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GYNAE SPECTRUM

Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "**Gynae Spectrum**", which contains latest and interesting news in the field of Obstetrics and Gynaecology.

This issue contains:

- Effect of Folic acid versus 5- methyl tetrahydrofolate supplementation in pregnancy.
- Treatment of Cervical Ectopic Pregnancy with Multi Dose Methotrexate Therapy- A case report.
- A novel test for couples struggling to conceive.

Should you require any article or, medical information, please feel free to contact us
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Looking forward to your valuable feedback.

Best Regards,

Medical Team, Micro Labs Limited



1. Effect of Folic acid versus 5- methyl tetrahydrofolate supplementation in pregnancy.

Folate (vitamin B9) protect against fetal neural tube defects. However, folic acid is inactive in the human body and must be converted by the liver into the active molecule 5-methyltetrahydrofolate (5-MTHF).

Methods:

A review was performed , the criteria for selection were a) the most recent evidences on folate metabolism, b) the possibility to exploit the content of each publication in order to compare the different molecular sources that eventually may be used by cell metabolism in the final structure of vitamin B9.

Results:

Folic acid supplementation is as effective as 5-MTHF supplementation in improving the level of folate in the organism. Nonetheless, 5-MTHF is the natural folate that represents 98% of all folates in plasma and does not need to be transformed by DHFR to become active.

Therefore the bioavailability of methylfolate is not limited by the saturation of this enzyme, and its intake does not lead to the accumulation in blood of a highly oxidized form of folate. Bioavailability of 5-MTHF is not affected by polymorphisms in the genes that encode MTHFR and DHFR, which instead affect that of folic acid.

Compared to folic acid, 5-MTHF is less reactive towards DHFR inhibitors such as methotrexate and presents a lower possibility of concealing hematological symptoms due to vitamin B12 deficiency in patients with megaloblastic anaemia .

5-MTHF is stable under visible light and UV-A irradiation which instead degrade folic acid.

Therefore, in persons exposed to sunlight, supplementation with 5-MTHF ensures a stability in serum folate levels that cannot be obtained with folic acid.

5-MTHF stimulates the endothelial production of nitric oxide, which has vasodilatory and antiplatelet activities

Folic acid supplementation during pregnancy is unable to enrich fetal serum, differently from 5- MTHF and THF. Therefore, supplementation with 5-MTHF during pregnancy could immediately supply folate to the fetus.

Discussion:

Folic acid can pose health risks in certain conditions, such as megaloblastic anemia, where it will conceal megaloblastic anemia due to vitamin B12 deficiency and in cases of reduced



hepatic transformation of folic acid (e.g. due to genetic variants or during some pharmacotherapies).

These risks can be avoided by supplementation with 5-MTHF rather than folic acid. Because 5-MTHF does not require activation, it is immediately available to mother and fetus and does not accumulate in blood like folic acid does in cases of reduced hepatic transformation.

Conclusion:

Dimethyl tetrahydrofolate has better properties than folic acid and hence can be a valuable option in pregnancy and other disorders.

Reference:

Ferrazzi E et al. Folic acid versus 5- methyl tetrahydrofolate supplementation in pregnancy, European Journal of Obstetrics and amp; Gynecology and Reproductive Biology (2020):1-32

2. Treatment of Cervical Ectopic Pregnancy with Multi Dose Methotrexate Therapy- A case report..

A cervical ectopic pregnancy (CEP) is implanted in the uterine endocervix. It is a rare condition with an incidence of less than 0.1% of all ectopic pregnancies.

Current is a case of cervical ectopic pregnancy.

Case report:

A 38-year-old lady, G3P0+2 pregnant for 9 weeks and 4 days, conceived by Invitro Fertilization (IVF) presented with bleeding per vagina and mild lower abdomen and back pain.

Initially started as brownish vaginal discharge and further progressed to frank vaginal bleeding. It soaked half a pad of blood over the span of 2 hours. Beta-hCG which done 5 days ago showed a reading of 950 mIU/mL.

History of two previous first trimester miscarriages. The first miscarriage was managed by Evacuation of Retained Products of Conception (ERPOC) and second miscarriage was medically managed.

current pregnancy was conceived by IVF- Intracytoplasmic sperm injection (ICSI) and 2 embryos were transferred.

known case of Grave's disease and had radioactive iodine therapy in 2004. Following that, she developed hypothyroidism and is currently on thyroxine 100 mcg for 4 days and 50 mcg for 3 days.

Her pain score was 1/10. She was vitally stable with BP of 138/84, Pulse: 85, Resp: 16, Temp: 36.7°C, SpO2: 100%.

On examination, she was anxious, lying comfortably with no acute distress. Her abdomen

was soft and non-tender without masses or organomegaly. The pad was soaked with period-like moderate bleeding and no clots were visible.

Vaginal exam showed no tenderness and closed cervical os. On speculum examination, minimal bleeding was noted along with ballooning of the cervix. Bedside transvaginal ultrasound scan elicited no probe tenderness, and revealed an empty uterus with a single gestational sac with a yolk sac measuring 7.4 mm in the cervical canal. It was corresponding to 5 weeks without a fetal pole and fetal heart. A small subchorionic hematoma behind the sac.

