Roll Back Malaria Partnership Malaria in Pregnancy Working Group:

Consensus Statement on Folic Acid Supplementation During Pregnancy

FEBRUARY 2015

The Roll Back Malaria (RBM) Partnership Malaria in Pregnancy Working Group supports the following for all pregnant women living in sub-Saharan Africa:

- In malaria-endemic areas, intermittent preventive treatment using sulfadoxine-pyrimethamine (IPTp-SP) should be provided to pregnant women at each scheduled antenatal care (ANC) visit for protection against malaria. This should start early in the second trimester and continue until the time of delivery, with the doses given at least one month apart [1].
  - IPTp-SP has been shown to reduce maternal anemia, antenatal maternal parasitemia, low birthweight infants and neonatal deaths.
  - Co-trimoxazole provides some protection through its antimalarial activity; however, IPTp-SP should NOT be given to women who are taking daily co-trimoxazole prophylaxis (i.e. mainly those living with HIV) as this increases the risk of adverse events.

- Daily oral supplementation of 30–60 mg elemental iron and 400 µg (0.4 mg) folic acid should be provided as early as possible in pregnancy to meet iron and folic acid requirements [2]. In cases where a combined folic acid–iron tablet is not available, a daily dose of 400 µg (0.4 mg) folic acid can be used separately.

- There is evidence that high doses of folic acid (i.e. 5,000 µg or more) may interfere with the efficacy of sulfadoxine-pyrimethamine as an antimalarial [3]. The higher 5,000 µg (5 mg) dose for pregnant women should be restricted for use in very specific clinical cases.

High doses of folic acid are not needed during low-risk pregnancies and may counteract the efficacy of both sulfadoxine-pyrimethamine and co-trimoxazole as antimalarials [4]. The RBM Malaria in Pregnancy Working Group strongly advises that countries currently prioritize the procurement and distribution of the available combined dose of 400 µg (0.4 mg) folic acid plus 30–60 mg elemental iron[1] as part of routine ANC. It also recommends that countries substantially reduce current stores and supplies of folic acid at a dose of 5,000 µg (5 mg) or higher at all facilities, as this dose should only be used for specific medical conditions as outlined by the World Health Organization (WHO) [2], and as indicated below in the answer to Question 2.

Frequently asked questions about iron and folic acid during pregnancy

1. What daily dose of iron and folic acid supplementation does WHO recommend during pregnancy?

Folate requirements are increased in pregnancy because of the rapidly dividing cells in the fetus and elevated urinary losses. Increased iron is needed to meet the demands for iron of the developing fetus and cell mass expansion. WHO recommends iron and folic acid supplementation for pregnant women, starting early in pregnancy and at a daily dose of 30–60 mg of elemental iron plus 400 µg (0.4 mg) of folic acid, as this has been shown to reduce the risk of low birthweight, maternal anemia and iron deficiency [2]. In settings where anemia in pregnant women is a severe public health problem (i.e. 40 percent or higher) a daily dose of 60 mg of elemental iron is preferred over a lower dose. If a woman is diagnosed with anemia, WHO recommends daily treatment with 120 mg of elemental iron and 400 µg (0.4 mg) of folic acid until her hemoglobin concentration rises to a normal level [5,6].

A combined dose of 60 mg of elemental iron and 400 µg (0.4 mg) of folic acid is included on the WHO Model List of Essential Medicines [7] and is provided by the United Nations Children's Fund (UNICEF). Using this preparation to treat anemia would provide 800 µg (0.8 mg) of folic acid daily, which would not interfere with sulfadoxine-pyrimethamine as an antimalarial [8]. A trial conducted on pregnant women in Gambia using a 1,500 µg (1.5 mg) daily dose of folic acid showed no reduction

1. The current iron and folic acid preparation is 400 µg (0.4 mg) of folic acid plus 60 mg of elemental iron.

in sulfadoxine-pyrimethamine efficacy [9]. However, to date, no data are available on sulfadoxine-pyrimethamine efficacy when administered with daily folic acid doses between 1,500 µg (1.5 mg) and less than 5,000 µg (5 mg) in pregnant women.

Women should be counseled when they receive iron and folic acid supplements to inform them why these supplements are needed, how to take them and for what duration. They should also receive information about how to manage the possible side effects of iron supplementation (mainly mild gastrointestinal symptoms), which may occur in some women.

