VOLUME - I

INTROSPECT

E-Journal by **OGSOS**, *Salem.*

JAN-2023

THE OBSTETRIC AND GYNAECOLOGICAL SOCIETY OF SALEM

Dr.G.JAYAMALA

President OGSOS

Dr.SARAVANA KUMAR

VICE PRESIDENT - OGSOS

Dr.L.SHANMUGAVADIVU

Secretary OGSOS

Dr.SURESH KRISHNAAMOORTHI

Hon.TREASURER - OGSOS

Dr. DHAVASHREE V

JOINT SECRETARY - OGSOS

EXECUTIVE COUNCIL MEMBERS

JOURNAL EDITORS

DR. KAVITHA NAGARAJAN,
MD OG, MRCOG, FRM, MICG.,

DR. ANUREKHA J P,
MD OG, DNB , FRM, FICOG.,

DR. MADHUMITHA ARUNKARTHIK
MS, DNB, FRM, FMAS.,

OUTREACH PROGRAMMES

DR. K. SUNDARA MEENAKSHI
MS OG, FICS.,

DR. P. SATHYA SUDHAKAR
DGO, DRM.,

DR. G. KIRANA SELVI,
MS OG, FMAS, DRM, FICS.,

SCIENTIFIC COMMITTEE

DR. D. NARMADA
MD OG.,

DR. ESAI AMUTHU
DGO, DNB, DRM.,

DR. ASHWIN RAO
MS, FRM, FMAS, PGDMLS.,

WEBSITE MAINTENANCE COMMITTEE

DR. G. DHIVYA,
DGO, DNB, MRCOG, DMAS, CIMP, MNAMS.,

DR. ARUNITA NANDY GOUTHAM
MS OG , FMAS, DRM.,

MTP COMMITTEE

DR. R. SUGANTHI
MD OG, DNB, MRCOG.,

DR. P. SATHYA SUDHAKAR
DGO, DRM.,

TNMC CREDIT POINTS COORDINATORS

DR. R.M. SORNAM
MD OG, Dip IBLM.,

DR. K. JEYALAKSHMI
DGO, DNB, MRCOG.,

NEW MEMBERS MOBILISING COMMITTEE

DR. ARUNITA NANDY GOUTHAM,
MS OG , FMAS, DRM.,

DR. D. PALLAVI
MD OG, FRM, DRM.,

ACADEMIC CO-ORDINATOR

DR. G. PREMAPRIYA
MS OG,, DNB., MNAMS., MRCOG.,

FOGSI VICE PRESIDENT'S NOTE

HAPPY NEW YEAR & HAPPY PONGAL!

FOGSI Presidential year 2023 has started off well with mega events – Anemia Mukht Yatra at Rishikesh and the mammoth AICOG at Kolkatta. And to this celebration there is one more addition from Salem – the Release of E Journal from Salem.

Salem OG Society has always been in the forefront in accepting and adopting newer concepts and activities in empowering women – be it in conducting the Adolescent Rally under Dr. Gnanasankar Natesan, conducting Badlaav's Clinic, the pet subject of our FOGSI President Dr. Hrishikesh Pai. And it has won laurels too – Winning the First Prize in the poster contest on Na Na Anemia Yatra at Jan 2023 AICOG, Kolkata. Their infectious zeal is rightly visible in the conduct of CMEs and Conferences.

I am amazed at the spike in their adrenalin level, proof of which is in the speed of their E Journal release. Kudos to Dr. Jayamala, President and Dr. Shanmugavadivu, Secretary, OGSOS. No doubt this scientific temper will flourish and benefit all OGcians not only in Salem and around but all over Tamilnadu and India.

I wish every success in this endeavour. I also congratulate all the members, editorial team and the executive committee of Salem Society.

JAI HO!

Prof. Dr. S. SAMPATHKUMARI,
MD, DGO, FICOG, FCD, FIME,
VICE PRESIDENT, FOGSI SOUTH ZONE

EDITOR'S NOTE

We are pleased to proudly present to you "INTROSPECT" – Official online journal from Obstetric and Gynaecological Society of Salem (OGSOS), commenced in order to acknowledge and recognize the work done by our very own members.The online media has become a vital component for the dissemination of knowledge and an imperative vehicle for wide access.

With this in mind, the first edition of our E-Journal has been curated meticulously. Our OGSOS has always turned heads, be it academics, conferences, skills, culturals, etc. This is our next step, where our vision has taken shape and this endeavor marks a major milestone in taking our society to greater heights.The objective of this journal is to promote research, share ideas, help in day to day clinical practice and promote a spirit of oneness among us. This would provide an exciting opportunity to showcase our work and share our skills. The journal aspires to be vibrant, engaging and accessible, and at the same time integrative and challenging. It will continue to evolve with fresh ideas and guidance at each step,encouraging debates and discussions.

We hope that this journal will offer ample opportunity to our members to learn about and reflect upon the practices and possibilities and help in their achievements and challenges at work.We are privileged to have the expertise and enthusiasm of our authors and believe that every member will play a pivotal role in leading the journal through the exciting phase of its development. Finally we remain very grateful to our President, Vice President, Secretary and Patrons for constant encouragement and guidance. Let us all join together in solidarity and introspect our ideas, thoughts and practices,with the aim of better practices and better outcomes, following the footsteps of our seniors and setting examples for those next in line.

HAPPY LEARNING!

DR. KAVITHA NAGARAJAN,
MD OG, FRM, MRCOG, MICG.,

DR. ANUREKHA J P,
MD, DNB, FRM, FICOG

DR. MADHUMITHA ARUNKARTHIK
MS, DNB, FRM, FMAS.

PRESIDENT'S NOTE

Greetings from the desk of the President of OGSOS! It is indeed a proud moment to be in this chair amidst our highly talented and esteemed members!

CHANGE is the only CONSTANT thing in this world. Likewise, Medical practice is something that keeps changing with newer inventions, interventions and evidence based modalities. So, it is inevitable for us to keep up with the trend, update our knowledge and enhance our clinical skills especially in this era, where patients are Google doctors with first hand information. We try hard to update ourselves by attending conferences, CMEs, reference articles and juggle between busy practice and family needs.

With our team of Editors, it is our maiden effort to bring out an E-journal every 4 months authored by our very own members. Our aim is to provide evidence based protocols, interventions and practical points needed for our day to day practice. My vision is to bring near uniform practice amongst us which is evidence based, for the benefit of our women to get standard treatment. Evidence based practice and following guidelines protect us legally too.

We have tried to cover all subspecialities with the experts in each. Hope our efforts help you in your practice. We are open to any suggestions to improve our quality and content of the journal.

I thank my team of council members who share responsibility and for their sincere efforts in all our proceedings. My heartfelt gratitude to all the enthusiastic authors for their contribution to the first edition of our journal!

My sincere thanks to my team of editors for their enthusiasm and hardwork shown in bringing out this journal!

Dr. G. JAYAMALA,
DOWH (IRE), MRCOG (UK), MRCPI (OG)., DRM.,
CONSULTANT, RAINBOW HOSPITAL

SECRETARY'S NOTE

Greetings and welcome to the first E-Journal of Obstetric and Gynaecological Society of Salem. I am honored to be the Secretary of our OGSOS family and I take this opportunity to thank our society members for their love and confidence on me and look forward to our continued teamwork to achieve greater excellence.

It's our proud moment in releasing the very first E-Journal of OGSOS and the credits are deeply shared by all the members of our OGSOS family. I am deeply obliged to Dr.G.Jayamala, the President of OGSOS who was the brain behind this baby.

My special thanks to the Journal committee members who played tremendous role in this beautiful compilation. In the months to come let us all join hands in making this E-Journal grow with impact factor and achieve its position among the indexed journals. For this, I kindly encourage all the OGSOS society members to actively contribute with original articles.

The culmination of our efforts in bringing out this first E-Journal shall lay the fundamental foundation of our society in uplifting the academic wing and thereby benefitting our society members by constant updation and knowledge upgradation. I believe that continued stability is dependent on continued support of its members and therefore I would encourage all members to actively participate and contribute to the upcoming issues.

LONG LIVE OGSOS!

Dr. L. SHANMUGAVADIVU, MD., (OG)
ASSOCIATE PROFESSOR, DEPARTMENT OF OG,
GMKMCH

TABLE OF CONTENTS PAGE

EVOLUTION AND EXCELLENCE OF THE NEW WHO PARTOGRAM

Dr. L. SHANMUGAVADIVU,
MD., (OG)
SECRETARY, OGSOS
ASSOCIATE PROFESSOR, DEPARTMENT OF
OBSTETRICS AND GYNAECOLOGY, GMKMCH

INTRODUCTION :

Every day many women die in pregnancy and childbirth, most of which are preventable. Regular and timely labour monitoring by partograph is of utmost importance. Monitoring of labour has been identified as a high priority for preventing maternal mortality by WHO.

EVOLUTION OF THE PARTOGRAPH :

The development of partograph provided health workers a pictorial overview of labor which can identify pathological labor to allow early intervention.

Most guidelines for normal human labor progress are derived from Friedman's clinical observations of women in labor. In 1954, he introduced the concept of partogram by graphically plotting cervical dilatation against time. The curve obtained was a sigmoid curve. He divided the first stage of labor into latent phase and active phase. Active phase was further divided into acceleration, maximum slope and deceleration.

Philpott's partograph is an improved version of the labor curve. He introduced the alert line and action line.

LAUNCH OF WHO PARTOGRAM :

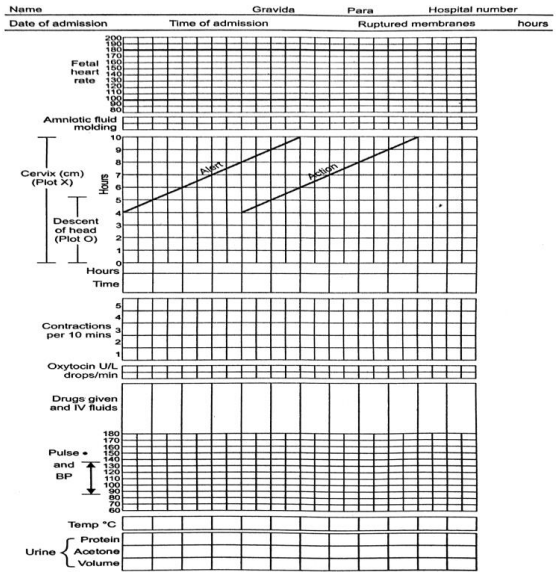
In 1987, WHO launched the safe motherhood initiative, since then WHO has published three different types of partographs.

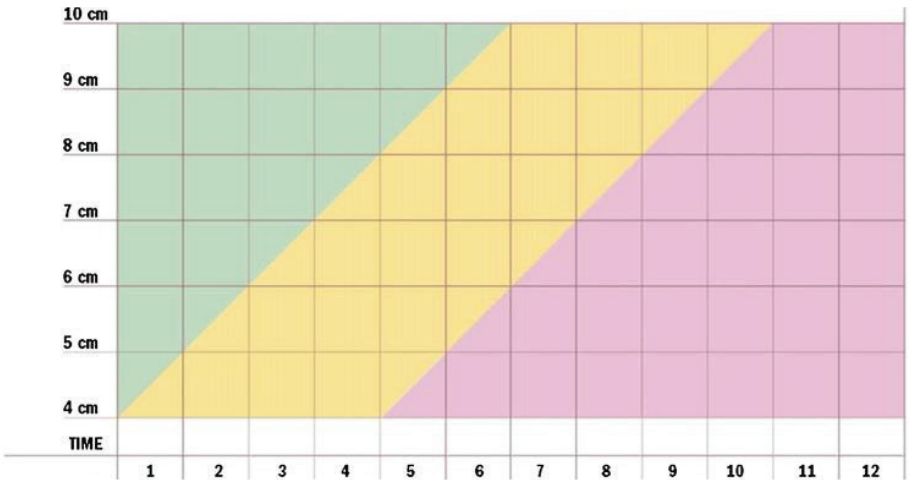
The first of these partograms also known as composite partograph includes latent phase of 8 h and an active phase starting at 3-cm cervical dilatation. It has an alert line with a slope at 1 cm/h and the action line 4 h to the right and parallel to alert line. It also provides space for recording descent of fetal head, maternal condition, fetal condition and medicines administered.

WHO MODIFIED PARTOGRAM :

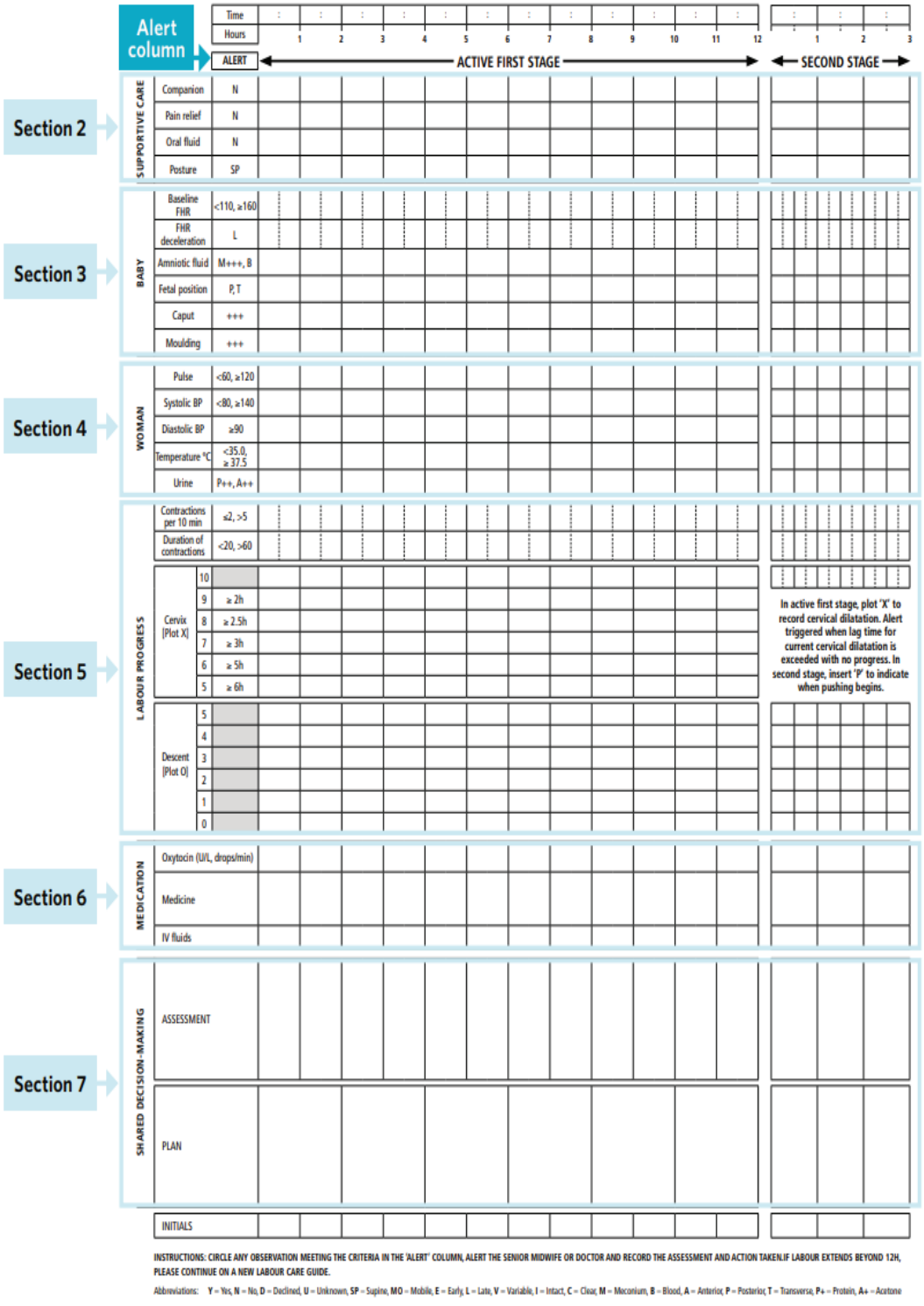
WHO modified the partograph in 2000, the latent phase was excluded, and the active phase commenced at 4-cm cervical dilatation. The other features remained the same. The reason for excluding the latent phase was more likelihood of interventions due to prolonged latent phase which was over diagnosed. There was also difficulty reported in transferring the dilatation from latent phase to active phase.

WHO further modified the partograph for the third time. This simplified partograph is color-coded. The area to the left of the alert line is colored green representing the normal progress. The area to the right of action line is colored red indicating dangerously slow progress. The area between the alert and action line is colored amber indicating the need for greater vigilance. Simplified partogram was rated more user-friendly over composite partogram.





WHO LABOUR CARE GUIDE NEWER RECOMMENDATION



STRUCTURE OF WHO - LABOUR CARE GUIDE :

The seven sections, adapted from the previous partograph design are: Identifying Information and Labour Characteristics at Admission, Supportive Care, Care of the Baby, Care of the Woman, Labour Progress, Medication, Shared Decision-making.

PRINICIPAL AIMS OF LABOUR CARE GUIDE :

To guide the monitoring and documentation of the well-being of women and babies and the progress of labour, to guide skilled health personnel to offer supportive care throughout labour, to ensure a positive childbirth experience for women, to assist skilled health personnel, to promptly identify and address emerging labour complications, to prevent unnecessary use of interventions in labour, to support audit and quality improvement of labour management.

TO MAXIMIZE THE POSITIVE OUTCOME :

To ensure the systematic and consistent application of the LCG, health providers are encouraged to use the Assess -> Record -> Check -> Plan approach, which involves: Assess (assess the well - being of woman and her baby, and progress of labour) Record (document labour observations) Check reference threshold (compare labour observations with reference values in the "Alert" column) Plan (decide whether and what interventions are required, in consultation with the woman, and document accordingly).

CRITICAL EVALUATION WHO LCG OVER THE WHO MODIFIED PARTOGRAPH ARE :

IMPROVED RESPECTFUL CARE DURING LABOUR AND CHILDBIRTH :

Providing and documenting non-clinical intrapartum practices (i.e. labour companionship, pain relief, maternal position, oral fluid intake) ensure women's comfort and well-being during labour and childbirth and thus their experience of care and improved outcomes.

IMPROVED LABOUR SUPPORT AND CARE LEADING TO IMPROVED OUTCOMES :

The partograph does not document nonclinical intrapartum practices that are essential components of care that should complement any necessary clinical interventions to optimize the quality of care provided to woman and her family.

MORE ACCURATE ASSESSMENT OF FETAL WELLBEING :

The partograph only includes assessment of the fetal heart rate; the WHO LCG requires additional assessment and documentation of presence/absence of decelerations. The identification of decelerations is important because there are

specific interventions for each type of deceleration that can improve fetal outcome; without this information, the fetus' status could deteriorate rapidly and result in poor peripartum outcomes.

MORE ACCURATE ASSESSMENT OF LABOUR PROGRESS :

The partograph only includes assessment of moulding of the fetal head; the WHO LCG requires additional assessment and documentation of caput. Marked caput can be a sign of cephalopelvic disproportion and is an important part of assessing poor progress in labour.

TIMELIER, EVIDENCE-BASED INTERVENTIONS :

Unlike the partograph, the WHO LCG has reference threshold values for labour observations that define normal, expected ranges for the different parameters. If an abnormal observation is identified, providers are triggered to reflect and then undertake a specific action(s).

CONCLUSION :

Introduction of WHO Labour Care Guide will facilitate effective implementation of the 2018 WHO recommendations: Intrapartum care for a positive childbirth experience and promote a shift towards improving the experience of childbirth, thus improving quality of care during labour and childbirth and maternal and newborn outcomes for all pregnant women.

THE DRUG CARBETOCIN - THE BOSS

Dr. SUNDARA MEENAKSHI,
MS.OG, F.I.C.S
CONSULTANT, SRI MEENAKSHI WOMEN CARE CLINIC,
PRIYAM SPECIALITY HOSPITALS

INTRODUCTION :

PPH causes ¼ of all maternal death world wide. PPH leading cause of maternal death in India. Prevalence in India is 38% and accounts for up to 56% of maternal death. PPH occurrence is about 2% to 4% vaginal delivery and 6% after CS. PPH is defined as cumulative blood loss of > 500ml following vaginal delivery and > 1000ml following CS. Blood loss causing haemodynamic instability is also termed PPH.