Patient was Diagnosed as an ectopic cervical pregnancy and was started on Methotrexate (MTX) Hybrid double dose Protocol with 2 equal doses of MTX 76 mg (50 mg/m²) each to be administered intramuscularly on day 1 and day 4.

For transfusion requirement, two units of blood were cross matched and saved. The couple were then explained about the risk of heavy bleeding, uterine perforation, ERPOC, laparoscopy repair, or a Hysterectomy in case of life threatening bleeding.

Complete Blood Count showed

Hemoglobin to be 11.8, MCV 84.9, WBC 9.2, HCT 36.0, and Platelets count of 290,000.

Total Beta-hCG before admission was 950 mIU/mL. The first dose of MTX was given on Day 1 and second dose of MTX was administered on day 4.

The value of BetaHCG kept rising and patient had continuous vaginal bleeding.

It was decided to proceed with Multi-dose MTX therapy and administer 2 more doses of MTX. She received the 3rd dose on Day 9 and 4th dose on Day 15. As she was clinically improving, and Beta-hCG was gradually falling, she was discharged with weekly follow up in clinic for Beta-hCG levels.



Discussion:

Cervical Ectopic Pregnancy (CEP) symptom is vaginal bleeding, which is often profuse and painless. Lower abdominal pain or cramps occur in less than one-third of the patients, however pain without bleeding is rare.

Presentation in early pregnancy should raise concern for CEP. Early diagnosis is critical to avoid severe blood loss and ensure successful treatment. Early CEP can be asymptomatic and is usually found incidentally on ultrasound scan.

Diagnosis is made on seeing the following features on Ultrasound--an empty uterus, a barrel-shaped cervix, a gestational sac present below the level of the internal cervical OS, the absence of the 'sliding sign' and blood flow around the gestational sac using color Doppler.

Conclusion:

Cervical Ectopic Pregnancy is extremely rare in occurrence, Methotrexate can be a valuable

addition for the treatment of ectopic pregnancy.

Reference:

Iqbal S et al. Successful Treatment of Cervical Ectopic Pregnancy with Multi Dose Methotrexate Therapy. Gynecol Obstet Case Rep. 2020; 6 (2):14.

IN FOCUS

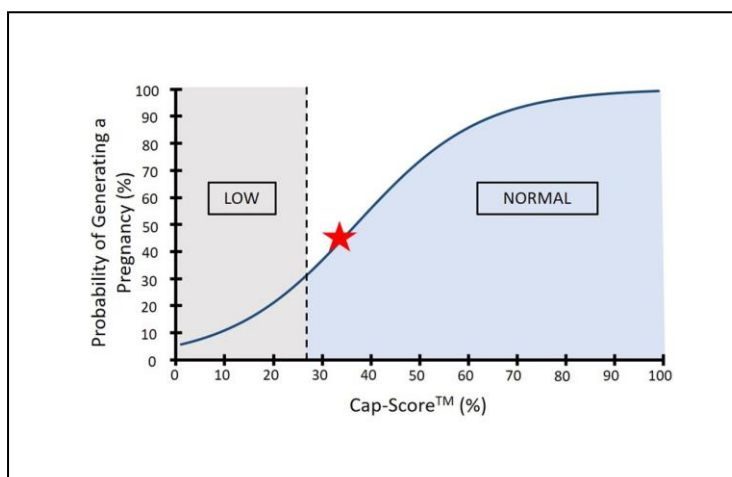
3. A novel test for couples struggling to conceive

Infertility contributes to 10% to 15% of couples globally, men contribute to around half of the cases.

A novel male fertility test help predict that men might need treatment and which couples might have success with different forms of assisted reproduction.

Cap-Score test is designed to provide information on the man's fertility.

The Cap-Score quantifies the ability of sperm to undergo a process called "capacitation," which enables the sperm to fertilize an egg. Only sperm that capacitate are capable of fertilizing.



In contrast, traditional male fertility exams rely primarily on semen analysis, which counts sperm and assesses whether they swim and look normal.

The new data shows that the man's fertility plays a key role in whether a couple will be able to conceive, even if they might have delayed having children and are older.

The researchers also compared Cap-Score results from more than 2,000 men having fertility exams against results from a control group of fertile men with a pregnant partner or young baby.

Results showed that Cap-Scores from the fertile men showed an expected bell-shaped curve. In contrast, the vast majority of men questioning their fertility had scores below the mean of the fertile population.

The researchers also examined the relationship between traditional semen analysis results and impaired capacitation which revealed that almost two-thirds of the men who had low Cap- Scores passed the traditional semen analysis.

With Cap-Score, doctors and couples can make informed decisions about whether to try to



conceive unassisted or choose one of several medical approaches.

Results can also be used to identify which men might benefit from treatment to improve their fertility, including changes in lifestyle, nutritional supplements or surgery.

Study concluded that Sperm capacitation predicted male fertility. Impaired capacitation affects normal semen analysis results, informing diagnosis versus idiopathic infertility.

Reference:

Sharara F et al, Multicentric, prospective observational data show sperm capacitation predicts male fertility, and cohort comparison reveals a high prevalence of impaired capacitation in men questioning their fertility, Reproductive BioMedicine Online. 2020; 41(1): 69-79



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