HiPP INFORMS

Study report

Clinical study proves safety and suitability of Metafolin® in infant formulae

Original title: Troesch B et al. (2019) Suitability and safety of L-5-methyltetrahydrofolate as a folate source in infant formula: A randomized controlled trial. PLoS ONE 14(8): e0216790.

Background

Folate is essential for the synthesis of RNA and DNA, and thus for cell division and tissue growth. This is why an adequate folate status is crucial for healthy development and growth, especially during pregnancy and infancy. L-5-methyltetrahydrofolate (5-MTHF) is the predominant bioactive folate form in breast milk, making Metafolin®* as a 5-MTHF calcium salt an ideal addition to formulae. Unlike synthetic folic acid and other folate forms, Metafolin® does not have to be metabolised into its bioactive form first and is therefore immediately available to the infant.

The safety and suitability of its use in formulae has been demonstrated in a clinical trial.

Objective of the study

To investigate the safety and suitability of Metafolin® as a folate source in infant formula.

Primary outcome parameters: the infant's average weight gain

Secondary outcome parameters: recumbent height, head circumference, stool characteristics, various blood parameters, adverse events

Study design

Design: A two-arm parallel, prospective, randomised, double-blind, controlled intervention study

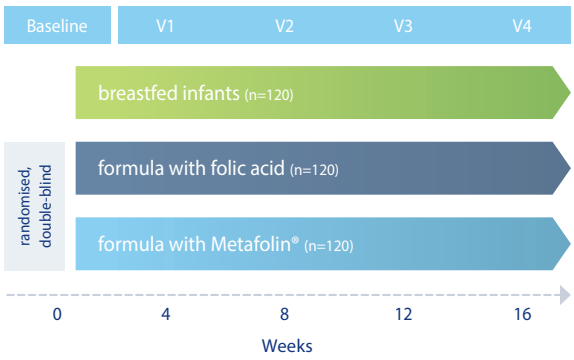
Study population: Healthy mature infants who were started on infant formula within the first 28 days after birth (n=240) and breastfed infants as a reference group (n=120).

Study structure

Control formula: Standard infant formula with 10.0 µg folic acid per 100 ml as per EU Regulation.

Intervention formula: Infant formula with 10.4 µg 5-MTHF per 100 ml as a folate source, which was added as 11.3 µg of the calcium salt of 5-MTHF (= Metafolin®).

Reference group: breast milk



Results

Of the 240 randomised infants, 120 received infant formula with Metafolin®. Both infant formulae were well accepted and showed no differences in acceptance and tolerability. Stool characteristics such as consistency, colour and odour were also comparable. No adverse events, anomalies in the blood samples, or haematological parameters were observed that would affect the safety and suitability of Metafolin® in infant formula.

Most of the folate-status relevant blood parameters did not differ between the intervention and the control groups.

However, at 4 months of age, significantly higher levels of unmetabolised folic acid were measured in the blood plasma samples of the control group. In contrast, the levels of unmetabolised folic acid in the intervention group were comparable to those in breastfed children. Red blood cell (RBC) folate also showed differences and was significantly higher in the intervention group than in the control group.

There was no significant difference in average daily weight gain, gain in recumbent height and head circumference between the intervention and control groups (see figures). Both formulae ensure age-appropriate growth.

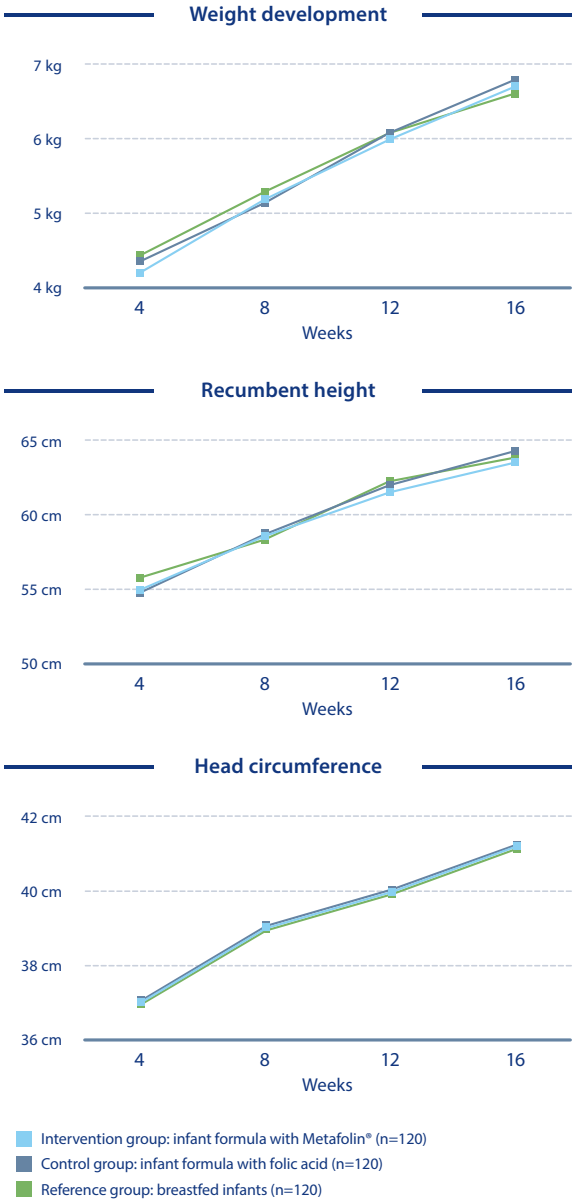
Discussion

Based on the comparable weight and length development, the study confirms that the administration of an formula with Metafolin® is safe.

The plasma samples from exclusively breastfed infants whose mothers did not ingest larger amounts of folic acid from dietary supplements or fortified foods contain only small amounts of unmetabolised folic acid. This is why adding a folic acid source to formulae that do not result in high levels of unmetabolised folic acid in plasma seems reasonable to the authors. The authors conclude that the addition of Metafolin® is a safe approach to provide sufficient folate without increasing the amount of unmetabolised folic acid.

To the authors' knowledge, this is the first and currently the only published study to determine the safety of 5-MTHF intake through formulae with respect to physical growth and formula tolerability.

Age-appropriate growth with Metafolin® in infant formula



CONCLUSION

5-MTHF is the predominant folate form in breast milk. The safety of its addition to infant formula was confirmed given the age-appropriate physical growth of the infants in the study. The use of Metafolin® instead of synthetic folic acid in formula is a safe alternative to ensure adequate folate supply in non-breastfed infants.

*Metafolin® is a registered trademark of Merck KGaA, Darmstadt, Germany.
HiPP COMBIOTIC® is the only formula with Metafolin®.

Scanning the QR code will take you directly to the original study by Troesch et al. PLoS ONE 2019.

For more information, have a look at our Metafolin® website at **hipp.com/hcp**

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