ETIOLOGY OF RISK FACTORS :

TONE	TRAUMA	TISSUE	THROMBIN
70- 90%	10-20%	10%	1%

CAUSES OF ATONIC PPH :

1 . Over distended uterus
   (a) multiple pregnancy
   (b) poly hydramnios
   (c) fetal macrosomia
2. Muscle Fatique
3. Uterine infections
4. Fibroid uterus
5. Uterine Inversion
6. GA

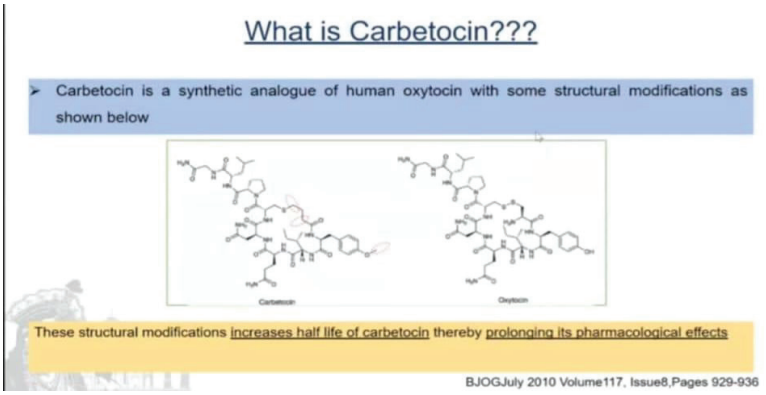
PREVENTION BETTER THAN CURE : AMTSL

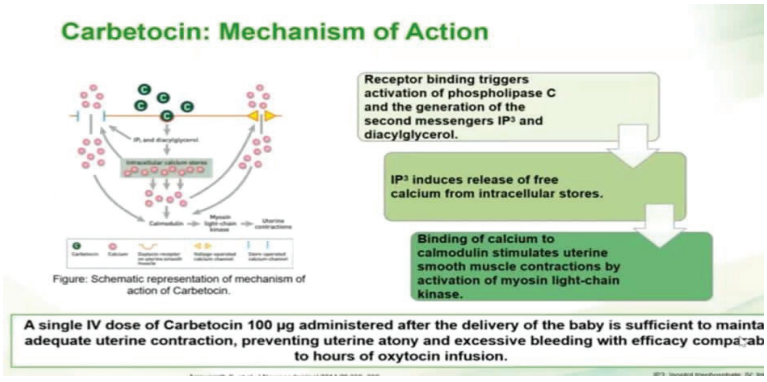
1. Treat anaemia
2. Ensure SBA
3. Using partogram to avoid prolonged / obstructed labour
4. Avoid unnecessary induction/augmentation

5. Ensure asepsis
6. Avoid fundal pressure
7. Controlled head delivery

WHO RECOMMENDATION :

Prophylactic effective uterotonics should be routinely offered in the management of the third stage of labour in all women as they reduce the risk of PPH and only one uterotonic should be used. Prophylactic uterotonics reduce the risk of PPH by almost 50%. The new drug CARBETOCIN, synthetic analogue of oxytocin, has now evolved as a game changer for the prevention of PPH.





COMPARE TO OXYTOCIN :

CARBITOCIN HAS SIMILAR EFFICACY AND SIMILAR ONSET OF ACTIONS
GOOD TOLERABILITY
LONG HALF LIFE AND SUSTAINABILITY
REDUCED NEED FOR ADDITIONAL UTEROTONICS
HEAT STABLE
LESS POTENT THAN OXYTOCIN AT V2 RECEPTORS
REDUCING THE RISK OF HYPONATREMIA

PHARMACOKINETICS AND PHARMOCODYNAMICS :

ABSORPTION - Peak concentration within 20 – 30 min

BIO AVAILABILITY - 80 %

HALF LIFE - Distributions half life – 5.5 min

Elimination half life – 41 min

METABOLISM - Eliminated primarily by non renal routes

MECHANISMS OF ACTIONS :

Binds to the same myometrial receptors as oxytocin

1. Durations of action after single dose - 1 hr given IV & 2 hrs given IM
2. Prolonged actions - longer half life. No drug interactions have been identified with anaglesics , spasmolytics and agents used for epidural or spinal anaesthesia.

CONTRANDICATIONS :

During pregnancy and labour before delivery of the infant

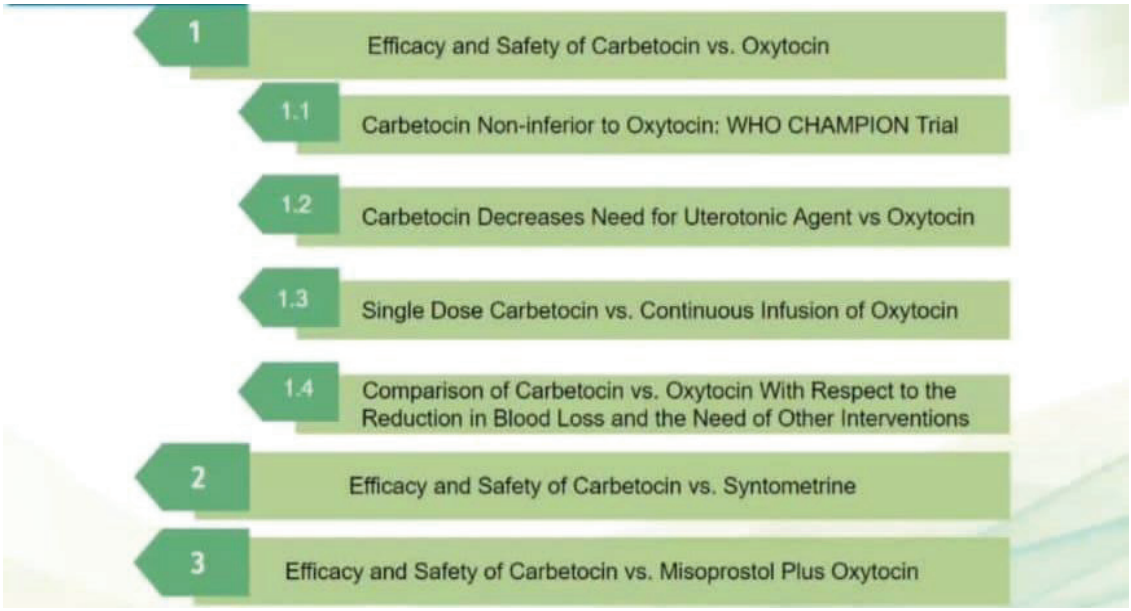
1. Carbetocin must not be used for the induction of labour
2. Hypersensitivity to carbetocin or oxytocin
3. Hepatic or renal disease
4. Serious cardiovascular disorders
5. Eclampsia
6. Epilepsy
7. Used with caution in PIH, SEVERE PET and ASTHMA

ADVERSE REACTIONS

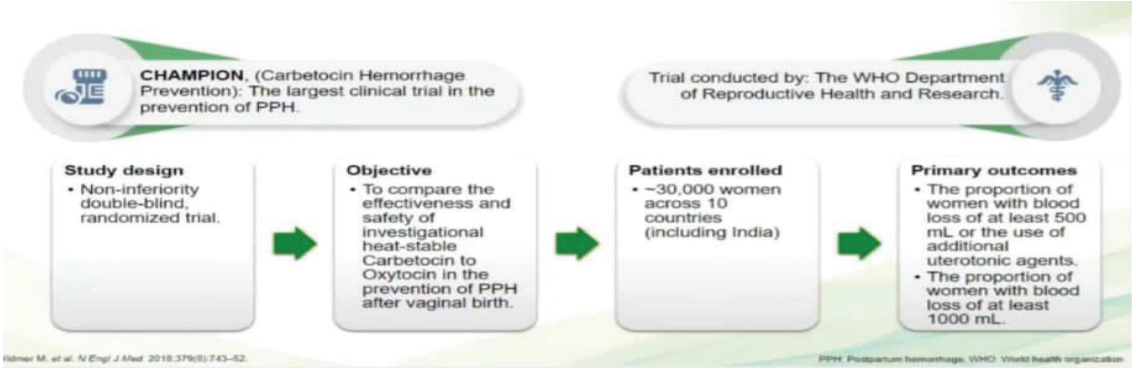
System organ class +	Very common>= 1/10	Common >=1/100 and <1/10
Blood and lymphatic system disorders	No drug interactions have been identified with anaglesis , spasmolytics and agents used for epidural or spinal anaesthesia	Anaemia
Nervous system disorders	Headache, Tremor	Dizziness, Anexity
Vascular disorders	Hypotension, Flushing	Tachycardia
Respiratory , thoracic and mediastinal disorders		Chest pain, Dyspnoea
Gastrointestinal disorders	Nausea, Abdominal pain, Vomiting	Metallic taste
Skin and subcutaneous tissue	Pruritus	

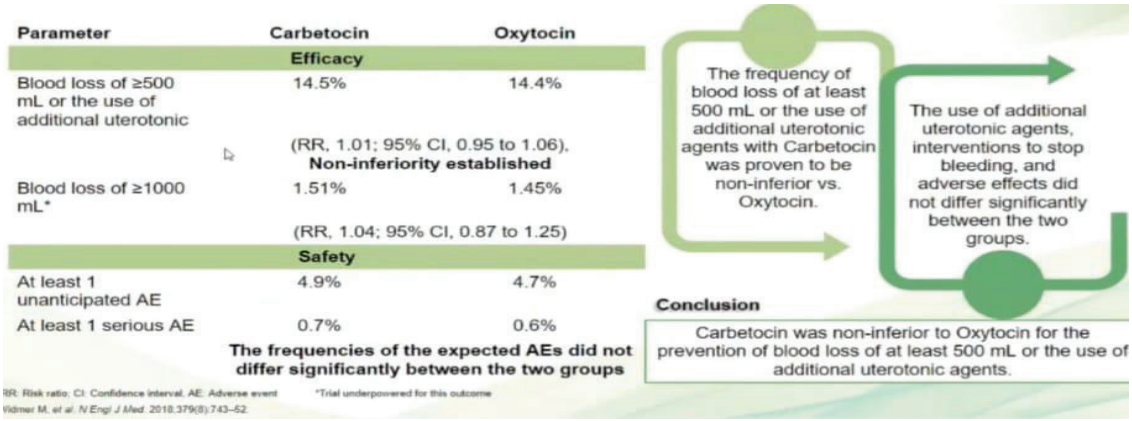
	CARBETOCIN		VS OXYTOCIN	
PARAMETERS	**IV**	**IM**	**IV**	**IM**
Onset of action	1.2 minutes	2.3 minutes	Almost immediate effect	2.5 minutes
Duration of action	60 minutes	119 minutes	-	-30 minutes
Half life	40 minutes	40 minutes	3-5 minutes	3-5 minutes

CARBETOCIN HAS BEEN STUDIED THROUGHOUT THE WORLD



WHO CHAMPION TRIAL - CARBETOCIN NON INFERIOR TO OXYTOCIN





Parameter	Carbetocin	Oxytocin
Efficacy		
Blood loss of ≥500 mL or the use of additional uterotonic	14.5%	14.4%
	(RR, 1.01; 95% CI, 0.95 to 1.06), **Non-inferiority established**	
Blood loss of ≥1000 mL*	1.51%	1.45%
	(RR, 1.04; 95% CI, 0.87 to 1.25)	
Safety		
At least 1 unanticipated AE	4.9%	4.7%
At least 1 serious AE	0.7%	0.6%
	The frequencies of the expected AEs did not differ significantly between the two groups	

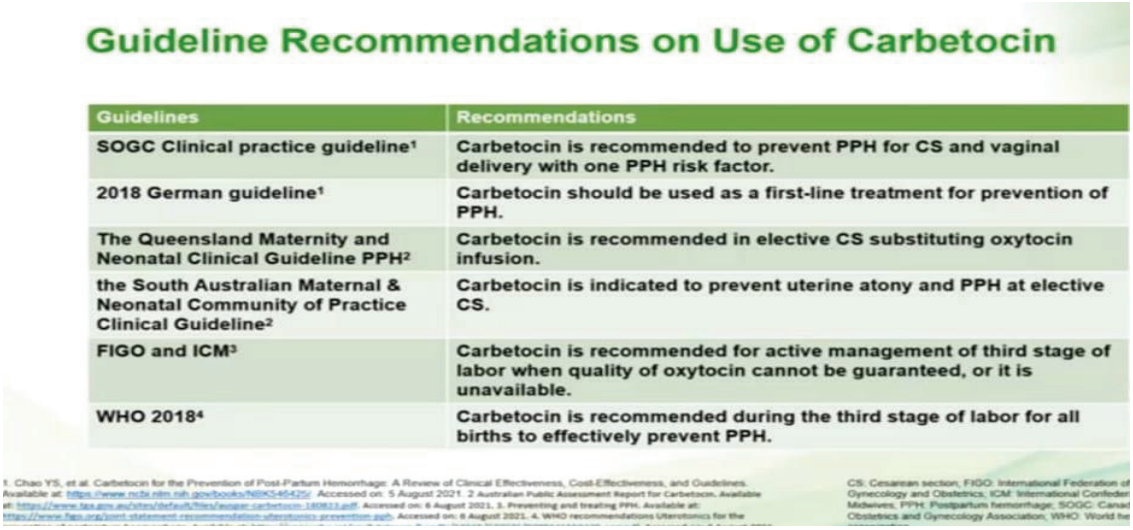
RR: Risk ratio; CI: Confidence interval; AE: Adverse event *Trial underpowered for this outcome

Widmer M, et al. N Engl J Med. 2018;379(8):743–52.

WHO RECOMMENDATION FOR CARBETOCIN :

The use of carbetocin (100ug, IM/IV)is recommended for the prevention of PPH for all births in contexts where its cost is comparable to other effective uterotonics.

AICOG 2019 62nd congress - Carbetocin has potent uterotonic effect.



Guideline Recommendations on Use of Carbetocin

Guidelines	Recommendations
SOGC Clinical practice guideline[1]	Carbetocin is recommended to prevent PPH for CS and vaginal delivery with one PPH risk factor.
2018 German guideline[1]	Carbetocin should be used as a first-line treatment for prevention of PPH.
The Queensland Maternity and Neonatal Clinical Guideline PPH[2]	Carbetocin is recommended in elective CS substituting oxytocin infusion.
the South Australian Maternal & Neonatal Community of Practice Clinical Guideline[2]	Carbetocin is indicated to prevent uterine atony and PPH at elective CS.
FIGO and ICM[3]	Carbetocin is recommended for active management of third stage of labor when quality of oxytocin cannot be guaranteed, or it is unavailable.
WHO 2018[4]	Carbetocin is recommended during the third stage of labor for all births to effectively prevent PPH.

1. Chao YS, et al. Carbetocin for the Prevention of Post-Partum Hemorrhage: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines. Available at: https://www.ncbi.nlm.nih.gov/books/NBK545425/. Accessed on: 5 August 2021. 2 Australian Public Assessment Report for Carbetocin. Available at: https://www.tga.gov.au/sites/default/files/auspar-carbetocin-180821.pdf. Accessed on: 6 August 2021. 3. Preventing and treating PPH. Available at: https://www.figo.org/joint-statement-recommendation-uterotonics-prevention-pph. Accessed on: 6 August 2021. 4. WHO recommendations Uterotonics for the

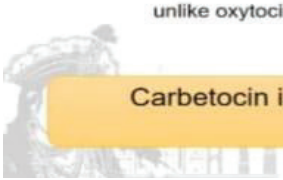
CS: Cesarean section; FIGO: International Federation of Gynecology and Obstetrics, ICM: International Confederation of Midwives; PPH: Postpartum hemorrhage; SOGC: Canadian Obstetrics and Gynecology Association; WHO: World he

Carbetocin Vs Oxytocin

- Half life for carbatocin (40 mins) is 10 folds higher than Oxytocin (4mins)
- Duration of action of carbatocin longer than IV & IM oxytocin

(It was found that a single intravenous bolus injection of carbetocin was at least as effective as 16 hours of continuous oxytocin infusion)

- Carbatocin need no repeated administration
- No dose variation/ single dose of carbatocin is found to be effective in controlling PPH, unlike oxytocin



Carbetocin is superior over oxytocin with respect to its pharmacokinetic parameters & single dose administration

PREGNANCY INDUCED HYPERTENSION

Dr. DHAVASHREE V,
DGO, MRCOG, DRM
JOINT SECRETARY - OGSOS
SKS HOSPITAL

INTRODUCTION :

The terminology Pregnancy induced hypertension has been replaced by Hypertensive disorders of pregnancy and is a spectrum of disorders that includes Gestational hypertension, Pre-eclampsia, Pre-eclampsia superimposed on Chronic hypertension. In this article, the practical aspects of Gestational hypertension and Pre-eclampsia would be dealt with.

DEFINITIONS :

Gestational hypertension: Hypertension that develops for the first time at ≥20 weeks without evidence of any features of preeclampsia.

PRE-ECLAMPSIA :

Gestational hypertension with new onset proteinuria or one or more adverse conditions (defined as a maternal end organ complication or evidence of uteroplacental dysfunction. PE further classified as non-severe (BP ≥140/90 and ≤160/110)and severe (>160/110).

Also can be classified as

Early onset PE: PE occuring before 34 weeks of pregnancy and associated with more severe maternal complications like LBW,FGR and iatrogenic prematurity.

Late onset PE: PE occuring after 34 weeks of pregnancy and complications are less severe.

How to measure the BP in pregnancy?

- Using a automated device or a caliberated aneroid device or a standardised mercury sphygmomanometer.
- Measured in the sitting position with the feet supported after 5 minutes of rest after reaching the office or in left lateral position(if bed bound) with the zero at the level of the heart.
- Appropriate size cuff should be used (≤ 33 cm - standard cuff, >33cm large cuff).

- BP taken on both arms at the first antenatal visit. Right arm used if no significant difference, or if significant difference then the arm with higher blood pressure should be used.
- SBP identified with appearance of the korotkoff I sound and DBP is recognised as korotkoff V sounds.
- Average of two BP measurements should be taken.

THE HDP-GESTOSIS SCORE

RISK FACTOR	SCORE
Age older than 35 years	1
Age younger than 19 years	1
Maternal Anemia	1
Obesity (BMI >30)	1
Primigravida	1
Short duration of sperm exposure (cohabitation)	1
Woman born as small for gestational age	1
Family history of cardiovascular disease	1
Polycystic ovary syndrome	1
Inter pregnancy interval more than 7 years	1
Conceived with Assisted Reproductive (IVF/ ICSI) Treatment	1
MAP>85 mm of Hg	1
Chronic vascular disease (Dyslipidemia)	1
Excessive weight gain during pregnancy	1
Maternal hypothyroidism	2
Family history of preeclampsia	2
Gestational diabetes mellitus	2
Obesity (BMI > 35 kg/M^2)	2
Multifetal pregnancy	2
Hypertensive disease during previous pregnancy	2
Pregestational diabetes mellitus	3
Chronic hypertension	3
Mental disorders$^{\$}$	3
Inherited / Acquired Thrombophilia	3
Maternal chronic kidney disease	3
Autoimmune disease (SLE / APLAS / RA)	3
Pregnancy with Assisted Reproductive (OD or Surrogacy) Treatment	3

Systemic Lupus Erythematosus ^ Anti-phospholipid Antibody Syndrome @ Rheumatoid Arthritis

PREDICTION OF PE :

Prediction can be based on clinical risk factors (sensitivity is 40%) identified during early pregnancy, biochemical markers and sonographic risk markers (UA- PI).

Clinical risk factors: Identification of clinical risk factors by Gestosis risk scoring method should be an universal screening method at the booking visit. Score of ≥3 implies identifies woman "At risk for Preeclampsia".

BIOCHEMICAL MARKERS :

PlGF is an angiogenic factor and is produced by placenta. Lower levels of PlGF in the first trimester (11-13 weeks) is associated with development of PE. Low levels of PAPP-A is also associated with delvelopment of early onset PE.

UA-PI :

The mean UA-PI is increased on ultrasound done at 11-13 weeks is associated with development of PE.

No single method is a reliable predictor of PE, but when combining clinical risk scoring along with the biochemical markers and UA-PI values increases the Prediction of PE. In low resource setting, clinical risk scoring should be undertaken to predict preeclampsia.

