variety of topics, enabling you to choose the deliberations specific to your area of interest and clinical practice. We are having a dedicated hall for the esteemed embryologist friends.

The best oral and poster presenters under various categories and the quiz winners will be honored with special awards and prizes. Do join us in large numbers and update your knowledge with most updated current standards in clinical practice, as well as get inspired to innovate further to overcome remaining enigmatic issues!

The three days of scientific program will encompass didactic lectures, keynote presentations, panel discussions and orations. There will be 9 Pre-conference workshops based on Ovulation Induction, Ultrasound, Andrology, Embryology, Hands on Embryo Transfer, Ovum Pickup and PGS and more. These workshops will be in addition to the special state of the art workshops by the faculty from IFFS and ESHRE. We expect delegates across India, Sri Lanka, Bangladesh, Nepal, Middle - East Countries and African Nations and the arrangements are being made to accommodate more than 2500 delegates.

The exhibition area will be one of the highlights of the conference. Exhibiting provides tremendous benefits to both participating industry and the society. Tea, coffee and lunch will be served confluent with the trade area to allow optimal interaction between the trade companies and delegates during beverage and lunch breaks.

We invite you to participate in the Fertivision 2019 and exchange your expertise with more than 2500 specialists in the field of Assisted Reproduction.

We look forward to your active participation and suggestions for successful conduct of the conference.

With Our Best Regards
and All Executive Committee of Current IFS team

Invitation

Dr. M Gouri Devi
Organizing Chairperson
FERTIVISION 2019

Dr. Pankaj Talwar
Organizing Secretary
FERTIVISION 2019
Title Prof/ Dr/ Mr/ Ms ____________________________
First Name ____________________________________ Last Name ____________________________
Institution ____________________________ IFS Member No. ____________________________
Correspondence Address ________________________________________________________________
City __________________________________________ Pin Code ____________________________ State __________________________
Mobile No. ____________________________ Email _____________________________________________

Choose from 10 Pre Conference Workshops | 6 December  
Choose Any 1 Workshop

1) □ IFFS Workshop on Do’s and Don’ts in Ovarian Stimulation
2) □ Reproductive Surgery
3) □ Ultrasonography Imaging In Infertility
4) □ Andrology & Semenology
5) □ Ovum Pickup and Embryo Transfer (With Simulators)
6) □ Cryobiology
7) □ QA / QC
8 A) □ Counselling & Psychological Support
8 B) □ Research Methodology
9) □ PGT and Genomics

Registration Fees

<table>
<thead>
<tr>
<th>Category</th>
<th>Early Bird Fees Till 15th July 2019</th>
<th>Regular Fees Till 15th October</th>
<th>Onspot</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFS Member</td>
<td>INR 10500</td>
<td>INR 12500</td>
<td>INR 14500</td>
</tr>
<tr>
<td>Non IFS Member</td>
<td>INR 12500</td>
<td>INR 14500</td>
<td>INR 16500</td>
</tr>
<tr>
<td>Conference Registration plus Life Time IFS Membership</td>
<td>INR 14500</td>
<td>INR 16500</td>
<td>INR 18500</td>
</tr>
<tr>
<td>Gynaecologist</td>
<td>INR 15000</td>
<td>INR 17500</td>
<td></td>
</tr>
</tbody>
</table>
| Embryologist                    | 18 Hrs of World Class Academic Program with Access to Best & Brightest International & National Faculty
| 3 Lunches and 6 Tea / Coffee Served During the Conference on 6, 7 & 8 December
| Banquet Dinner on 7 December
| Conference Kit (Including Bag, Badge, Notepad, Certificate & Pen)
| 1 Pre Conference Workshop
| Accompanying Person is Entitled for Food Coupons Only
| PG Students (No Dinner)          | INR 6000                            | INR 7000                       | INR 8000        |
| Accompanying Person             | INR 10500                           | INR 11500                      | INR 12500       |
| Foreign Delegates               | $ 350                               | $ 400                          | $ 500           |

Conference Registration Fees Includes

- 18 Hrs of World Class Academic Program with Access to Best & Brightest International & National Faculty
- 3 Lunches and 6 Tea / Coffee Served During the Conference on 6, 7 & 8 December
- Banquet Dinner on 7 December
- Conference Kit (Including Bag, Badge, Notepad, Certificate & Pen)
- 1 Pre Conference Workshop
- Accompanying Person is Entitled for Food Coupons Only

Cancellation Policy

- Cancellation till 31st October, 2019 – 50% Refund.
- Cancellation from 1st November, 2019 – No Refund.
- All refunds will be made after the congress.

Cheque / Draft No. ________________ Total Amount ________________

Note: Kindly email us bank deposit slip / UTR number once you made the payment for our record. Payment confirmation will take 7-10 working days post deposit of cheque, DD or RTGS

Mode of Payment

1. Bank Draft/Cheque - To be made in favor of “INDIAN FERTILITY SOCIETY”
2. Bank Transfer Details
   IFS Account Name: Indian Fertility Society
   Account Number: 50562010067180
   IFSC Code : ORBC0100179
   Bank Name: Oriental Bank of Commerce
   Branch: Connaught place, New Delhi- 110001

Please send Registration Form along with cheque / draft at the following address:
www.fertivision2019.com
Looking for your Own IVF Lab setup?

**Biocell Enterprise** offers “One Stop Shop” solutions for all your needs in ART

We provide complete hand holding support to setup your very own IVF (ART) centre.

Services offered:

- Site visit & Lab design assistance
- Supply & Installation of high end IUI-IVF-ICSI equipment
- Supply of Labware & Consumables
- Supply of entire range of IVF media
- IVF Lab Quality Control services
- Clinical and Embryology Support
- Trainings
- AMC & After Sales Support

For any query or information please contact us at:

Mobile: +91 9891470707
Email: biocellenterprise@gmail.com