2. What are the clinical indications for higher dose folic acid during pregnancy?

Folic acid insufficiency is associated with an increased risk of neural tube defects, a debilitating congenital anomaly in which the neural tube does not close properly. This occurs in 0.5–6.5 out of every 1,000 pregnancies. The neural tube forms in the first month after conception, with closure by about 28 days; thus, in order to prevent neural tube defects maternal intake of folic acid should begin before conception and continue through early pregnancy.

There are limited cases (e.g. for prevention of recurrent cases of neural tube defects [10] and for women on anticonvulsant treatment, diabetics and women with sickle cell anemia) where it is recommended that pregnant women take folic acid at a daily dose of 5,000 µg (5 mg).

In particular, women who have had a previous pregnancy resulting in a baby with neural tube defects are at higher risk of having another baby with neural tube defects. These women should receive folic acid at a dose of 5,000 µg (5 mg) a day starting at least one month – though preferably two to three months – before they conceive, and continuing until 12 weeks of gestation, while increasing their dietary folate intake. Given the need for supplementation prior to conception, fortification of staple foods with folic acid should also be considered as a cost-effective public health measure to reduce the incidence of neural tube defects [11].

3. How does folic acid interfere with the efficacy of sulfadoxine-pyrimethamine against malaria?

Folic acid is an essential nutrient for all organisms. Humans get folate from food or dietary supplements. Other organisms, such as the malaria parasite, synthesize folic acid de novo, or endogenously. Both sulfadoxine-pyrimethamine and co-trimoxazole are anti-folates and prevent malaria by blocking the synthesis of folic acid. Without folic acid, the parasite cannot complete its lifecycle. However, if blood folate concentrations are high enough, the malaria parasite can use this folate instead of making its own, allowing the infection to continue unchecked.

References

1. Policy brief for the implementation of intermittent preventive treatment of malaria in pregnancy using sulfadoxine-pyrimethamine (IPTp-SP). Geneva: World Health Organization; 2013.
2. Guideline: daily iron and folic acid supplementation in pregnant women. Geneva: World Health Organization; 2012.
3. Peters PJ, Thigpen MC, Parise ME, Newman RD. Safety and toxicity of sulfadoxine-pyrimethamine: implications for malaria prevention in pregnancy using intermittent preventive treatment. Drug Saf. 2007 June; 30(6):481–501.
4. Cotrimoxazole (Septrin) [Internet]. NAM Aidsmap; 2015. Available from: http://www.aidsmap.com/Cotrimoxazole-iSeptrini/page/1731332/
5. World Health Organization (WHO), United Nations Children's Fund (UNICEF), United Nations University (UNU). Iron deficiency anaemia assessment, prevention, and control: a guide for programme managers. Geneva: WHO; 2001.
6. Iron and folate supplementation. Integrated Management of Pregnancy and Childbirth (IMPAC). In: Standards for maternal and neonatal care, 1.8. Geneva: World Health Organization; 2007.
7. WHO model list of essential medicines, 18th edition. Geneva: World Health Organization; 2013. Available from: http://apps.who.int/iris/bitstream/10665/93142/1/EML_18_eng.pdf
8. Ouma P, Parise ME, Hamel MJ, et al. Randomized controlled trial of folate supplementation when treating malaria in pregnancy with sulfadoxine-pyrimethamine. PLoS Clin Trials. 2006 Oct 20; 1:e28. Available from: http://journals.plos.org/plosclinicaltrials/article?id=10.1371/journal.pctr.0010028
9. Mbaye A, Richardson K, Balajo B, et al. Lack of inhibition of the anti-malarial action of sulfadoxine-pyrimethamine by folic acid supplementation when used for intermittent preventive treatment in Gambian primigravidae. Am J Trop Med Hyg. 2006 Jun; 74(6):960–4. Available from: http://www.ajtmh.org/content/74/6/960.long
10. Prevention of neural tube defects. Integrated Management of Pregnancy and Childbirth (IMPAC). In: Standards for maternal and neonatal care, 1.5. Geneva: World Health Organization; 2007.
11. World Health Organization (WHO), Food and Agriculture Organization (FAO). Guidelines on food fortification with micronutrients. Geneva: WHO; 2006.

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