PREVENTION :

Women "At risk of PE" should be started on Aspirin 75-150mg per day earlier than 12 weeks but atleast by 16 weeks and can be continued throughout the pregnancy. (ASPIRE trial - 150mg of Aspirin at bedtime was associated with good adherence(80%) and reduction in preterm PE by 62%).

There is a strong recommendation to start Calcium 1-1.5 gm daily in women with low calcium intake.

DIAGOSIS :

All women detected to have a raised blood pressure ≥140/90 should be offered proteinuria testing.

Proteinuria testing is done using urinary dipstick method or by spot urine protein: creatinine ratio. Routine 24 hour urine testing should not be offered for the quantification of urinary protein.

Significant protenuria is defined as urinary excretion of >300mg protein in 24 hour period. Urine dipstick of ≥2+ or spot urine PCR ≥30mg/mmol is considered significant proteinuria.

Urine dipstick allows a quick assessement of significant proteinuria.

When there is a significant proteinura along with the raised blood pressure in women of ≥20 weeks, the diagnosis of preeclampsia is made.

MANAGEMENT OF GESTATIONAL HYPERTENSION AND PREECLAMPSIA :

The goals of management includes

1. Assessing the severity of the disease
2. Appropriate control of the blood pressure
3. Prevent Ecalmpsia
4. Obstetric management

ASSESSMENT OF SEVERITY OF THE DISEASE ON THE MOTHER AND THE BABY :

Maternal surveillance: involves a baseline blood investigations which includes

• Complete blood count: for anaemia assessment and for a baseline platelet count check

• LFT: AST, ALT, LDH and S.Bilirubin

• RFT: S.Creatinine

• S.Uric acid

Additional investigations may include coagulation profile (if platelets is <1,00,000/ mm3) and serum electrolytes if severe disease is suspected.

MATERNAL USG of the abdomen and pelvis: for the evaluation of liver for sub-capsular heamatoma/ hepatomegaly, kidney for any signs of renal cause of HT, Ascites and pleural effusion which are other worsening signs of PE.

FETAL SURVEILLANCE: At the diagnosis of PE, fetal evaluation for fetal biometry, AFI, UA and Umbilical artery doppler should be performed to identify FGR and doppler abnormalities.

TREATMENT OF HYPERTENSION :

Antihypertensives are warranted if the SBP 140 and DBP 90mm Hg and the target SBP should be <140 mm Hg and DBP <90 mm Hg. CHIPS trial showed a target DBP of 85 mm Hg halves the risk of severe hypertension.

ANTI-HYPERTENSIVE MANAGEMENT OF NON-SEVERE HYPERTENSION :

1. **Labetalol:** This is the first line medication especially when the baseline pulse is >100/min. It is contraindicated in asthma, CCF, DM and cases of bradycardia. It is started at a dose of 100 mg TID or QID and if BP not controlled increase it to 200 mg TID or QID. A maximum dose of 2200mg /day is suggested.

2. **Nifedipine:** (20-120mg/day and slow release preparation in 2 divided doses) This is a preferred antihypertensive when the baseline pulse is <100/min. It should never be given sub-lingually. Maternal adverse effects include tachycardia, headache, palpitations, flushing. Nifedepine is contraindicated in woman with aortic stenosis.

3. **Methyldopa:** 500 -2000mg per day in 2-3 divided doses, safe anti-hypertensive in the antenatal period but is not available these days. If the woman is on antenatal methyldopa, it should be discontinued in the postpartum period to avoid postpartum depression.

ANTI-HYPERTENSIVE MANAGEMENT OF SEVERE HYPERTENSION (RAPID CONTROL) :

Anti-hypertensives for rapid control (Severe Preeclampsia)

Drug	Dosage	Points to remember
Nifedipine[21]	10-30 mg orally (Not sublingually) If BP is not controlled, can be repeated within 30-45 minutes. Max total dose of 120 mg is not to be exceeded. Once controlled, slow release preparations are to be started.	Contraindicated in CCF and AV or SA nodal abnormalities
Labetolol[21]	Slow IV injections: 10 to 20 mg IV, then 20 to 80 mg every 20 to 30 minute Max total dose of 300 mg is not to be exceeded Alternate IV infusion regimen: After initial loading dose, an infusion can be started at 1–2 mg/min and is titrated until desired effect. Oral tablets can be used in a conscious patient in the dose of 200mg	Contraindicated in CCF, DM, Asthma and bradycardia.
Hydralazine[21]	5 mg, IV or IM, then 5 to 10 mg every 20 to 40 minutes; once BP controlled repeat every 3 hours; for infusion: 0.5 to 10.0 mg/h; if no success with 20 mg IV or 30 mg IM, consider another drug	It has been associated with more maternal and perinatal adverse effects than intravenous labetolol or oral nifedipine such as maternal hypotension, cesarean sections, placental abruptions and oliguria.[24]
Nicardipine[25,26]	The average starting dose is 1.5 mg/h It can be increased up to 6 mg/h for desired effect according to 0.5 µg/kg/min equation.	It is 100 times more water soluble than nifedipine, so it can be administered i.v. making it an easily titratable i.v. calcium channel blocker.

Target – < 140 / 90 mm Hg Lower the blood pressure promptly but slowly.

SEIZURE PREVENTION :

Loading dose of Magnesium sulphate 4 gms intravenously is recommended in all cases of severe preeclampsia. There is no contraindication of using MgSo4 when nifidepine is used. This is the same dose that is given to treat eclampsia.

Intramuscular regimen (Pritchard)

Loading dose	(Total 14 gram = 4g slow IV as 20 ml (20% solution) + 5 g (50% solution) deep IM
Intravenous:	4gram (4 ampoules of 50% w/v MgSO4 + 12 ml distilled water in 20 ml syringe) slow IV at the rate of 1 gram over 1 minute.
Intramuscular:	5gram (5 ampoules of 50% w/v MgSO4 +0.5 ml 2% Lignocaine) deep i.m. (In 10 cc syringe& with 20-G long needle) in each buttock.
Maintenance dose	(5 g deep IM in alternate buttock 4 hourly)
Intramuscular:	5gram (5 ampoules of 50% w/v MgSO4 +0.5 ml 2% Lignocaine) deep IM in alternate buttock.

Intravenous regimen (Zuspan)

Loading dose	(4 gram slow IV as 20 ml 20% solution)
Intravenous:	4gram (4 ampoules of 50% w/v MgSO4 + 12 ml distilled water) slow i.v.
Maintenance dose	5 gm (5 ampoules of 50% w/v MgSO4 to add in 500 ml RL) Intravenous infusion rate 100 ml/ hour = 1 gm / hour preferably administered through infusion pump

MONITORING OF WOMEN WITH GHT OR PE :

Women with GHT : Weekly maternal blood investigations, and 2-4 weekly Fetal assessment in case of non-severe GHT and every 2 weekly fetal assessment in case of severe GHT is recommended.

WOMEN WITH PE :

1. Non-severe PE:maternal blood investigations repeated twice weekly and fetal assessment done 2 weekly.

2. Severe PE: maternal blood investigations repeated 3 times a week and fetal assessment if baseline normal repeated 2 weekly and if FGR identified, dopplers repeated more often.

OBSTETRIC MANAGEMENT :

In women with uncontrolled hypertension despite using 3 or more classes of antihypertensives in appropriate doses, or women with progressive deterioration in LFT, RFT, platelet count, neurological symptoms, placental abruption, when FGR with abnormal doppler flow studies should be offered termination after steroid prophylaxis and Magnesium sulphate infusion for prevention of eclampsia and for the fetal neuroprotection.

In women with Uncomplicated GHT, Pregnancy can be continued till term. In women with mild PE, delivery of the baby is recommended by 37 completed weeks and in case of severe PE, delivery is often recommended beyond 34 completed weeks.

Induction of labour can be safely done using appropriate method. Caesarean section is indicated only for obstetric indications. Women with PE are at increased risk of PPH, so Active management of third stage of labour should be done. Ergometrine should not be administered to women with any hypertensive disorder of pregnancy.

Fluid management in woman with pre-eclampsia during labour should be restricted to about 80ml/hr to prevent pulmonary edema.

POSTPARTUM MANAGEMENT :

Following delivery, BP monitoring should be done at least once daily on D3-7 postpartum. Women with persistant SBP>150 mm Hg and DBP >100 mm Hg in the post natal period will need anti-hypertensive treatment.

The preferred medication in the post natal period is enalapril or nifedipine/ amlodipine. Labetalol is preferably avoided as it causes neonatal hypoglycemia. The second line medications include atenalol or labetalol.

REFERENCE :

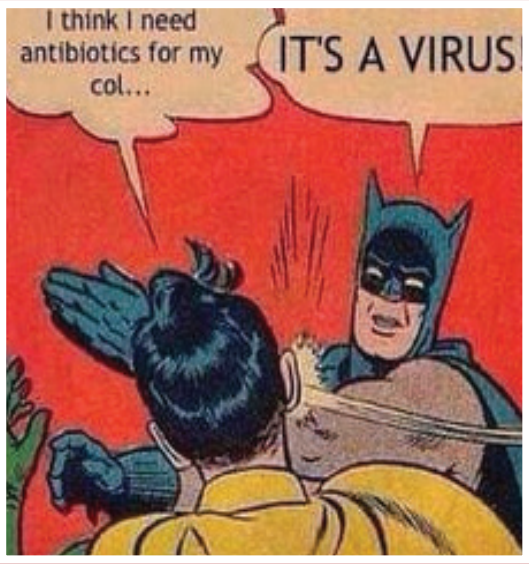
1. Good clinical Practice recommendations 2019: Hypertensive disorders in pregnancy: FOGSI-GESTOSIS-ICOG.
2. Guideline no.426; Hypertensive disorders of pregnancy: Diagnosis, Prediction, Prevention and Management: SOGC clinical practice guideline May 2022.
3. Hypertension in Pregnancy: diagnosis and management: NICE GUIDELINE ; June 2019.

BREAK


Is this Gluten Free?
No, it costs money.


Meanwhile, Inside the fridge


"Your medical records are safe with us. We take patient privacy very seriously."


I think I need antibiotics for my col...
IT'S A VIRUS!

NON DESCENT VAGINAL HYSTERECTOMY

Dr. SARAVANA KUMAR,
MD (OG)
VICE PRESIDENT, OGSOS
CONSULTANT, MALAR MATERNITY HOSPITAL

INTRODUCTION :

Like midcavity forceps, like breech delivery, vaginal hysterectomy also is progressively obscuring into oblivion. The reasons are many, but the interest in endoscopic surgeries and proceeding laparoscopically for a hysterectomy is mainly deemed a rider to avoid vaginal hysterectomies.

All that said, we need mentors to teach a difficult task and supervision when we do on our own. The learning curve is steep and sometimes it is difficult to avoid complications in the journey to master the technique.

The feel of the bladder, the cervix, the vesico cervical fascia and the anterior pouch is obtained by constantly trying hysterectomy from below. Nevertheless, the posterior pouch is not much easier either, but it is a rare chance that there is obliteration of posterior pouch and adhesion of bowel therein.

Even like a laparoscopic hysterectomy, NDVH has different techniques by different surgeons. Learning and trying all such methods, and developing our own technique will define our safety and ease of doing NDVH.

Good selection of cases, adequate training, and good assistants are essential for NDVH. Recourse to laparoscopy or laparotomy if difficulty arises are the options to be kept as plan B. With experience majority of the hinderances will be overcome and NDVH can be accomplished for larger uteri, uterus with previous scars, removal of adnexae, and adnexal masses too.

SELECTING A CASE OF NDVH :

The usual indications of hysterectomy applies, after careful consideration of medical methods of management, especially LNG IUS. This one revolution of usage of LNG IUS has robbed the luxury of trying a vaginal hysterectomy for small uteri, especially for beginners.

THERE ARE FEW CONTRAINDICATIONS FOR NDVH

1. Uterine size more than 20 weeks
2. Uterine volume more than 400 ml
3. Associated endometriosis
4. Restricted uterine mobility
5. Inaccessible cervix
6. Reduced vaginal space.

INSTRUMENTS NECESSARY FOR NDVH :

Discussing only the set of different instruments necessary for the operation.

Always check the clamps – a good set of clamps which have good grip and do not jump is very essential. Retracted vessels may be a messy problem.

Myoma screws in various sizes.

Single blade speculum – usual double blade sims speculum is cumbersome to retract the posterior vaginal wall as the lower blade will hitch against the OT table.

Good pair of mayo scissors, slender and sharp to dissect out the bladder. The bladder pillars yield to meticulous defining of anatomy and sharp dissection rather than heavy blunt scissors which make the surgery crude and liable to injure the bladder.

Curved blade handle, so that it can access the areas of the uterus in depth(for morcellation) without compromising safety.

Allis forceps and tenaculum (cats paw, single toothed) with good grip, which can help do vaginal morcellation for larger uteri.

Vaginal use of vessel sealing devices are now a boon, which help us complete the hysterectomy without the fear of slippage of knots. Beware, the prongs have residual heat and be careful enough not to touch tissues beyond uterus.

ACTUAL STEPS :

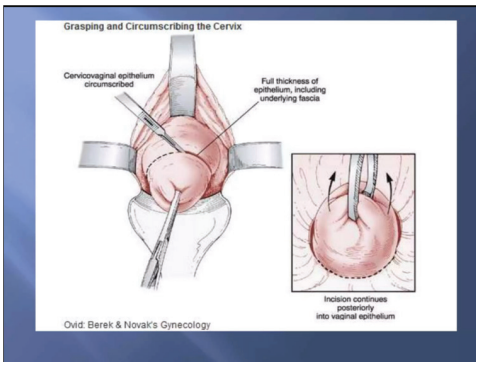
The Three important aspects of a successful vaginal hysterectomy is Opening Posterior pouch, bladder dissection and debulking of uterus.

Of all these , the opening of POD is easiest, as in most of uteri, that is a relative area free of major structures posteriorly unless obliterated by previous PID or endometriosis.

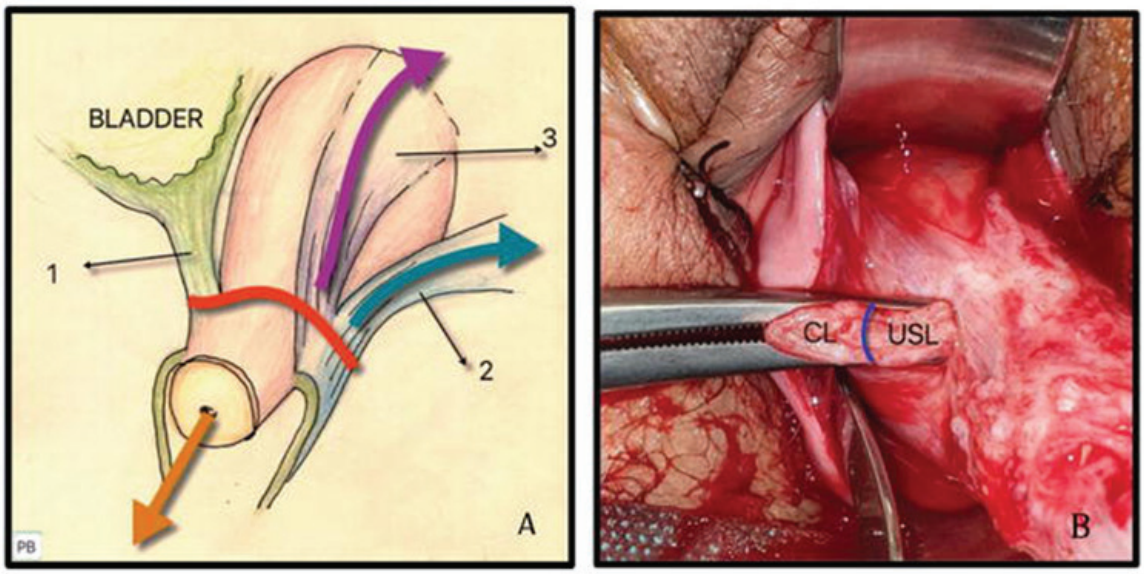
Good lithotomy to accommodate your assistants is important, if your assistants stand beyond the stirrups, both of you will feel the difficulty.

Assess the case under anesthesia, The location of cervix beyond or above the ischial spines. Gently tug the cervix to see if they move further down. A massage to uterosacral ligaments also helps coaxing the ligaments to amenable to a vaginal surgery. Assess the mobility of uterus and the space available in the vagina for manipulations and morcellation.

It is a routine practice of some surgeons to inject saline all around the cervix, a little bit of patience in this step to inject quite a lot of saline +/- 2 drops of adrenaline (in 100-150 ml saline) will define tissue planes, push the bladder up (auto dissection), provide a vascular tourniquet of the small vessels in the vagina and makes the tissue blanched making a feel that you are doing a ovarian cystectomy.



Clearly define the bladder sulcus. Because beyond the sulcus , the vaginal mucosa is firm to the cervix and if plane is lost, we may end up digging into the stroma of cervix.



1 = cervicovesical ligament, 2 = uterosacral ligaments, 3 = cardinal ligament. Redline mark where the same pedicle might secure bladder pillar, uterosacral ligaments, and cardinal ligaments. B. Lower connective pedicle at vaginal hysterectomy with distinct uterosacral ligament (USL) and cardinal ligament (CL) in the same pedicle.

It is good to start with the opening of POD. If Saline is used, a simple circumferential incision over the cervix is enough and a finger dissection over the posterior vaginal wall will gently push the vagina out of way from cervix. The POD can be picked up with a allis or toothed tenaculum. If saline is not used, an allis can be used to tent the posterior vaginal wall with a good traction of the cervix cephalad, beyond the attachment of uterosacrals and a sharp cut with mayo's scissors will open up the POD. Do not be disheartened when a large amount of fluid comes as you open up

the POD. Usually some amount of fluid is seen normally when you cut POD. It may also be an ovarian cyst which was ruptured with all manipulations.

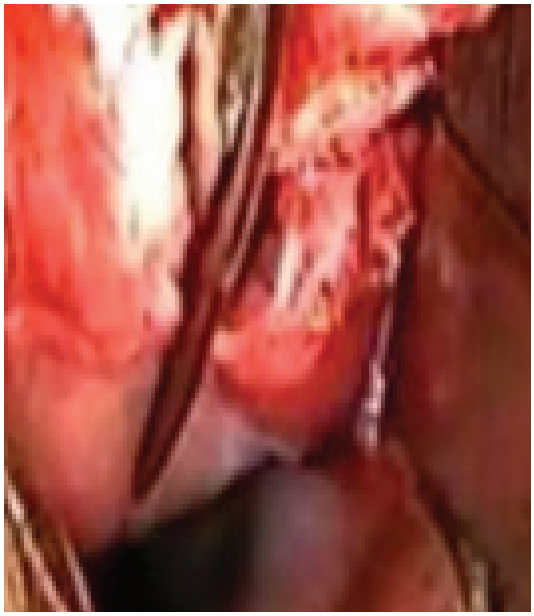
Lifting the bladder up along with the anterior incision over the cervix and downward traction over the cervix exposes the UV fold of peritoneum which is seen tented here.

Tug the uterosacrals to assess further descent of the uterus. Extend the incision anteriorly. Again the same principle can be used . Lift the bladder with an allis just above the bladder sulcus and give a sharp cut by a mayo's scissors with the curve of the scissors pointing downwards. In majority of the patients , a good traction of cervix by your assistant, the pull of the bladder above by the allis and the incision below will show up the stretched vesico cervical ligament. Cut the vesico cervical ligament with sharp scissors. If there is a descent with anesthesia and the cut of vesico cervical ligament exposes the vesical space , the bladder can be gently pushed with the blade of a speculum. If the bladder appears to be high up and the anterior pouch is high up, do not try to reach further up by extending the blade of speculum and trying to chase the UV fold. With descent and further clamping of Uterosacral ligaments, the body of uterus will definitely come into view.

Always clamp, cut and ligate the uterosacral ligaments rather than using the recent vessel sealing devices from the first clamp, because the cauterized uterosacral ligaments will retract and vault support may not be possible. Sometimes it may not be possible to clamp and cut the uterosacral ligaments in one go. Use further clamps to advance uterosacral by which time the mackenrodt's ligament also will be caught in the clamp.

Anteriorly now, trying to reach the UV fold may be wiser now, as the major portion of cervix will be freed and uterus will descend down further. An index finger may be used to dissect out the bladder from the uterus and the speculum blade now readjusted. If the bladder pillars have not been divided till now, it is good to give traction down on the cervix and gently graze the vesico cervical ligament over the body of the uterus to release the bladder. Once this is done, the ureter will be out of the field. This will expose the UV fold of peritoneum and can be opened.

Uterine arteries are best clamped if both the pouches are opened and a sturdy clamp applied directly over the surface of uterus without any intervening tissues. This is a time that we can switch over to Vessel sealing device, so that we can be sure of uterine arteries being coagulated and cut without the fear of slippage. The vessel sealing device have the advantage of nibbling small portions of uterine artery precisely even if we had not opened the anterior pouch. If it is a big uterus filling the pelvis from side to side, we may encounter difficulty in descent further unless we start debulking the uterus. If the UV fold is opened, a speculum blade can be used to retract the bladder away from the field, and can start with bisecting the uterus.



Bisecting at this point will help us reach the anterior and posterior aspect of the uterus further and wedges of uterus can be removed. If we encounter fibroids at this level, use a myoma screw to fix the fibroid and gently dissect out the pseudo capsule of the myoma. In fact it is easy to do NDVH in myomatous uterus rather than huge adenomatous uterus. Curved blade handle comes very handy to cut wedges of tissue surrounding the myoma here. If it was a single big myoma and when plane has been reached and gentle traction will bring down the myoma along with the fundus in a EUREKA moment (as happy as delivering a fetal head).

There are various methods to tackle a non-yielding big uterus after opening the anterior and posterior pouches. At times a deep lateral cut will elongate a globular uterus into an ovoid one and will descend down. Sometimes , you need to make the bisected uterus stand on one leg, that is , push one half of the the bisected cervix and uterus into the pelvis and give traction on the other half , which will expose the deep uterine vessels which can be clamped and cut. Repeat it on the opposite side too.

Intramyometrial coring, removing wedges of tissues, Cone shaped cuts made over the anterior and posterior walls , myomectomy will reduce the bulk of the uterus. All we need is good pair of instruments which hold the uterus (like a cats paw/ vulsellum) or a cutting cautery which will reduce the strain on your shoulders in cutting.

Once the fundus is seen, uterus can be totally bisected, one half can be pushed inside pelvis and the space utilized to clamp cut and tie the cornual structures . Alternatively, the prongs of vessel sealer also works well, caution is the whole instrument is visible and catching only the cornua. Special clamps can be used to tug down the ovaries and clamp the infundibulopelvic ligament if needed.

CLOSURE OF VAULT :

A gauze on an instrument is used to push the bowels inside and inspect the pedicles. Use a long allis forceps to hold the posterior wall of the vagina along with the portion of pelvic peritoneum which will ensure all bleeding points are taken care off.. The anterior vagina can be held with 3 small allis so that they do not hang too low and be a hindrance in suturing. Vault can be sutured with 1 vicryl with fixation of uterosacral ligaments on both sides.

POST OPERATIVE MONITORING :

Most of vaginal hysterectomy patients are well up and sitting after 6 hours of the surgery. Still the 24 hours is crucial in monitoring her vitals , which may point towards any sort of internal hemorrhage.

Remove cathether by 12 hours and make the patient ambulate. This will give her confidence to walk away from the hospital after another 12 hours.

NDVH IN SPECIAL SITUATIONS :

Previous LSCS – If in doubt use saline to define planes and then a lateral window approach can lead to the plane between bladder and uterus. Do not try to push the bladder with a blade of sims unless the pillars are cut. The scar may be adherent to the bladder and rough pushing the bladder may cause injury. Go lateral, find the plane, use sharp dissection, pick up the bladder tissue with babcocks or allis and then approach the scar area from the plane already formed.

Remember, every great surgeon has made mistakes. What we see is just their expertise which comes with experience. Overcoming the fear of failure and trying newer things is the first step towards becoming a confident surgeon.

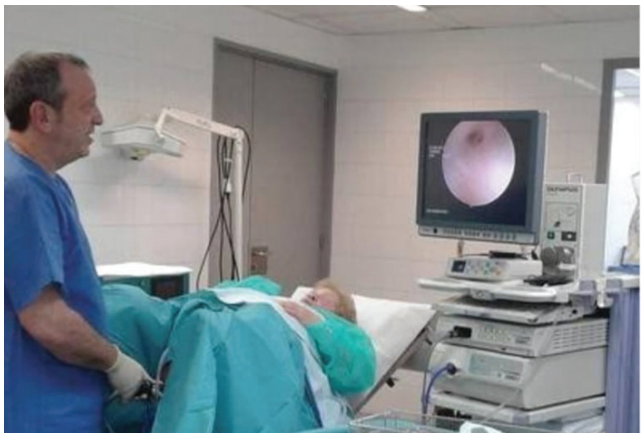
NAVIGATION TIPS AND TACKLING COMPLICATIONS IN HYSTEROSCOPY

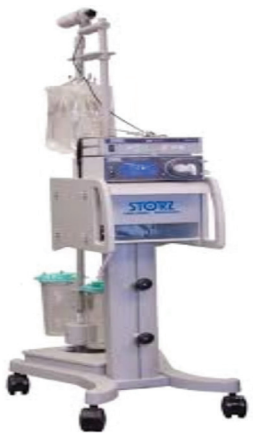
Dr. G. JAYAMALA,
DOWH (IRE), MRCOG (UK), MRCPI (OG)., DRM.,
PRESIDENT, OGSOS
CONSULTANT, RAINBOW HOSPITAL

- Hysteroscopy has become the "Third eye of gynaecologist" as Transvaginal ultrasound the "3rd finger".
- Hysteroscopic procedures have replaced older, invasive techniques.
- Innovative techniques and new hysteroscopic interventions like smaller diameter, morcellators (myosure / truclear) enable us to perform these procedures in an office setting.
- As with any other procedure , the Success of Hysteroscopic procedure starts with choosing the "Right Surgery for the Right Patient by the Right (experienced) Surgeon".

EQUIPMENTS :

- Commonly used hysteroscope- 2.9mm Bettocchi scope with operating sheath size 4.3mm with channel for semirigid 5 Fr. Operating instruments. Continuous flow operating sheath size 5 mm.
- 30 degree Rigid hysteroscope.
- Monitor.
- Fluid management pump (Endomat).





SURGICAL INSTRUMENTS :

- Scissors
- Biopsy forceps
- Grasper
- Loop electrode
- Roller ball
- Scalpel
- Vaporizing electrode
- Morcellator

ENERGY SOURCES :

- Monopolar Resectoscope
- Bipolar versapoint system

DISTENSION MEDIA :

- Diagnostic procedure – Normal saline / Electrolytes
- Operative procedure – 1.5% glycine (Electrolyte poor media) for monopolar system.

Table 1. Hysteroscopic Distending Media

Type	Maximum Fluid Deficit	Advantages	Disadvantages and Safety Precautions*	Complications
Low-Viscosity Fluid Media: Electrolyte-Poor Fluid (eg, glycine, 1.5%; sorbitol, 3%; and mannitol, 5%)	1,000 mL	Compatible with radiofrequency energy Monopolar devices require electrolyte-poor fluids	Excessive absorption of these fluids can cause hyponatremia, hyperammonemia, and decreased serum osmolality with the potential for seizures, cerebral edema, and death.	Excessive absorption of these fluids can lead to hyponatremia, hyperammonemia, and decreased serum osmolality, with the potential for seizures, cerebral edema, and death.
Low-Viscosity Fluid Media: Electrolyte-Containing Fluid (eg, normal saline, sodium lactated solution)	Maximum fluid deficits with isotonic solutions are based only on expert opinion but consensus would be approximately 2,500 mL.	Readily available Isotonic Media of choice during diagnostic hysteroscopy and in operative cases where mechanical, laser, or bipolar energy is used	Although the risk of hyponatremia and decreased serum osmolality can be reduced by using these media, pulmonary edema and congestive heart failure can still occur. Careful attention should be paid to fluid input and output, with particular attention to the fluid deficit.	Fluid overload causing pulmonary edema and congestive heart failure

*Careful attention should be paid to fluid input and output, with particular attention to the fluid deficit, particularly in in elderly patients and patients with cardiopulmonary or renal compromise, in whom lower fluid thresholds should be considered.

Data from Munro MG, Storz K, Abbott JA, Falcone T, Jacobs VR, Muzii L, et al. AAGL practice report: practice guidelines for the management of hysteroscopic distending media: (replaces hysteroscopic fluid monitoring guidelines. J Am Assoc Gynecol Laparosc. 2000;7:167–8). AAGL Advancing Minimally Invasive Gynecology Worldwide. J Minim Invasive Gynecol 2013;20:137–48.

INDICATIONS :

DIAGNOSTIC	OPERATIVE
Abnormal uterine bleeding	Removal of IUCD
Recurrent pregnancy loss	Removal of Polyps
Unexplained Infertility	Submucous myoma resection
Amenorrhea	Lysis of IU Adhesions/ Ashermann's syndrome
Abnormal HSG	Resection of uterine septum
Chronic pelvic pain	Tubal Cannulation
Postoperative evaluation	Tubal Sterilization
Assisted reproductive techniques	Endometrial ablation
	Removal of retained products of conception
	Isthmocele repair
	Subendometrial injection of PRP / Stem cells

CONTRAINDICATIONS :

- Active cervical or uterine infection.
- Pregnancy
- Advanced uterine or cervical cancer
- Medical conditions precluding surgery.

PRE-OP ASSESSMENT :

- Transvaginal ultrasound, preferably 3D USG
- Saline sonography
- Hysterosalpingogram
- Get Informed consent

These will complement our diagnosis , to plan for the right surgical procedure.

PRE-OP PREPARATION :

- There is insufficient evidence to recommend routine cervical ripening before diagnostic or operative hysteroscopy, but it may be considered for those patients at higher risk of cervical stenosis or increased pain with the surgical procedure.
- Misoprostol 400mcg per vaginal 4 hours before procedure or the night before for nulliparous, post-menopausal or patients with suspected cervical stenosis patients.

- Endometrial preparation with progestins, OCPs or GnRH Analogous helps to thin endometrium and gives good visualisation during operative procedures.

TIMING OF PREDECURE :

In premenopausal women with regular menstrual cycles, the optimal timing for diagnostic hysteroscopy is during the follicular phase of the menstrual cycle after menstruation.

Some women with unpredictable menses can be scheduled at any time for operative hysteroscopy, but ideally patients who are actively bleeding may not undergo the procedure because adequate visualization could be impaired.

PATIENT POSITION :

- Dorsal Lithotomy with legs in adjustable stirrups
- Avoid Trendelenburg position as it increases the risk of air embolism

BLADDER CATHETERIZATION – Ask patient to void before procedure to avoid unnecessary intervention.

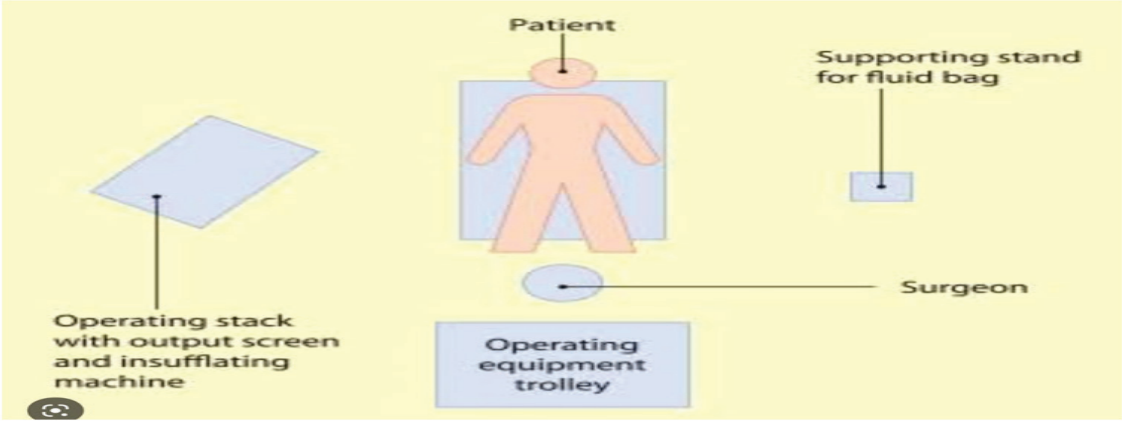
ROUTINE ANTIBIOTICS – Not necessary .But selected cases done for Infertility, better to screen pre operative for infection or to give a course of antibiotics post operatively.

OFFICE HYSTEROSCOPY :

In randomized trials, patients reported a preference for office-based hysteroscopy, and office-based procedures are associated with higher patient satisfaction and faster recovery when compared with hospital-based operative hysteroscopy. Other potential benefits of office hysteroscopy include patient and physician convenience, avoidance of general anaesthesia, less patient anxiety related to familiarity with the office setting, cost effectiveness, and more efficient use of the operating room for more complex hysteroscopic cases. Appropriate patient selection for office-based hysteroscopic procedures for women with known uterine pathology relies on thorough knowledge and understanding of the target pathology, size of the lesion, depth of penetration of the lesion, patient willingness to undergo an office-based procedure, physician skills and expertise, assessment of patient comorbidities, and availability of proper equipment and patient support.

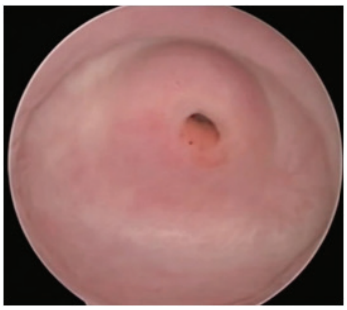
The office hysteroscopy analgesia regimens commonly described in the literature include a single agent or a combination of multiple agents, including a topical anesthetic, a nonsteroidal antiinflammatory drug, acetaminophen, a benzodiazepine, an opiate, and an intracervical or paracervical block, or both.

Vaginoscopy is the preferred mode especially for office hysteroscopy.

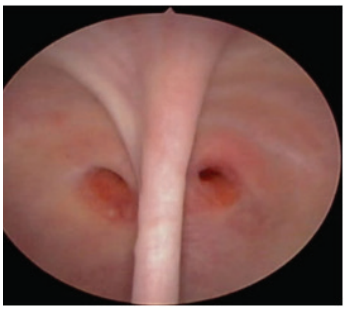


VAGINOSCOPY :

- Reduce pain and discomfort to patient.
- Ask your assistant to occlude introitus, for beautiful visualization of vaginal walls, fornices and external os to diagnose any pathology in the vagina.
- 1st entry always the best.
- To navigate cervical canal, follow cervical mucus. Be patient ,wait for fluid to open up the canal and then to distend the cavity.
- Direct view helps to navigate the canal.
- Avoid friction for a clear view.
- Extreme retroversion or anteversion may be due to adhesions.
- Traction with tenaculum on anterior lip of cervix will straighten uterine axis if any difficulty to navigate.
- If distension is lost due to back flow / leakage, partially occlude the OS with allis forceps.
- Know your landmarks . Both ostia are our GPS.
- Open and close outflow valve to remove clots and debris when poor visualization occurs.



VAGINOSCOPY



VAGINAL SEPTUM

COMPLICATIONS - 0.22%

Diagnostic vs operative hysteroscopy – 0.13% vs 0.95%.

1. Mechanical
2. Distension media related
3. Energy source related
4. Late complications

1. MECHANICAL :

Excessive traction on cervix by tenaculum

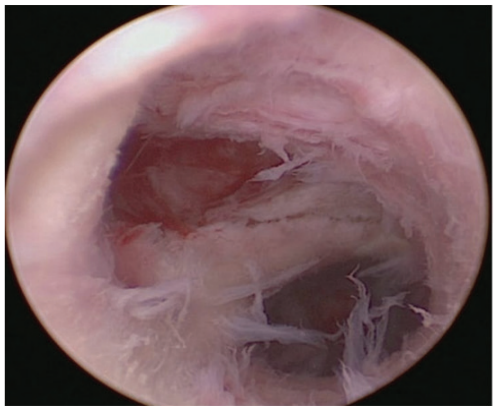
Forcible dilation of cervix, Especially in nulliparity, menopausal women, cervical hypoplasia or atresia

PREVENTION OF MECHANICAL COMPLICATIONS :

- Preparation with misoprostol
- Deep intracervical injection of vasopressin 0.05units/ml-0.1u/ml. 4ml each at 4 and 8'O clock position.
- In case of adhesions/synechiae, hysteroscopic scissors can be used to cut through to facilitate entry.
- Use smaller diameter hysteroscope or only inflow channel scope alone in stenotic cervix.
- Vaginoscopy will help.

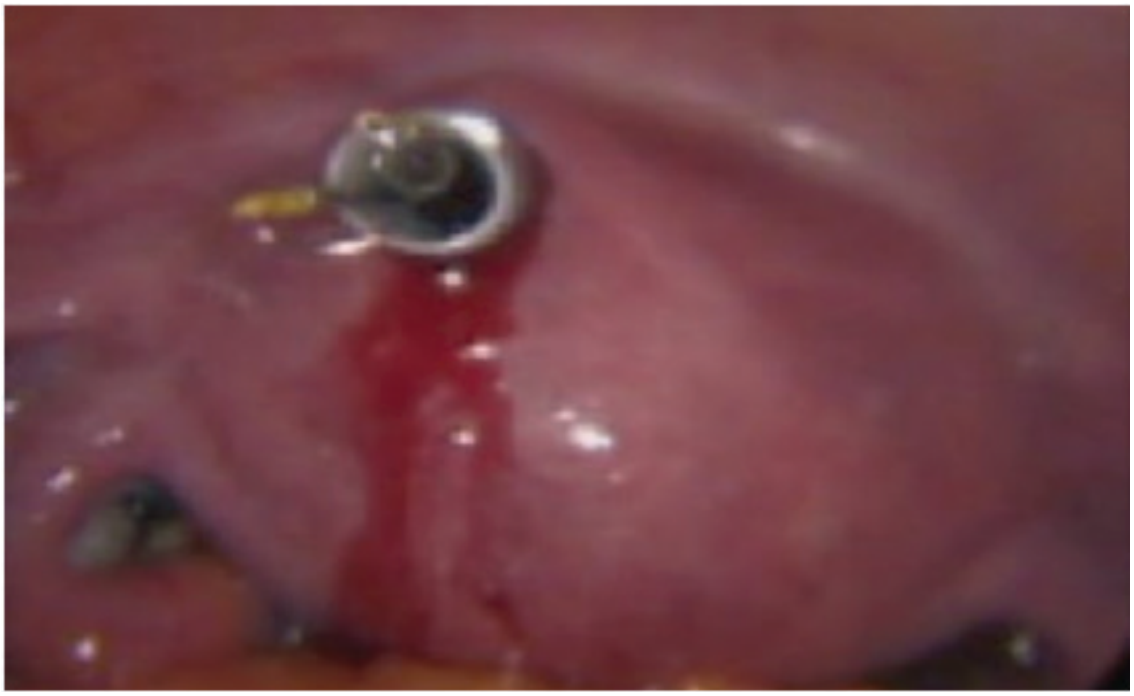
FALSE PASSAGE :

- Visualisation of concentric myometrium with absence of endometrium and cornua – Diagnostic of false passage.
- No need to abandon procedure.
- Withdraw scope and again follow the cervical canal.
- Usually no consequence.



UTERINE PERFORATION :

- Abandon procedure.
- Small perforation by mechanical instrument can be observed expectantly. Usually no intervention required.
- Large perforations / ones caused by active electrode requires Laparoscopy



PERFORATION WITH RESECTOSCOPE

ON LAPAROSCOPY :

- Bleeding from perforation can be controlled by Bipolar coagulation or suturing.
- Thorough examination of bowel, bladder and other vitals structures should be done and corrected accordingly.
- Repeat hysteroscopy after 6 weeks.

BLEEDING INSIDE THE UTERUS :

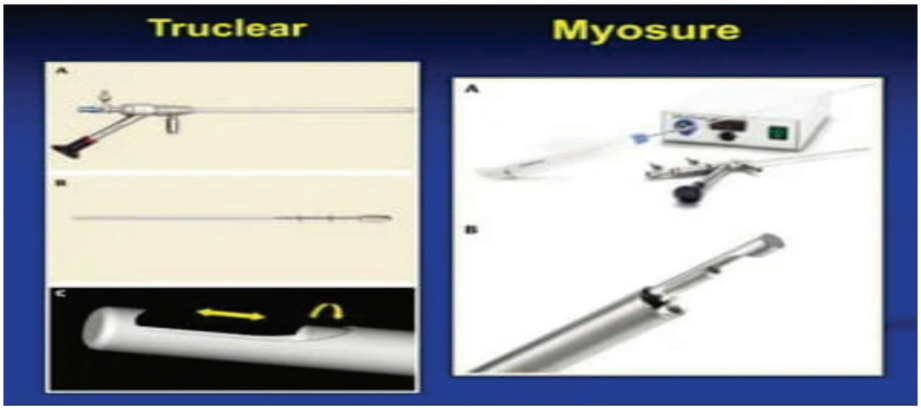
- Can be reduced by intraoperative injection of dilute vasopressin.
- Temporarily increase intrauterine pressure.
- Roller ball coagulation of bleeding site.
- Uterine packing.
- Foleys tamponade with 20-30ml of saline and observe. Catheter can be removed after 6-8 hours.

2. DISTENSION MEDIA RELATED COMPLICATIONS

PREVENTION OF FLUID OVERLOAD AND HOW TO AVOID COMPLICATIONS :

- Careful history and physical examination
- Pre operative assessment of intracavitary abnormalities
- Advance hysteroscope in a clear view
- Strict adherence to fluid deficits
- Stop and reschedule surgery if fluid deficit is reached or if full resection cannot be completed.
- To prevent absorption and hyponatremia use automated fluid pumps and monitoring system.
- If not available , fluid bag in large BP cuff and inflating the cuff. Input and output recorded manually.
- Maintain intrauterine pressure – 70 to 80mmHg.
- Monitor fluid deficit closely. Halt procedure if Electrolyte poor fluid deficit of > 1500ml Electrolyte fluid deficit of > 2500ml
- Minimize operating time .
- Avoid entering vascular channels
- Early detection of systemic absorption and recognition of warning symptoms of fluid overload and hyponatremia.
- Termination of procedure when indicated.

WITH THE USE OF NEW HYSTEROSCOPIC MORCELLATORS (TRUCLEAR/ MYOSURE) OPERATING TIME IS LESS, THUS AVOIDING COMPLICATIONS IN AN OFFICE SETTING.



RECOGNITION AND TREATMENT OF HYPONATREMIA :

Serum Na+ level	Symptoms	Treatment
135-145	Normal	Nil
120-135	Restlessness	Oxygen, Inj. Furosemide 40-60mg IV 0.9% normal saline
110-120	Nausea, headache,confusion, cardiac irregularities	Ventilator support if pulmonary edema, Inj. Furosemide 1mg/kg 4-0 hourly, 3% hypertonic saline

3. ELECTROSURGERY COMPLICATIONS

- Injury due to active electrode needs Immediate Laparoscopy and thorough inspection of bowel and bladder.
- Energy sources can lead to adhesion formation and Secondary Amenorrhea.

4. LATE COMPLICATIONS

- Intrauterine adhesions
- Infection and pelvic inflammatory disease
- Complications in subsequent pregnancies(uterine rupture, placenta accreta, percreta, increta)
- Haematometra

CONCLUSION :

HYSTEROSCOPIC INJURIES CAN BE MINIMIZED BY

- Careful history and physical examination.
- Appropriate case selection.
- Pre operative assessment of intracavitary abnormalities.
- Advance hysteroscope in a clear view.
- Recognition of learning curve and surgeon's skill.

- Knowledge of equipment.
- Thorough knowledge of energy sources and Distension media.
- Strict adherence to fluid deficits.
- Termination of procedure when warranted.

OVULATION INDUCTION

Dr. MADHUMITHA ARUNKARTHIK
MS, DNB (OBG), FRM, FMAS
CONSULTANT, ALPHALIFE FERTILITY & WOMEN'S CENTER

INTRODUCTION :

Ovulation induction is the process of stimulating the ovarian folliculogenesis in order to treat infertility. Initially it was used in women with anovulation. The goal of ovulation induction is to produce a single healthy egg for fertilization. The clinical approach to ovulation induction requires an understanding of the causes of anovulation.

The four most common ovulatory disorders include

- Hyperprolactinemia
- Primary ovarian insufficiency (POI)
- Hypogonadotropic hypogonadism (HA)
- Polycystic ovary syndrome (PCOS)

PHYSIOLOGY OF OVULATION :

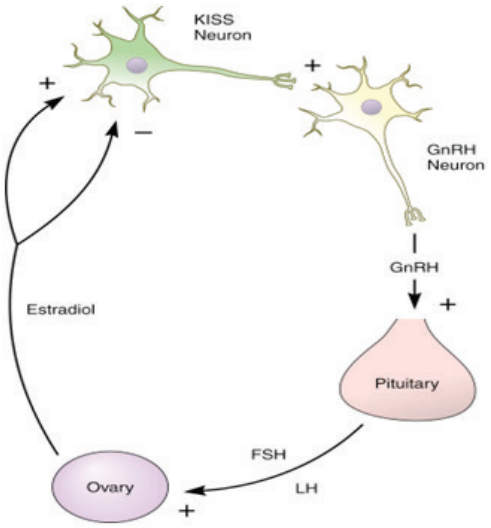
The hypothalamo pituitary ovarian axis works to regulate the menstrual cycle, under neuroendocrinological control.

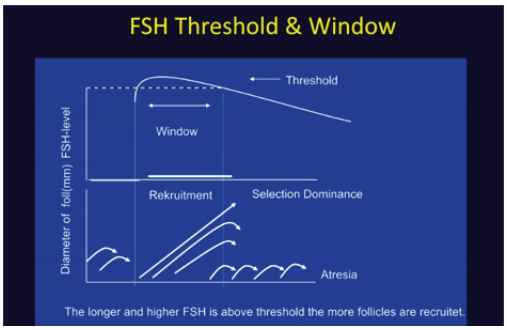
The hypothalamus contains gnrh neurons which secrete pulsatile gnrh into the hypophyseal portal blood system which is transported to the anterior pituitary gland. Gnrh binds to its receptor on gonadotrope cells, stimulating biosynthesis and secretion of the gonadotropins, LH and FSH. LH and FSH travel through the peripheral circulation, acting at the gonads to stimulate gametogenesis and steroidogenesis. The gonadal steroids feedback at the hypothalamus and pituitary to decrease GnRH and gonadotropin secretion. An exception is at the time of the periovulatory LH surge in females, due to positive feedback by rapidly rising E2 levels. Gnrh pulse characteristics vary depending on the time of the menstrual cycle with more frequent but lower amplitude pulses during the follicular phase.

- High frequency pulses of every 60–90 min -> LH secretion in the follicular phase
- Low frequency pulses of every 200 min -> FSH secretion in the late luteal phase.

The high levels of progesterone and proportionally lower levels of estrogen during the luteal phase contribute to the preferential release of FSH at this time. This increase in FSH is critical for the initiation of follicular recruitment during the early follicular phase of the next cycle.

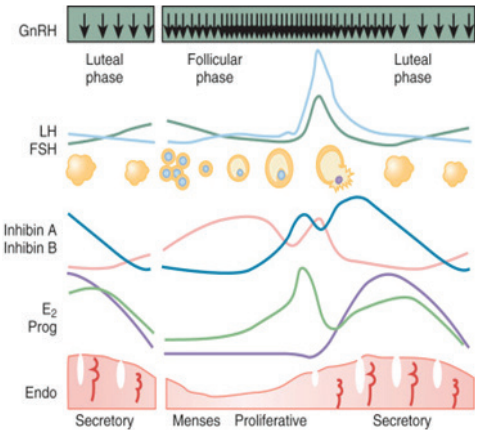
FSH leads to recruitment of a cohort of follicles from the pool of non-proliferating follicles. Between cycle days 5 and 7, selection of a follicle takes place whereby only one follicle is selected from the cohort of recruited follicles to ovulate, and the remaining follicles will undergo atresia. This follicle exerts its dominance by promoting its own growth and suppressing the maturation of the other ovarian follicles thus becoming the dominant follicle. The E2 levels which rise as the follicle grows causes a LH surge due to positive feedback, resulting in ovulation.





INDICATIONS OF OVULATION INDUCTION :

1. WHO Group II patients having anovulatory cycles
2. Unexplained infertility
3. Polycystic ovarian syndrome
4. Superovulation in intrauterine insemination (IUI)
5. Hyperprolactinemia
6. Poor responders



WHO Classifications of ovulatory dysfunction

Group	Gonadotropin levels	Estrogen secretion	Cause
I	Low	Low	Hypothalamic-pituitary failure
II	Normal	Normal	Hypothalamic-pituitary-ovarian axis failure
III	High	Low	Ovarian failure

GOALS OF OVULATION INDUCTION :

-Induce mono follicular rather than multi follicular development

-Subsequent ovulation and

-Ultimately, a singleton pregnancy and birth of a healthy newborn.

GENERAL PRINCIPLES OF OVULATION INDUCTION :

The method of ovulation induction selected by the clinician should be based upon the underlying cause of anovulation, efficacy, costs, risks and potential complications. Both FSH and LH are required for the follicular growth.

PRETREATMENT EVALUATION :

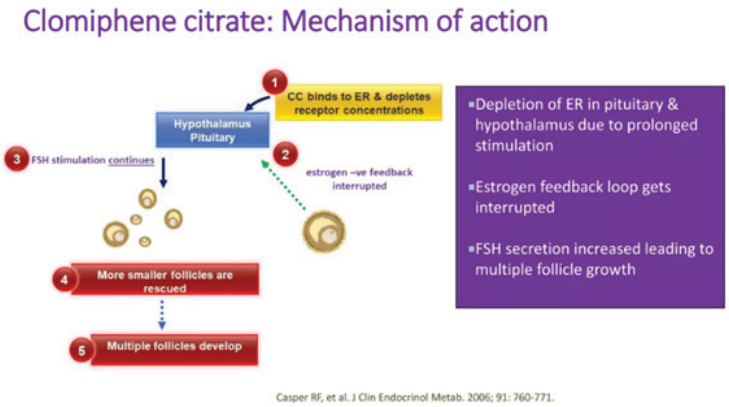
Pretreatment evaluation generally should exclude abnormalities of thyroid function and hyperprolactinemia and should include evaluation of the uterine cavity and fallopian tubes. While evaluation for hyperprolactinemia is not indicated in the general infertility workup, it is indicated in anovulatory women. Blood count and screening for STD is also done. As male factor is present in approximately 50% of infertile couples, complete history and examination of the male partner, in addition to a semen analysis should be done.

METHODS OF OVULATION INDUCTION

CLOMIPHENE CITRATE (CC) :

It is an anti-estrogenic drug. It binds with estrogen receptors at the hypothalamus, blocking the binding of estrogen hormone to estrogen receptors. Hypothalamus detects a lack of estrogen binding at the receptors and releases gonadotropin-releasing hormone. GNRH signals the pituitary to secrete more follicle-stimulating hormone and luteinizing hormone.

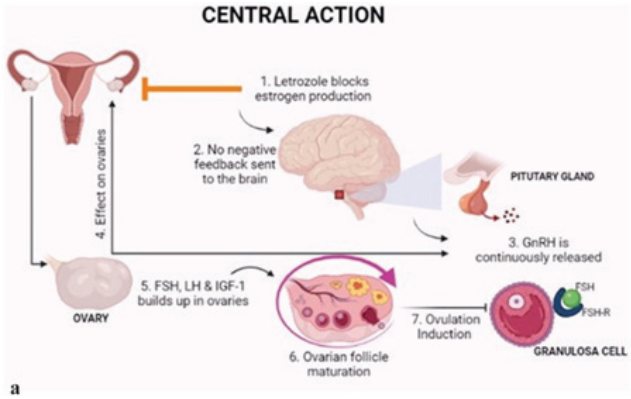
FSH and LH stimulate the development of ovarian follicles. Estrogen level rises after follicular development but it does not decrease the levels of FSH and LH because there is no negative feedback on the hypothalamus as estrogen receptors are occupied by clomiphene citrate.



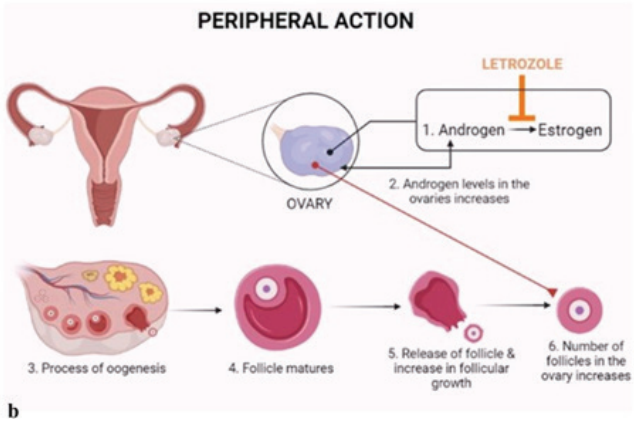
CC dosage varies with body weight however, there is no reliable way to accurately predict what dose will be required in an individual woman. Therefore, a 'stair-step' protocol is often employed to enable optimal dosing without excessive stimulation. The initial dosing of CC is typically 50 mg orally for 5 days beginning on day 2–5 of the menstrual cycle with ovulation occurring 5–10 days afterwards. However, if a dominant follicle is not identified at this time, the patient can be given a 50 mg higher dose of CC for another 5 days until maximum daily dose of 250 mg is reached or ovulation has occurred. Patients who fail to respond to CC at doses of 250 mg/day or do not ovulate after six treatment cycles are considered CC-resistant and will require alternative or combination therapies.

LETROZOLE :

Letrozole is an aromatase inhibitor and is used for ovulation induction. The main advantage of Letrozole is that it is a reversible enzyme inhibitor. It blocks the conversion of androgen to estrogen and thus increases the level of testosterone. By negative feedback, FSH rises and stimulates folliculogenesis. The initial dose is usually 2.5 mg daily for 5 days, with ovulation normally occurring 5–10 days later. Comparable to CC, if a patient does not ovulate or recruit a dominant follicle, the patient can immediately be redosed with an additional 2.5 mg of Letrozole. A maximum dose of 7.5 mg daily is usually employed for individuals undergoing ovulation induction with Letrozole. If a patient does not ovulate after 6 cycles, then further review of infertility should be evaluated, along with consideration for other OI medications.



a



b

GONADOTROPHINS :

Gonadotropin therapy has more risks and is more expensive than oral ovulation induction agents. Individuals that are type I in the WHO classification system are ideal candidates for exogenous gonadotropin treatment as these patients do not have an intact HPO axis. These patients would not respond to OI medications that act within this axis such as CC or Letrozole and, therefore, require a medication that supersedes the HPO axis's normal ability to produce FSH in order to directly stimulate follicular growth and ovulation. However, anovulatory or PCOS individuals who have failed traditional OI may also be good candidates for Gonadotrophin treatment, with the idea that the FSH had not reached threshold level required to generate a dominant follicle. These directly stimulate the ovaries. The various FSH hormone preparations available are hMG, hMGhp, urinary FSH, FSHhp, recombinant FSH and recombinant LH combination. There are three standard protocols for Gonadotrophin therapy: step-up, low dose step-up, and step-down. The step-up protocol is most traditional, with Gonadotrophin given at an initial dose of 75–150 IU for 2–4 days beginning on cycle day 2 or 3. Following this, estradiol levels and transvaginal ultrasound are utilized to determine follicle recruitment. If no increase in estradiol or recruitment of follicles is noted, then the dose is slowly increased until an appropriate response is seen. When estradiol levels start to rise, TVUS is required more frequently to ensure that a dominant follicle is observed when it has reached 16–18 mm. Once the follicle is between 16 and 20 mm, hCG is given to trigger ovulation, which occurs 36–48 h later and intrauterine insemination (IUI) or intercourse is encouraged.

MONITORING OF OVULATION INDUCTION :

A baseline scan is done on day 2/ day 3 to look for residual cysts and endometrial shedding before OI is started. The follicles and endometrium are monitored by serial transvaginal ultrasonogram and estradiol levels which rise as the follicle increases in size. Follicular vascularity and flow indices give an idea about the oocyte quality.

COMPLICATIONS OF OVULATION INDUCTION :

The complications encountered after ovulation induction are multiple pregnancy and OHSS which can be effectively reduced by stringent monitoring.

CONCLUSION :

Infertility secondary to ovulatory dysfunction is a common condition encountered these days. An understanding of reproductive physiology and common etiologies of anovulation is imperative for effective administration of CC or Letrozole or gonadotropins for promoting positive treatment outcomes. Monitoring of the follicular growth and endometrium helps to optimize outcomes. In those who fail initial treatment, further infertility evaluation may be warranted.

REFERENCES :

1. Gonadotrophins for ovulation induction in women with polycystic ovary syndrome. Cochrane Database Syst Rev 2019.
2. A personalized medicine approach to ovulation induction/ovarian stimulation: development of a predictive model and online calculator from level-I evidence. Fertil Steril 2022. Irene Souter et al.
3. Anovulation and ovulation induction Katsikis et al, 2006.
4. Use of exogenous gonadotropins for ovulation induction in anovulatory women: a committee opinion. Practice Committees of the American Society for Reproductive Medicine and Society for Reproductive Endocrinology and Infertility American Society for Reproductive Medicine. Fertil Steril 2019.
5. Ovulation Induction for the General Gynecologist. Steven R. Lindheim et al. J Obstet Gynaecol India. 2018

BREAK


SICK PATIENTS
GOOGLE
FAMILY DOCTORS


Doctor: You need to take one of this pills everyday for the rest of your life
Him: But there's only 3 pills doctor
Doctor: Exactly


Am I dying?
We are all dying, just at different speeds.
But what about me?
You're like the Usain Bolt of dying, lmao


WANT THE GOOD NEWS OR THE BAD NEWS FIRST?
GOOD NEWS, PLEASE, DOCTOR
WELL, THEY'RE NAMING A DISEASE AFTER YOU

HORMONAL REPLACEMENT THERAPY

Dr. ANUREKHA J P,
MD, DNB, FRM, FICOG
ASSISTANT PROFESSOR, GMKMCH
CONSULTANT, ARMC IVF FERTILITY CENTRE

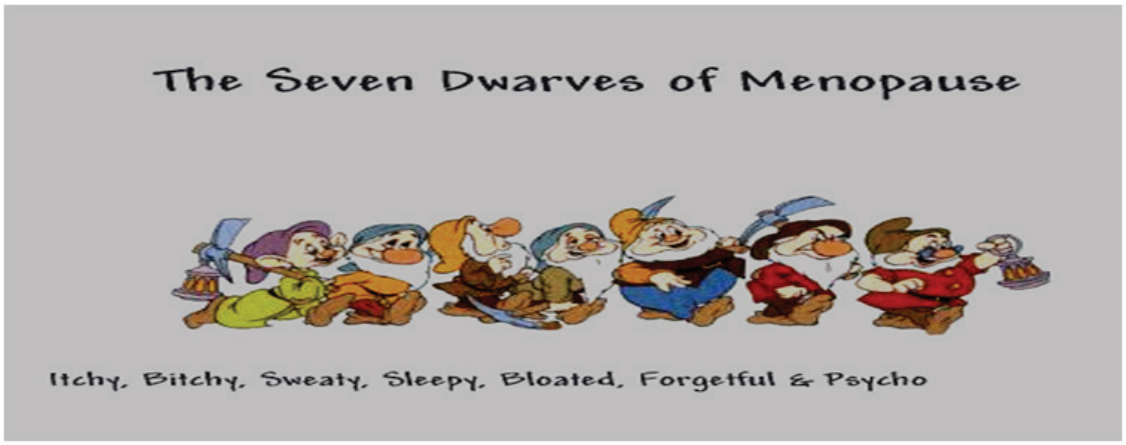
INTRODUCTION :

Life span is increased over last decades and as a result a woman has to spend 1/3 rd of her living years after menopause. Hormone replacement therapy (HRT) or Hormone therapy (HT) in postmenopausal women is proven to prevent bone loss and reduce fracture along with symptomatic improvement in Vasomotor symptoms (VMS) like hot flushes, night sweats and genitourinary symptoms of menopause (GSM). But the hype is always there HRT is associated with side effects or in someone's views more risky! This chapter aims to intrude the recent updates regarding the role of HRT.

WHOM- INDICATIONS :

Recently menopausal women with moderate or severe postmenopausal symptoms (seven dwarfs) are appropriate candidates for HT; spectrum extends to surgically induced menopause and Premature menopause before 40 years of age. Assessment of Bone mineral density by Dual Xray absorptiometry (DXA) with resulting T score <-1 to 2.5 (osteopenia) or T score < -2.5 (osteoporosis) is a definite indication.

Fig 1 Seven dwarfs of menopausal symptoms



WHEN/HOW :

If HRT is started within a decade of menopause or less than 60 years of age benefits outweigh the risks. Before starting HRT patient has to be adequately counselled regarding the benefits and risks, to be questioned for the history of thromboembolic events and baseline screening of hemogram along with renal and liver function tests. In case of in utero HRT endometrial hyperplasia by 2 D or 3 D Ultrasound has to be ruled out.

WHAT- TYPES OF DRUGS :

HORMONAL

1. ESTROGEN

oral (Conjugated equine estrogen (0.3/0.45/0.625mg/d), synthetic conjugated estrogen (0.625-1.25 mg/d), Micronized estradiol - 1-2 mg/d

Transdermal (25, 50, 75 and 100µg per day)

Vaginal

Cream - Vagifem – contains 25µg estradiol. Ring- Estring – 55mm silicone ring containing 2mg estradiol with a release rate of 7.5µg/day

Implants- Estradiol pellets available in doses of 25,50 and 70mg for subcutaneous twice yearly. 25 mg pellet provides blood levels in the range of 40-60pg/ml, comparable with those obtained with standard oral doses. Significant blood levels of estradiol will persist for up to 2yrs after last insertion. Blood levels of estradiol > 200pg/ml should be avoided

Intranasal spray -Aerodiol pulsed estrogen therapy Dose - 300µg/day (1 spray in each nostril per day) Comparable to oral estradiol 2mg/day.

2. COMBINED ESTROGEN AND PROGESTERONE

Progesterone is used to protect endometrium against unchecked proliferation; Estrogen and progestin can be given as either sequential or continuous regimens.

Sequential regimen: progesterone administered 2 weeks of every month, using the comparable doses of the following progestins

5mg Medroxy progesterone acetate or 0.7mg norethindrone, or 1mg norethindrone acetate or 200mg micronized progesterone

Progestin withdrawal bleeding occurs in 80-90% of women on a sequential regimen

Continuous, combined regimen: progestins are combined with estrogen in the following comparable doses

1.5 or 2.5mg medroxy progesterone acetate daily or 0.35mg norethindrone, or 0.50 or 1mg norethindrone acetate or 100mg micronized progesterone

Progesterone supplementation has a role in patients with past history of endometriosis / underwent supracervical hysterectomy or past history of adenocarcinoma of endometrium. Monthly withdrawal bleeding occurs in 80–90 per cent of women after the last dose of the progestogen or during the last days of taking it.

Levonorgestrel-releasing intrauterine system (LNG-IUS) can be used for endometrial protection in HT. LNG-IUS contains 52 mg of LNG, initially releasing 20 µg/ day, followed by a mean release of 12 µg of LNG daily for a period of 5 years.

CONTRAINDICATIONS TO ESTROGENS AND PROGESTOGENS

1. Unexplained vaginal bleeding
2. Acute liver dysfunction
3. Patients with estrogen-dependent cancer such as breast cancer.
4. Women with risk factors for stroke / VTE should be advised to take transdermal estradiol in preference to oral estradiol.

3. ANDROGENS

Testosterone patch of 150mcg/300 mcg or Testosterone undecanoate 40 mg oral daily or alternate days is advisable specially to treat menopause related female sexual dysfunction. Though androgenisation and an absolute fall of HDL values is proven deleterious, evidence is scarce either to support or deter.

ALTERNATIVE THERAPY :

1. SELECTIVE ESTROGEN RECEPTOR MODULATORS (SERM) / TISSUE SELECTIVE ESTROGEN COMPLEX TSEC

Triphenylethelene: Clomiphene, Tamoxifen, Toremifene

Benzothiophene: Raloxifene, Iodoxifene, Droloxifene and Leuormeloxifene,

Recent/ New gen SERM: ospemifene

Favorable safety/tolerability profile with no increased risk of endometrial hyperplasia makes SERM an attractive option;

Raloxifene at 60 mg/day is the most convenient regimen, earlier advocacies of Tamoxifen for 5mg / day in breast cancer survivors has a risk of endometrial hyperplasia. But these drugs carried risk of altered breast density though correlation to breast cancer is limited.

TISSUE SELECTIVE ESTROGEN COMPLEX

Bazedoxifene 20 mg with CEE 0.45 mg daily effective for VMS and urogenital atrophy but carries potential risk of endometrial cancer, breast cancer, Venous thromboembolism, coronary heart disease and stroke.

2. TIBOLONE

Mild oestrogenic androgenic and progestational agent and STEAR (Selective Tissue Estrogen Activity Regulation). Tibolone 1.25 mg to 2.5 mg daily to be taken at the same time shows favorable effects on bone health and at the same time without adverse effect on breast and endometrium.

3. BISPHOSPHONATE

Non-nitrogen like Etidronate, Clodronate and Fludronate

Nitrogen-containing like Alendronate, Risedronate, Ibandronate and Zoledronic acid

Alendronate 70 mg daily before first meal of the day with plenty of water is effective treatment for osteoporosis.

SERMs can be drugs of choice to counteract postmenopausal bone loss in younger women or at low risk of fracture, while bisphosphonates are appropriate for women with high risk or at an older age.

NEWER DRUGS :

Teriparatide, Abzioparatide and Tenosumab - monoclonal antibody to receptor activator of nuclear factor kB ligand

NON-HORMONAL :

Calcitonin, Phytoestrogen, Multivitamins, minerals are supposed to provide supportive role. It is advisable to combine HRT with Supplementation of calcium 500mg and vitamin D 400 IU/ 800 IU per day.

EVIDENCE :

1. The first randomized clinical trial was a study of secondary prevention of cardiovascular disease, the Heart and Estrogen/Progestin Replacement Study (HERS).

Cochrane analysis published in 2015 showed that women who started HT within 10 years of their menopause had lower coronary heart disease, non-fatal myocardial infarction as well as lower cardiovascular mortality compared to placebo or no treatment.

2. WOMEN'S HEALTH INITIATIVE (WHI) In 1998, the Women's Health Initiative (WHI) was started, which was the largest randomized study to date that was aimed at evaluating the effect of HRT on the most common causes of death and disability in postmenopausal women, such as cardiovascular disease, cancer, and osteoporosis. The first results of the WHI were published in 2002 after a mean follow-up period of 5.2 years. In the group with intact uteri, an increased incidence of coronary heart disease and breast cancer was observed in concomitance with a reduction of osteoporotic fractures and colorectal cancer. Given these results, it seemed that the risks outweighed the benefits, and the trial was prematurely discontinued.

The data were largely disseminated to the media, creating panic among HRT users and forcing new guidance for doctors on prescribing HRT. The trial with only estrogen (performed in hysterectomized women) continued, and the preliminary data were published in 2004. In addition, this trial was stopped prematurely after 6.8 years of follow-up due to evidence of a small increased risk of ischemic stroke in the absence of other significant cardiovascular benefits. In spite of the benefits (such as a reduction of osteoporotic fracture and colon cancer) the overall message on HRT remained negative.

3. WOMEN'S HEALTH INITIATIVE MEMORY STUDY (WHIMS 2005)- The Women's Health Initiative Memory Study (WHIMS) was a multicentre, randomised, double-blind, placebo-controlled clinical trial in which a subgroup of women who participated in the Women's Health Initiative study were assessed for the effects of HT on dementia and mild cognitive impairment

4 THE MILLION WOMEN STUDY -1,08,110 women recruited between 1996 and 2001, Based on an average follow up of 2.6 yrs (a very short exposure; indeed, the breast cancers were diagnosed on an average of 1.2 years after the study begin). No significant difference was found between specific estrogen and progestogens or their doses or between continuous or sequential regimens.

5 SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS (SEER) STUDY, showed a 6.7% decrease in breast cancer incidence linked to reduced HRT use in 2003.

6 THE STUDY OF WOMEN'S HEALTH ACROSS THE NATION (SWAN) showed that women with hot flushes had higher subclinical CVD, including greater aortic calcification, poorer endothelial function, and higher intima media thickness, than did women without menopausal symptoms.

BREAST CANCER :

The WHI study linked the effects of combined estrogen and progestin HT to an increased risk of breast cancer. Results indicated a hazard risk for breast cancer of 1.24 after 5 years of HT; this correlates to a 26% increase in risk. The attributable risk was 8 per 1000 women. But detailed analysis showed increase in breast cancer was observed over a timetable of 1 year itself. This suggests that the cancer was pre-existing, as a focus of malignant cells is thought to take 8 years to become detectable. Most significantly, the breast cancers were also observed in the women who had taken hormone therapy prior to enrolment, suggesting that the trial exposure required at least 5 years before an effect was noted.

Sweetland et al 2012 concluded that oral HT users had twice the risk of VTE in the first 2 years after starting HT than later (Pheterogeneity = 0.0006); effect is more with medroxy progesterone acetate. Associations were similar for deep vein thrombosis with and without pulmonary embolism

ADVANTAGES :

THE FOLLOWING TABLE HAS ENUMERATED THE ADVANTAGES OF HT.

TABLE.1 ADVANTAGES OF HORMONAL THERAPY

Effects	Outcome	Reference
Vasomotor symptoms	75% fall in frequency, 87% fall in severity	Cochrane 2015 NICE 2015 - SSRI/SNRI/clonidine for VMS alone
Urogenital symptoms	75 - 805 relief, Grade I b recommendation	Rahn D 2014
Female sexual functi	Transdermal testosterone with effective relief	Nappi RE 2022
Mood depression and anxiety	68 - 80% improvement	Baber 2016 climacteric
Osteoporosis and fractures	30% reduction in osteoporotic fractures	Cochrane 2015
Cognition	30% reduction of Alzheimer's disease	Baber 2016 climacteric

Long-term estrogen therapy appears to reduce the risk of cataract by 60–80 per cent as well as small absolute reduction in the risk of developing glaucoma.

DISADVANTAGES- WHERE TO STOP :

Nausea vomiting, headache and breast discomfort are all estrogen dependent side effects; Breakthrough bleeding is common when commencing HRT. Unscheduled bleeding beyond the first 3–6 months of starting sequential regimens should be investigated

The duration of HRT should be based on the menopausal symptoms experienced by the woman and should not be subject to arbitrary limits and women should be informed that favourable benefit–risk profile exists before the age of 60.

In patients on estrogen alone HT or in SERM endometrial thickness has to be evaluated annually if patient remains asymptomatic, endometrial thickness less than or equal to 4mm is non troublesome. In case of recurrent AUB or when the endometrium thickness is greater than 4mm in a postmenopausal woman, additional uterine investigations (hysteroscopy and histology) are recommended.

In the presence of diffuse breast pain without abnormalities on clinical examination, it is not recommended to change the usual indications for screening. For focal breast pain, breast imaging (mammography and possibly ultrasound) is recommended, doses of estrogens should be reduced until the breast pain decreases, or even stop the HRT if this symptom persists despite the use of low doses.

CONCLUSIONS :

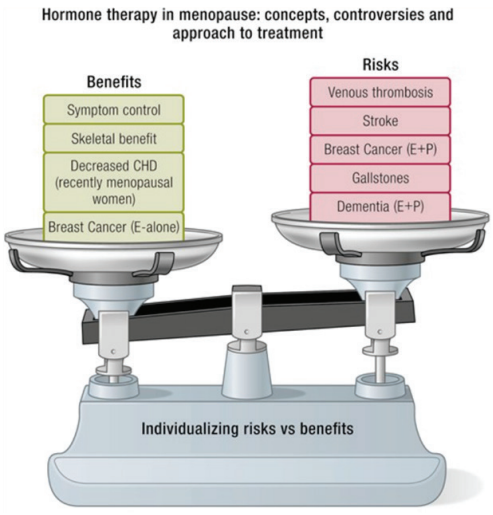
Women with intolerable menopausal symptoms may benefit with short-term use of low-dose HT, provided they do not have specific contraindications.

HT should be considered the first-line therapeutic intervention for the prevention and treatment of osteoporosis in women with premature ovarian insufficiency (POI) and menopausal women below 60 years of age, particularly those with menopausal symptom. But Cochrane 2017 concludes that HT is generally recommended as an option only for women at significant risk for whom non-oestrogen therapies are unsuitable.

HT may be contraindicated for some women, including those at increased risk of cardiovascular disease, increased risk of thromboembolic disease (such as those with obesity or a history of venous thrombosis) or increased risk of some types of cancer (such as breast cancer, in women with a uterus). The risk of endometrial cancer among women with a uterus taking oestrogen-only HT is well documented.

HT is not indicated for primary or secondary prevention of cardiovascular disease or dementia, nor for prevention of deterioration of cognitive function in postmenopausal women.

Ovarian transplantation- a logical futuristic option !!



REFERENCES :

Bonaccorsi G, Rizzati M, Salani L, Giganti M. Postmenopausal osteoporosis: risk evaluation and treatment options. Minerva Obstet Gynecol 2021;73:714-29. DOI: 10.23736/S2724-606X.21.04896-X

Baber RJ, Panay N, Fenton A. IMS recommendations on women's midlife health and menopause hormone therapy. Climacteric 2016;19(2):109–50.

Menopause: diagnosis and management NICE guideline [NG23]. November 2015. ww.nice.org.uk/guidance/ng23

Sweetland S, Beral V, Balkwill A, Liu B, Benson VS, Canonico M, Green J, Reeves GK; Million Women Study Collaborators. Venous thromboembolism risk in relation to use of different types of postmenopausal hormone therapy in a large prospective

study. J Thromb Haemost. 2012 Nov;10(11):2277-86. doi: 10.1111/j.1538-7836.2012.04919.x. PMID: 22963114.

Rahn DD, Carberry C, Sanses TV, Mamik MM, Ward RM, Meriwether KV, Olivera CK, Abed H, Balk EM, Murphy M; Society of Gynecologic Surgeons Systematic Review Group. Vaginal estrogen for genitourinary syndrome of menopause: a systematic review. Obstet Gynecol. 2014 Dec;124(6):1147-1156. doi: 10.1097/AOG.0000000000000526. PMID: 25415166; PMCID: PMC4855283.

Nappi RE, Tiranini L, Martini E, Bosoni D, Righi A, Cucinella L. Medical Treatment of Female Sexual Dysfunction. Urol Clin North Am. 2022 May;49(2):299-307. doi: 10.1016/j.ucl.2022.02.001. PMID: 35428435.

Jane Marjoribanks, Cindy Farquhar, Helen Roberts, Anne Lethaby, Jasmine Lee Long-term hormone therapy for perimenopausal and postmenopausal women. Cochrane Database of Systematic Reviews: 17 January 2017. https://doi.org/10.1002/14651858.CD004143.pub5

Valerie A Flores, Lubna Pal, JoAnn E Manson, Hormone Therapy in Menopause: Concepts, Controversies, and Approach to Treatment, Endocrine Reviews, Volume 42, Issue 6, December 2021, Pages 720–752, https://doi.org/10.1210/endrev/bnab011

INVERSION OF CHROMOSOME 9 AS A CAUSE OF PREGNANCY LOSS:
EVIDENCE FROM 2 INDEPENDENT PRODUCTS OF CONCEPTION

Dr. MEENAKSHI BHAIRAVI KANNAN,
MS. Medical Genetics (UK), PhD Experimental Medicine (Canada),
GENETICS CONSULTANT, KANSHYA GENETICS CENTRE

ABSTRACT :

About 5 to 8% of couples experience recurrent pregnancy loss (RPL) and the etiology remains unexplained in nearly half those cases. Chromosomal aberrations are the leading cause of RPL among unexplained cases. Chromosomal investigations in the couple and foetal samples could reveal relevant details on the cause of RPL, the risks of recurrence and alternative methods to improve pregnancy outcome. Inversion of chromosome 9 (inv(9)) is considered to be a normal variant, and inv(9) in patients is often ignored in couples with RPL. However, there are few reports concerning the outcomes of pregnancy in patients with RPL when either of the partner is a carrier of inv(9). In this study, we analysed the outcomes of pregnancy in two independent cases, where the father was a carrier of inv(9). Tissue biopsy from product of conception (POC) samples were evaluated for chromosomal microdeletions and duplications. Both POC samples presented with deletion in chromosome 9, resulting in partial monosomy. While some individuals carrying chromosomal inversions may produce healthy offspring, these two case scenarios represent the potential pathogenic effects of these parental inversions in couples with RPL. Patients carrying chromosomal inversions should therefore be counselled on a case-to-case basis, depending on clinical history and foetal chromosomal assessments to validate pathogenicity, whenever possible. This study also emphasizes the significance of chromosomal evaluations in POC samples, which is a vital tool to investigate unexplained pregnancy loss.

INTRODUCTION :

Recurrent Pregnancy Loss (RPL) occurs in about 5-8% of reproductively active couples, which is typically defined as 2 or more consecutive early pregnancy losses. The etiology remains unexplained in 35-60% of cases. There are several risk factors for RPL, including Mullerian anomaly, inherited thrombophilia, hormone deficiency, metabolic disorder, infectious diseases, autoimmune abnormalities, chromosomal

and genetic abnormalities. Chromosomal anomalies are one of the most relevant risk factors for RPL, occurring at a frequency of 3%-8%, [2-5] in couples with RPL. The most common forms of chromosomal anomalies are balanced translocations between two chromosomes in one individual. It has been reported that this anomaly occurs in approximately 5%-6% of couples with RPL, [6- 8]. The partner that carries this balanced translocation presents with a higher risk of infertility, RPL, and producing chromosomally abnormal offspring.

Chromosomal inversion refers to the occurrence of a two-break event in a chromosome, and the segment rotates 180 degrees before reinserting [9]. Inversions are functionally similar to translocations in that alterations affect the structure or activity of genes near one or the other breakpoint. Inversion carriers may produce abnormal gametes through meiosis, which may lead to partial duplication/deletion of the embryonic chromosome (Fig. 1). This then results in spontaneous abortion, a foetus with multiple anomalies, or birth of a malformed child [10]. Pericentric inversion 9 is a common chromosome variant with an incidence of approximately 2%-4% in the general population. Despite the relatively high incidence of this finding, the pathogenicity of this variant is under debate. Inversion 9 has been associated with non-viable embryos, early miscarriages, or livebirths with multiple anomalies, RPL and male infertility [10]. However, there hasn't been sufficient clinical evidence for inversion 9 being an isolated cause of pregnancy loss. It is therefore considered to be a normal variant and has been reported to be a harmless anomaly in couples with RPL. Here we report pregnancy loss due to chromosomal deletions in foetuses in 2 independent cases, occurring as a result of parental chromosomal inversion 9. This report emphasizes the significance of parental chromosomal investigations, as well as potential chromosomal anomalies that may occur in foetuses of parents with chromosomal inversion.

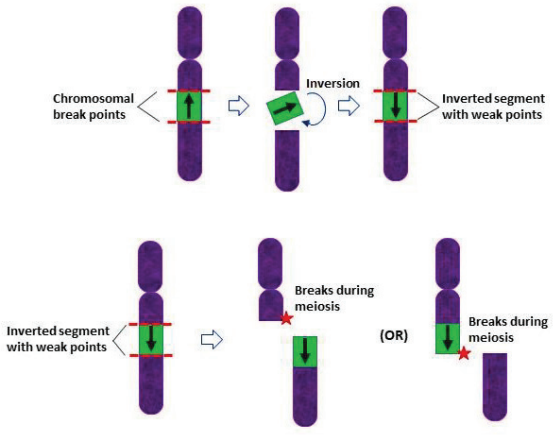


Figure 1. Chromosomal inversion leading to breakpoints. An inversion occurs when a single chromosomal segment undergoes breakage and rearrangement within itself, in an inverted position. The inversion process leads to breakpoints that may occasionally remain weak through the process of meiosis and lead to chromosomal aberrations in the offspring.

MATERIALS :

CYTOGENETIC ANALYSIS

Peripheral blood (2 mL) was collected from all patients in sterile tubes containing heparin anticoagulant. Lymphocytes were cultured in RPMI-1640 culture medium (including phytohemagglutinin) for 72 h. Then, G-banding was performed using standard operating procedure. At least 30 metaphases were analyzed for each patient. The karyotypes were described according to the International System for Human Cytogenetic Nomenclature (ISCN 2016).

CHROMOSOMAL MICROARRAY ANALYSIS :

Product of conception (POC) in the form of tissue biopsy was temporarily preserved in normal saline with gentamycin. The microarray and associated software (Chromosome Analysis Suite) is designed by Affymetrix and used for the purpose of identifying DNA copy number gains and losses associated with chromosomal imbalances. The resolution corresponds to 750kbp for clinically relevant losses and 1MB for gains. The test cannot detect balanced chromosomal rearrangements, genetic disorders due to point mutations, repeat expansions or low-grade mosaicism (<20%) for chromosomal abnormalities. The protocol followed the ACMG guidelines (South et. al., Constitutional Microarray Guidelines, Genetics in Medicine, Vol 15, Number 11, Nov 2013) for reporting of CMA findings.

RESULTS :

CASE 1.

Mother aged 22 and father 33 years at the time of conception, presented with a history of 1 biochemical pregnancy (G1: 8w) and 1 spontaneous abortion (G2: 8w). Routine gynecological examination showed that his wife had normal reproductive function. Semen analysis of the husband showed that semen parameters were within the normal range. Examination of the family history (pedigree analysis) revealed no further relevant abnormalities. The product of conception from G2 was assessed via chromosomal microarray analysis to rule out spontaneous chromosomal deletions and/or duplications. The foetal sample was negative for maternal cell contamination. Chromosomal microarray analysis on the foetal sample (POC) revealed deletion in chromosome 9 (9p21.2-->qter) in a non-mosaic state. Cytogenetic analysis of the couple revealed that the husband was a carrier of an inversion in chromosome 9: 46,XY,inv(9)(p11q13)[30]. His wife presented with normal karyotype 46,XX [20].

CASE 2.

Husband ages 28 years and wife 26 years presented with no live children after 3 years of marriage and 2 early spontaneous abortions and 1 missed abortion at 7w4d. Routine gynecological examination showed that his wife had normal reproductive

function. Clinical examination of the couple showed normal intelligence and phenotype. Examination of the family history (pedigree analysis) revealed no further relevant abnormalities. Semen analysis revealed asthenozoospermia in the husband, but the couple were able to achieve spontaneous conceptions. POC from the third missed abortion was assessed for chromosomal deletions and duplications via chromosomal microarray analysis. The foetal POC sample was negative for maternal cell contamination and presented with deletion in chromosome 9 (del 9p21- ->qter) in a mosaic state (nearly 45% of the cells carried the deletion). Cytogenetic analysis revealed the husband to be a carrier of chromosomal inversion. His karyotype was 46,XY,inv(9)(p21q21)[30], whereas that of his wife was 46,XX[20].

DISCUSSION :

Chromosomal inversion is a significant chromosomal structural abnormality. Male inversion carriers may be infertile because of spermatozoa production with unbalanced chromosome [11]. DNA fragmentation is found to be significantly higher in sperm with unbalanced chromosomal content [12]. Although inversion carriers are at higher risk of being infertile, patients with normal fertility have often been observed in clinical practice. Genetic counselling remains a challenge for inversion carriers. This study reported 2 males showing pericentric inversion in chromosome 9. One of these had asthenospermia, and the other normal semen parameters. Both wives presented with pregnancy loss that was a result of paternal inversion. This study also emphasizes the importance of chromosomal investigations on POC samples to identify spontaneous or inherited chromosomal aberrations. It is most likely that deletion in chromosome 9 was a recurring pathogenic event in these couples. However, previous foetal samples in both cases were unavailable for assessment or validation.

It is considered that circularized configuration is formed at the pachytene stage of meiosis in cases of chromosomal inversion, and that various unbalanced karyotypes would emerge in the gametes (oocytes or sperms), prior to fertilization. Young et al. [13] reported on the aneuploidy rates in embryos from 28 patients who carried the inversion 9 variant and demonstrated that a similar rate of aneuploidy was seen in a group of age-matched controls. Collodel et al. [14], hypothesized that the inversion 9 variant could have an effect on meiotic segregation. Deletions in chromosome 9 have been associated with intrauterine death, failure to thrive, psychomotor developmental delay, facial dysmorphism (trigonocephaly, midface hypoplasia, upslanting palpebral fissures, dysplastic small ears, flat nasal bridge with anteverted nostrils and long philtrum, micrognathia, choanal atresia, short neck), single umbilical artery, omphalocele, inguinal or umbilical hernia, genital abnormalities (hypospadia, cryptorchidism), muscular hypotonia and scoliosis. Large deletions in chromosome 9, leading to partial monosomy of chromosome 9 could result in early abortions

All inversions cannot be classified as pathogenic, since some individuals with chromosomal inversions may produce healthy biological children and have no other clinical abnormalities. Genetic counselling should depend on individual clinical history, type of inversion and the type of chromosomal anomalies detected in the foetal sample (POC analysis), if applicable. For inversion carriers with recurrent spontaneous abortion, the couples can choose PGT to reduce the abortion rate and increase the chances of pregnancy. Alternatively, these carriers can opt for natural pregnancy along with prenatal diagnosis. For inversion carriers with asthenospermia, PGT treatment may be recommended.

REFERENCES :

1. Branch DW, Gibson M, Silver RM. Clinical Practice: Recurrent Miscarriage. N Engl

J Med. 2010;363:1740-1747.

2. Bryns JP, Van Buggenhout G. Structural chromosome rearrangements in couples with recurrent fetal wastage. Eur J Obstet Gynecol Reprod Biol. 1998;81:71-76.

3. Elghezal H, Hidar S, Mougou S, Khairi H, Saâd A. Prevalence of chromosomal abnormalities in couples with recurrent miscarriage. Fertil Steril. 2007;88:721-723.

4. Meza-Espinoza JP, Anguiano LO, Rivera H. Chromosomal abnormalities in couples with reproductive disorders. Gynecol Obstet Invest. 2008;66:237-240.

5. Dutta UR, Rajitha P, Pidugu VK, Dalal AB. Cytogenetic abnormalities in 1162 couples with recurrent miscarriages in southern region of India: Report and review. J Assist Reprod Genet. 2011;28:145-149.

6. Ostovics MK, Toth SP, Wessely JA. Cytogenetic investigation in 418 couples with recurrent fetal wastage. Ann Genet. 1982;25:232-236.

7. Fryns JP, Kleczkowska A, Kubien E, Petit P, Van den Berghe H. Cytogenetic survey in couples with recurrent fetal wastage. Hum Genet. 1984;65:336-354.

8. Portnoi MF, Joye N, van den Akker J, Morlier G, Taillemite JL. Karyotypes of 1142

couples with recurrent abortion. Obstet Gynecol. 1988;72:31-34.

9. Young D, Klepacka D, McGarvey M, Schoolcraft WB, Katz-Jaffe MG. Infertility patients with chromosome inversions are not susceptible to an inter-chromosomal effect. J Assist Reprod Genet. 2019;36:509–16.

10. Balasar Ö, Zamani AG, Balasar M, Acar H. Male infertility associated with de novo pericentric inversion of chromosome 1. Turk J Urol. 2017;43:560–2

11. Caer E, Perrin A, Douet-Guilbert N, Amice V, De Braekeleer M, Morel F. Differing mechanisms of meiotic segregation in spermatozoa from three carriers of a pericentric inversion of chromosome 8. Fertil Steril. 2008;89(6):1637–40

12. Perrin A, Nguyen MH, Bujan L, Vialard F, Amice V, Guéganic N. et al. DNA fragmentation is higher in spermatozoa with chromosomally unbalanced content in men with a structural chromosomal rearrangement. Andrology. 2013;1(4):632–8.

13. Young D, Klepacka D, McGarvey M, Schoolcraft WB, Katz-Jaffe MG. Infertility patients with chromosome inversions are not susceptible to an inter-chromosomal effect. J Assist Reprod Genet. 2019;36(3):509–16.

14. Collodel G, Moretti E, Capitani S, Piomboni P, Anichini C, Estenoz M, et al. TEM,

FISH and molecular studies in infertile men with pericentric inversion of chromosome

ALL WE NEED TO KNOW ABOUT PRP AS A PRACTISING GYNAECOLOGIST

Dr. KAVITHA NAGARAJAN,
MD OG, MRCOG, MICG.,
FELLOW (REPRODUCTIVE MEDICINE)
CLINICAL DIRECTOR
SKS WOMEN'S CENTRE & FERTILITY FOUNDATION

INTRODUCTION :

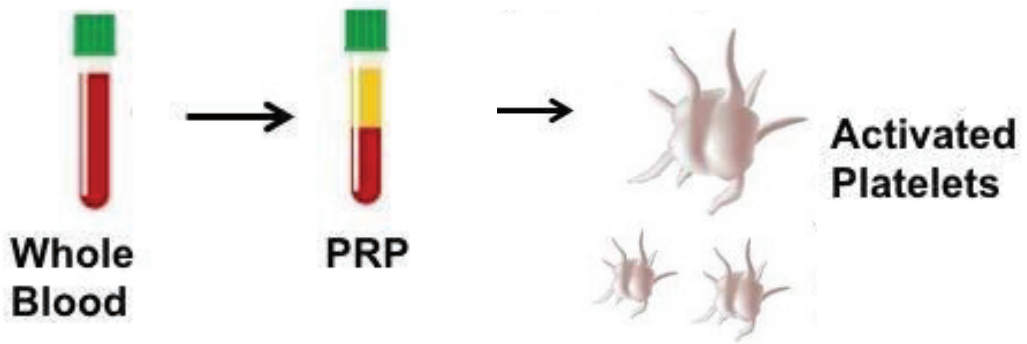
Platelet-rich plasma (PRP) is becoming more popular as a nonoperative treatment option for a broad spectrum of medical disorders. PRP is widely used in orthopedic and sports medicine to relieve pain through the natural promotion of healing in musculoskeletal diseases.

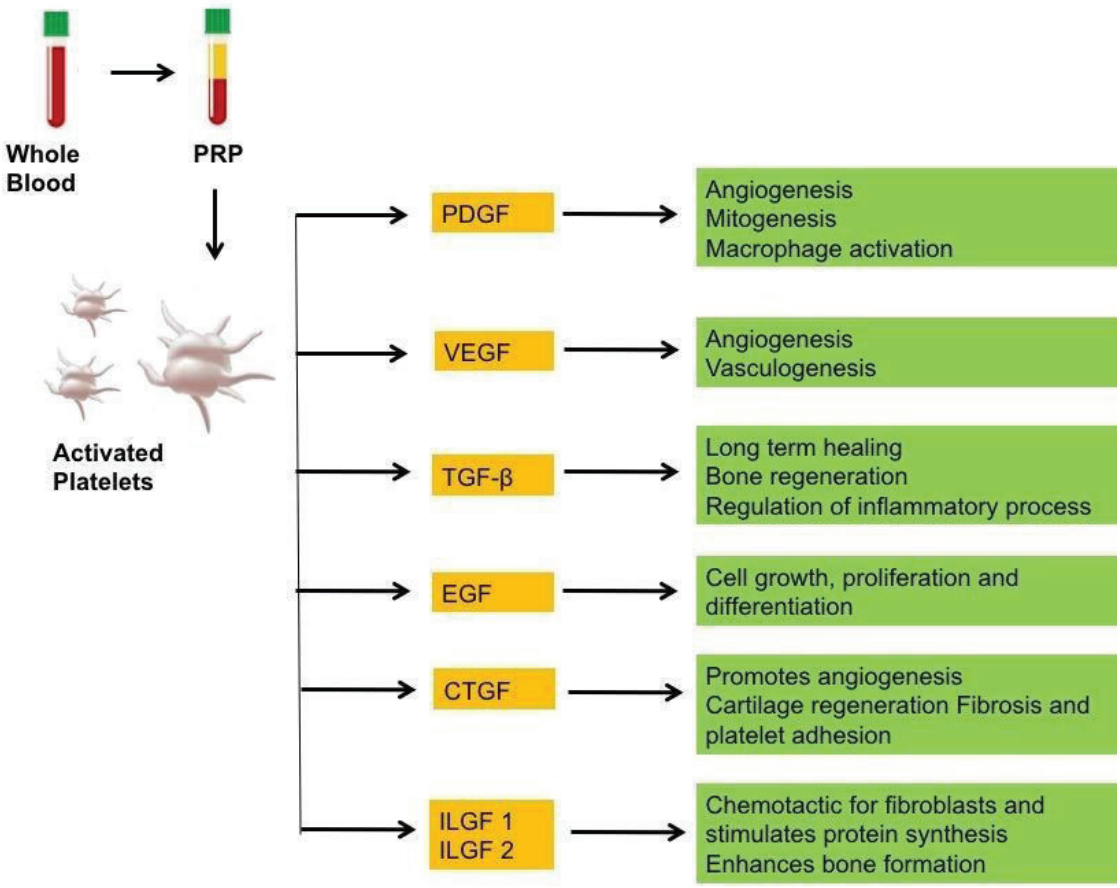
PRP is currently considered a new therapeutic modality for some disorders that are refractory to conventional drugs . The goal of this discipline is to enhance the body's innate ability to repair and regenerate. PRP therapy has lately gained a lot of attention as a safe, non-surgical, biological treatment.

The theory underlying this treatment modality was derived from natural healing processes, as the body's first response to tissue injury is to deliver platelets to the injured area. Platelets promote healing and attract stem cells to the site of the injury.

MECHANISM OF ACTION OF PRP :

Various growth factors are produced by activated platelets at the site of tissue injury and accelerate the healing and tissue regeneration. PRP: Platelet-rich plasma, PDGF: Platelet derived growth factor, VEGF: Vascular endothelial growth factor, TGF-: Transforming growth factor beta, EGF: Epidermal growth factor, CTGF: Connective tissue growth factor, ILGF: Insulin like growth factor.



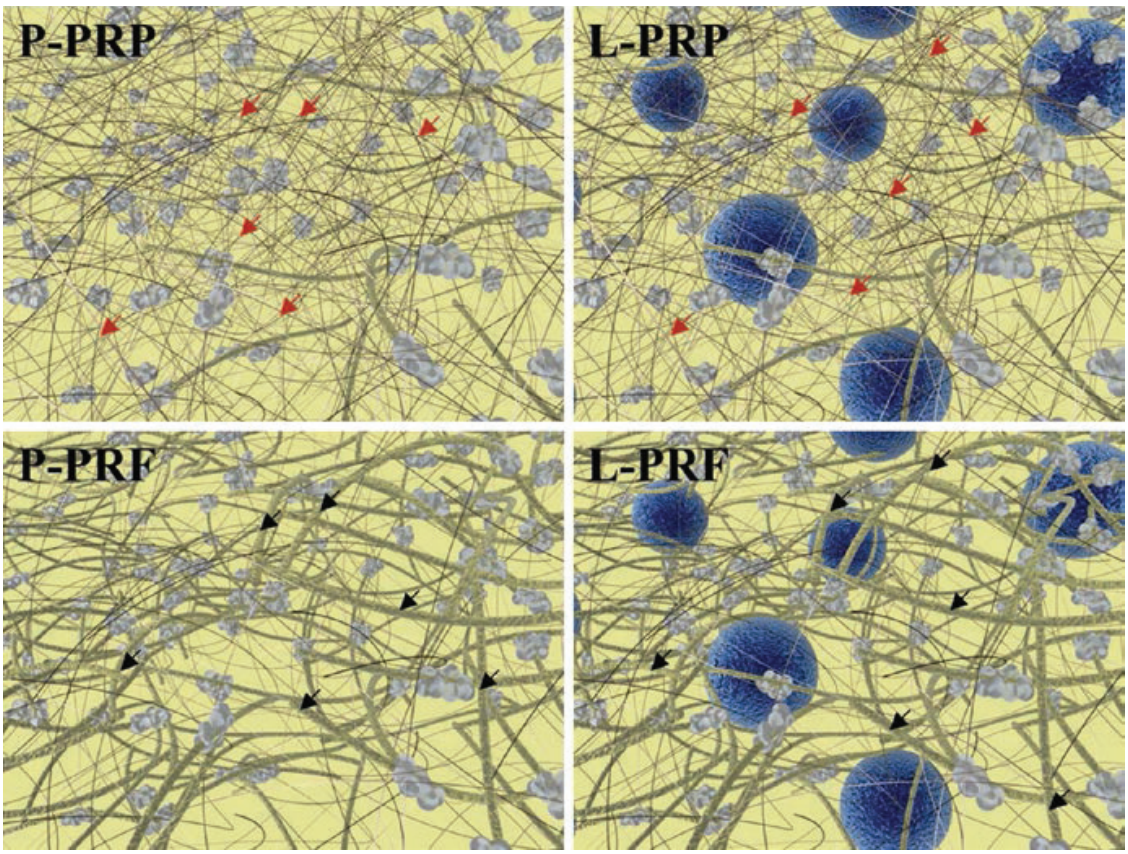


PRP SUBTYPES AND DEFNITIONS :

Various sub classifications exist through different formulations based on additional products found in the final collection. Clinical formulations of PRP used across disciplines vary in their concentration of platelets and other cell types, such as leukocytes, erythrocytes, and fibrin. While the consensus on optimal protocols and classifications remain debatable, four classifications of PRP are commonly used when defned in the literature:

Table 1. Platelet-containing preparations, as classified by Dohan Ehrenfest et al. [8]

Preparation	Acronym	Leukocytes	Fibrin density
Pure platelet-rich plasma	P-PRP	Poor	Low
Leukocyte- and platelet-rich plasma	L-PRP	Rich	Low
Pure platelet-rich fibrin	P-PRF	Poor	High
Leukocyte- and platelet-rich fibrin	L-PRF	Rich	High



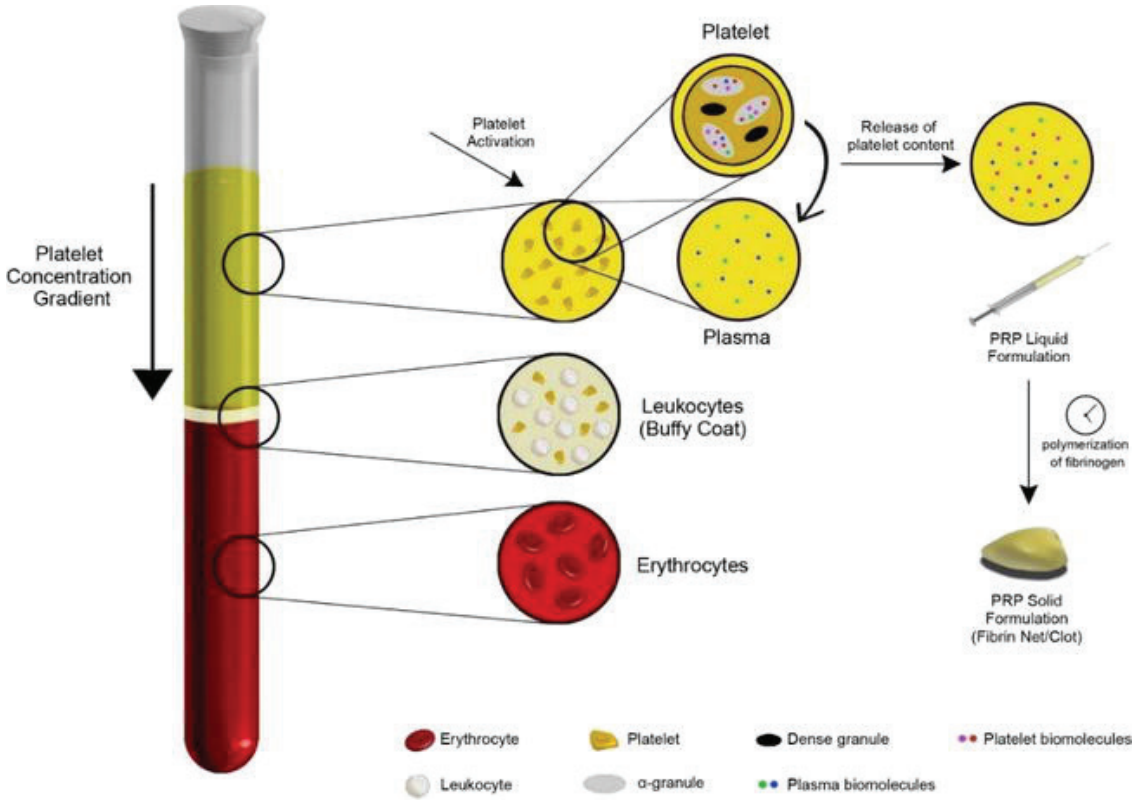
The fibrin frameworks present over platelets support the regenerative matrix leading to the rapid establishment of the proper morphological and molecular configuration for wound healing

PRP PREPARATION :

The preparation of PRP is an outpatient procedure that involves a blood draw, preparation of the PRP, and the injection of PRP into the diseased area. Multiple methods have been developed for PRP preparation, with variation in the speed and timing of centrifugation .

1. Venous blood (15–50 ml) is drawn from the patient's arm in anticoagulant-containing tubes;
2. The recommended temperature during processing is 21°–24° C to prevent platelet activation during centrifugation of the blood;
3. The blood is centrifuged at 1,200 rpm for 12 minutes;
4. The blood separates into three layers: an upper layer that contains platelets and white blood cells, an intermediate thin layer (the buffy coat) that is rich in white blood cells, and a bottom layer that contains red blood cells;

5. The upper and intermediate buffy layers are transferred to an empty sterile tube. The plasma is centrifuged again at 3,300 rpm for 7 minutes to help with the formation of soft pellets (erythrocytes and platelets) at the bottom of the tube;
6. The upper two-thirds of the plasma is discarded because it is platelet-poor plasma;
7. Pellets are homogenized in the lower third (5 ml) of the plasma to create the PRP;
8. The PRP is now ready for injection. Approximately 30 ml of venous blood yields 3–5 ml of PRP;
9. The affected area is disinfected before the PRP injection;
10. Providing assurance to the patient and discussing the procedure make the injection easier and less painful;
11. PRP stimulates a series of biological responses, and the injection site may become swollen and painful for roughly 3 days.



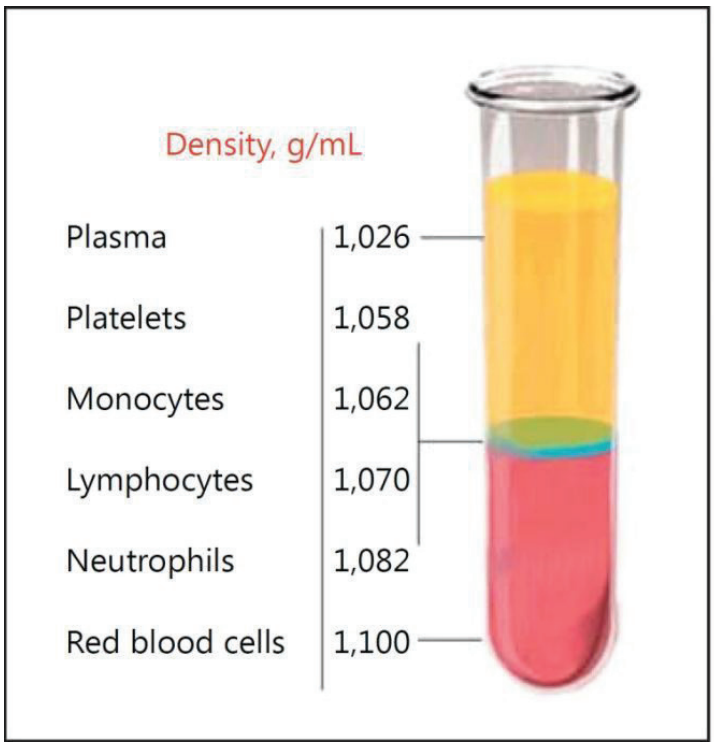


Fig. 1 DEPA classification system. (Modified from Magalon et al. 2016)

D	**Dose of injected platelets**
E	**Efficiency of production**
P	**Purity of PRP**
A	**Activation of PRP**

Fig. 2 FIT PAAW classification system. (Modified from Frautschi et al. 2017)

F	**Force of centrifugation**
I	**Iteration/sequence of centrifugation**
T	**Time of centrifugation**
P	**Platelet concentration**
A	**Anticoagulant use**
A	**Activation method**
W	**White blood cell composition**

These easy-to-remember classification systems will help the clinician to choose a PRP preparation system that will provide a reliable, replicable, and effective product.

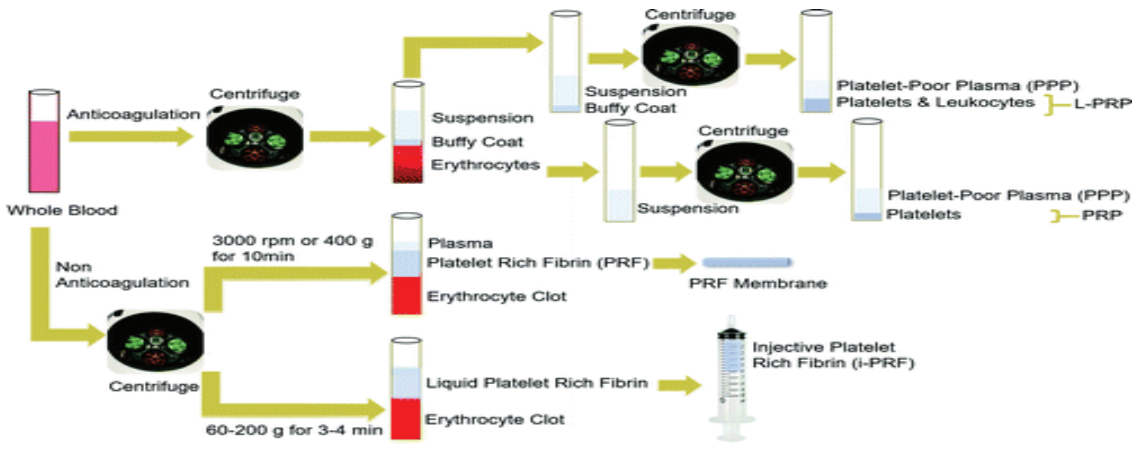
Table 2. DEPA classification of PRP preparations

DEPA classification	Subgroup	Description
Dose of injected platelets	Very high	>5 Billion injected platelets
	High	3–5 Billion injected platelets
	Medium	1–3 Billion injected platelets
	Low	<1 Billion injected platelets
Efficiency of production	High device efficiency	Recovery rate in platelets >90%
	Medium device efficiency	Recovery rate in platelets 70%–90%
	Low device efficiency	Recovery rate in platelets 30%–70%
	Poor device efficiency	Recovery rate in platelets <30%
Purity of the PRP	Very pure PRP	Platelets in the PRP >90%
	Pure PRP	Platelets in the PRP 70%–90%
	Heterogeneous PRP	Platelets in the PRP 30%–70%
	Whole-blood PRP	Platelets in the PRP <30%
Activation process	Autologous thrombin Calcium chloride	-

Modified from Magalon et al. BMJ Open Sport Exerc Med 2016;2:e000060 [11]

Each one has a particular bioaction and has been applied in a specific clinical field. However, the overall goal is to achieve a concentrating platelet, as well as factors of two to three times in whole blood, in order to make PRP a more effective instrument than peripheral blood.

This summarizes the most often initial step, additional cycles may be performed with varying protocols to yield the varying PRP subtypes discussed previously. The collected concentrate is then activated for use. Bovine thrombin and calcium chloride are common activators (Hausauer and Humphrey 2020a).Bovine thrombin however comes with a small risk of patients developing antibodies to bovine thrombin leading to a systemic immune coagulopathy (Foster et al. 2009)



1. APPLICATIONS OF PRP IN AESTHETIC GYNECOLOGY

I) PRP IN BREAST RECONSTRUCTION

PRP together with adipose tissue has been used in breast reconstruction . PRP mixed with fat grafts led to improvements in the maintenance of breast volume in patients affected by breast soft-tissue defects.

II) PRP IN FEMALE SEXUAL DYSFUNCTION

O-Shot therapy PRP use in sexual dysfunction is considered to be a revolutionary new nonsurgical outpatient treatment that helps improve sexual dysfunction through using a woman's own growth factors. The PRP is injected into specific areas of the vagina with the aid of local anesthetic cream. PRP immediately activates tissue regeneration, and the enhancement in sexual response is dramatic. The desired response includes improved arousal, stronger orgasm, decreased dyspareunia, and increased natural lubrication

III) VAGINAL REJUVENATION

Aesthetic practitioners have used PRP for the regeneration of vaginal mucosa, muscles, and skin. After PRP injection, vaginal vascularity is increased, with a subsequent dramatic increase in sensitivity. In addition, the skin becomes thicker and firmer, making the vagina look much more youthful. Moreover, the ligaments and muscles supporting the urethra become stronger, alleviating urinary incontinence .

2. APPLICATIONS OF PRP IN VARIOUS GYNECOLOGICAL DISORDERS

PRP preparations are used in gynecology for various diseases based on its known mechanisms, which involve the wound healing process and the initiation of inflammatory reactions

I) PRP IN SKIN LESIONS AND WOUND HEALING

Due to the ability of PRP to promote angiogenesis and wound healing, it is widely used in dermatology for purposes including the treatment of ulcers, scars, and alopecia.

Faster wound healing can be expected when PRP is used due to the presence of more platelets and growth factors.

II) PRP IN CERVICAL ECTOPY

Autologous PRP application appeared promising for the treatment of cervical ectopy in symptomatic women, as it yielded a shorter tissue healing time and milder adverse effects than laser treatment.

III) PRP IN VULVAR DYSTROPHY

PRP has been tried in many dermatological and autoimmune conditions nonresponsive to corticosteroids, such as lichen sclerosus (LS) and eczema.

Application of PRP in cases of LS resistant to steroid therapy was tried by Behnia-Willison et al.in 28 patients with LS. They injected PRP into the vulva in a fanning pattern. Patients received three PRP treatments 4 to 6 weeks apart and again at 12 months. Nearly all patients exhibited clinical improvements in the size of their lesions, and in 28.6% of the patients, the lesions disappeared completely after PRP treatment. They concluded that PRP injections could therefore be considered an effective therapy for LS

IV) PRP IN UROGENITAL DISORDER

PRP in genital fistulae Genital fistulae are treated by many modalities, as listed by Bodner Adler et al in a systemic review that assessed conservative and surgical treatments. They found that small fistulae could be treated conservatively with various therapies, including PRP, with success rates ranging from 67% to 100%.

PRP has been tried in the treatment of vesicovaginal fistulae as a novel, minimally invasive approach for the closure of genital fistulae. Shirvan et al., in a series of 12 patients, injected PRP around the fistula into the tissue, and platelet-rich fibrin (PRF) glue was interpositioned in the tract. They followed the cases for 6 months and found that 11 patients were clinically cured, with normal findings on transvaginal physical examinations and cystography. They concluded that PRP injection and PRF glue interposition offered a safe, effective, and novel minimally invasive approach for the treatment of vesicovaginal fistulae that obviated the need for open surgery.

3. APPLICATIONS OF PRP IN REPRODUCTIVE MEDICINE

I) PRP IN PREMATURE OVARIAN FAILURE

The successful use of PRP in regenerative medicine has led investigators to study its effect in the treatment of conditions like decreased ovarian reserve, poor responders, and premature ovarian insufficiency

Intraovarian PRP was performed based on the theory that degenerative processes lead to ovarian insufficiency through molecular pathway dysfunction, which regulates the ovarian vascularization.

Intraovarian PRP for diminished ovarian reserve, poor ovarian response, or POI is still experimental. There is a need for research on cellular and molecular level to improve our knowledge on PRP mode of action,standardization of PRP preparation methods, and application methods.

Table 1 Studies for poor ovarian reserve

Study	Type of study	Number of patients	Outcome
Sills et al. 2019, [6]	Case series	4	Improved ovarian function in all cases, Increase AMH, Decrease FSH or both. IVF: retrieval of 5.3 ± 1.3 MII oocytes.
Petryk et al. 2020 [8]	Interventional	38	Significant improvement in hormone levels; 6 babies were born, 10 pregnancies were achieved, and 4 out of the 10 were from natural conception.
Singh et al. 2020 [9]	Interventional	30	No benefit in increasing AMH, AFC, ovarian response to COS or IVF outcome
Mello et al. 2020 [10]	Controlled non randomized	46	PRP Vs control G: Sig improvement in FSH, AMH, AFC. Biochemical (26.1% vs 5.4%) and cl pregnancy (23.9% vs 5.4%) were higher.
Sills et al. 2020 [11]	Case series	182	Improved AMH in (28%) with median increase of 167%. Mean interval to maximum AMH increase was 4 w (range 2–10 w).
Jacman et al. 2020 [12]	Case series retrospective	140	PRP can stimulate follicular development for at least 6 weeks following the intraovarian injection.
Total		369	

II) PRP IN REFRACTORY ENDOMETRIUM

Endometrium is one of the most prominent factors in implantation and pregnancy. It has been suggested that the minimal endometrial thickness required for embryo transfer is 7 mm at the end of follicular phase . Thus, endometrial thickness less than 7 mm is considered to be thin.

Most studies have led to the conclusion that infertile women with thin endometrium benefit from PRP treatment, whereas the experimental conditions should be noticed and controlled, including PRP preparation process, PRP infusion dose, inclusion criteria etc.

III) CHRONIC ENDOMETRITIS

Chronic endometritis is a persistent inflammatory condition of the endometrial mucosa with plasmacyte infiltration in the endometrial stromal compartment caused by various bacterial pathogens Since CE could modify the endometrial decidualization, it may affect the endometrial receptivity to accommodate pregnancy . Oral antimicrobial regimes are considered to be a traditional remedy for CE. Recent research suggested that PRP may be employed as an ideal CE treatment. Clearly more studies on larger patient population, as well as more RCTs, are needed for clinically meaningful conclusions.

IV) ASHERMAN SYNDROME

Asherman Syndrome (AS) consists of the development of intrauterine adhesions as a consequence of trauma, radiation, or infection in the endometrium. AS remains one of the most challenging pathologies fertility specialists encounter in daily practice.

PRP may not only help endometrial growth, but also enhance its functional properties. It can be interpreted that the removal of scar tissue, leading to the exposure of the normal endometrial cells to the GFs and cytokines in PRP, helps boost the existing cellular functions involved in tissue regeneration.

COMPLICATIONS OCCURRING MORE FREQUENTLY IN PATIENTS TREATED WITH PRP :

- Hematoma
- Infection
- Nausea and dizziness
- Pain
- Swelling

SPECIAL CONSIDERATIONS :

- Immunocompromised patients may not respond to PRP
- Use caution when harvesting autologous PRP from patients who have low hemoglobin levels.
- Autologous PRP is safer than allogeneic PRP for avoiding infectious disease transmission
- Bovine thrombin as an activator for PRP has been reported to cause immune-related factor V deficiency
- Avoid PRP use near precancerous or cancerous lesions
- Avoiding nonsteroidal anti-inflammatory drugs (NSAIDS) within 48 h to 1 week

CONCLUSION :

PRP is an innovative therapeutic modality, as it is affordable, simple, easily performed, and effective. It is also a noninvasive modality with promising results and no side effects.

As the field of medicine and surgery continue to report on the use of PRP, we hope that greater attention will be paid to looking for and acknowledging any complications that arise.

The idea of exploiting an autologous blood product as a therapeutic treatment is now scientifically and clinically accepted. However, it is important to appreciate the challenges and scientific questions that earlier scientists addressed to allow modern-day practice

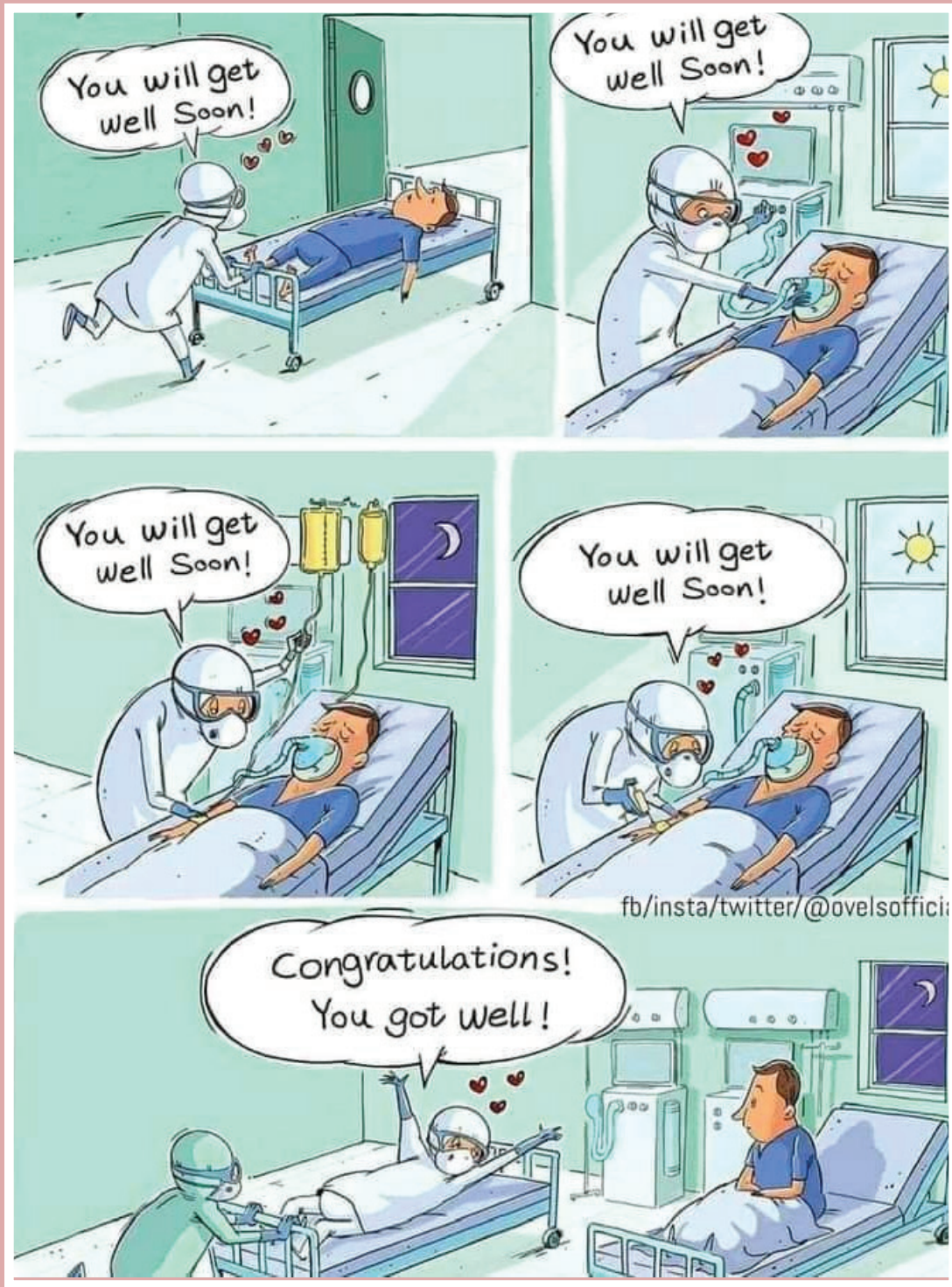
There is still much to be learned and discovered regarding PRP and its specific factors. The utility of platelets and PRP will only continue to evolve as we move forward in the everlasting quest of scientific advancement. Hopefully, with the available technological resources at our disposal, unrealized questions with respect to PRP will be answered in time

REFERENCES :

- Current clinical applications of platelet-rich plasma in various gynecological disorders: An appraisal of theory and practice 2018
- Platelet-rich Plasma: Properties and Clinical Applications RICK G. SMITH, B.S., C.C.P., CRAIG J. GASSMANN, C.C.P., AND MARK S. CAMPBELL, B.A., C.C.P. Perfusion Management Group, Ltd., Lancaster, PA 2017
- The use of Platelet-Rich Plasma in the Gynaecological Clinical Setting.

  A review. Vasileios Sanoulis1 , Nikolaos Nikolettos2 , Nikolaos Vlahos 2018
- Textbook of Aesthetic Clinician's Guide to Platelet Rich Plasma Shilpi Khetarpal
- Text book of Platelet Rich Plasma in Medicine Basic Aspects and Clinical Applications Elie M. Ferneini Regina Landesberg Steven Halepas
- Platelet-Rich Plasma as a Potential New Strategy in the Endometrium Treatment in Assisted Reproductive Technology Yunying Lin1,2† , Jia Qi 1,2† and Yun Sun 2021
- Intraovarian platelet-rich plasma: current status Aboubakr Mohamed Elnashar 2022

BREAK


You will get well Soon!
You will get well Soon!
You will get well Soon!
You will get well Soon!
fb/insta/twitter/@ovelsoffici
Congratulations! You got well!

END