

Clinical THYROIDOLOGY

VOLUME 24 • ISSUE 7

JULY 2012

Neuropsychological Development in Children of Mothers with Hypothyroidism Is Normal When Euthyroidism Is Achieved after Conception

Downing S, Halpern L, Carswell J, Brown RS. Severe early maternal hypothyroidism corrected prior to the third trimester associated with normal cognitive outcome in the offspring. Thyroid 2012;22:625-30. Epub May 10, 2012.

Background

Concern about potential harmful effects of early maternal hypothyroidism (MH) on fetal brain development has led to calls for universal screening early in, or even before, pregnancy. However, evidence in humans that adverse effects are irreversible if thyroid-hormone replacement is initiated after the first trimester is limited. The authors sought to determine the outcome if treatment is given in early pregnancy.

Methods

The authors identified three women who had TSH receptor blocking antibody-induced MH during pregnancy and were treated with levothyroxine (L-T₄), starting at 27 weeks, 5 weeks, and the first month of gestation. The corresponding pretreatment serum TSH levels in the 2 women in whom data were available were 68 mU/L at 25 weeks of gestation and 65 mU/L at 24 weeks of gestation, falling, in each case to 6 mU/L. The third woman with MH required 0.5 mg of L-T₄ to normalize her thyroid hormone levels by 4 months of gestation. Their infants were also treated with L-T₄ after neonatal screening identified congenital hypothyroidism (CH). A battery of neuropsychological tests was administered to assess intelligence, language, memory, and visualmotor performance. All testing of these three infants at 5.4 years of age (range, 5.1 to 6.1) and of three sibling controls at 6.8 years (range, 9.1 to 3.0) was performed by two experienced pediatric clinical psychologists who had no knowledge of the maternal thyroid function during pregnancy.

Results

Children born to women with MH had average or above average results on all parameters. Comparative scores of the neuropsychological tests in sibling *continued on next page*

Email: clinicalthyroidology@thyroid.org

Los Angeles, CA 90073

and UCLA School of Medicine Endocrinology 111D 11301 Wilshire Blvd

Editor-in Chief

Associate Editors: Albert G. Burger, MD Professor, University of Geneva Geneva, Switzerland Email: clinicalthyroidology@thyroid.org

VA Greater Los Angeles Healthcare System

Telephone: 310-268-3852 Fax: 310-268-4879

Stephanie L. Lee, MD, PhD

Director of the Thyroid Health Center Boston University Medical Center Boston, MA Telephone: 617-638-8530 Fax: 617-638-7221 Email: clinicalthyroidology@thyroid.org

Jorge H. Mestman, MD

Professor of Clinical Medicine and OB/GYN University of Southern California Keck School of Medicine Los Angeles, CA Telephone: 323-442-6179 Email: clinicalthyroidology@thyroid.org

Stephen W. Spaulding, MD

Professor of Medicine Department of Medicine University at Buffalo, SUNY Telephone: 716-862-6530 Fax: 716-862-6526 Email: clinicalthyroidology@thyroid.org

President James A. Fagin, MD

Secretary/Chief Operating Officer John C. Morris, MD

Treasurer David H. Sarne, MD

President-Elect Bryan R. Haugen, MD

Past-President Gregory A. Brent, MD

Executive Director

Barbara R. Smith, CAE American Thyroid Association 6066 Leesburg Pike, Suite 550 Falls Church, VA 22041 Telephone: 703-998-8890 Fax: 703-998-8893 Email: thyroid@thyroid.org

Designed By Karen Durland (kdurland@gmail.com)

Clinical Thyroidology Copyright © 2012 American Thyroid Association, Inc. Printed in the USA.All rights reserved.

Neuropsychological Development in Children of Mothers with Hypothyroidism Is Normal When Euthyroidism Is Achieved after Conception

pairs for full-scale IQ and performance IQ were variable; some scores were higher and some lower in children with CH.

Conclusions

Although the findings do not exclude a subtle impact of MH on intellectual function during early gestation, the normal cognitive outcome despite overt MH should provide data with which to counsel mothers who have overt hypothyroidism early in pregnancy. Aggressive thyroid-hormone replacement as soon as possible is important, but early termination of the pregnancy because of fear that the baby will have significant cognitive delay is not warranted.

ANALYSIS AND COMMENTARY • • • • •

Low intelligence quotient (IQ) scores in children of pregnant women with poorly treated hypothyroidism have been of great concern to health care professionals and to the lay population. Very early reports of cretinism in infants of women with hypothyroidism were related to severe iodine deficiency and/or maternal hypothyroidism (1). In 1999, Haddow et al., in a retrospective study, found that a group of children born to women with untreated hypothyroidism had a 7-point deficit in their IQ at 7 to 9 years of age as compared with matched children from mothers whose serum TSH levels were within reference range (2). However, the deficit was only 4 points (not statistically significant) when children of mothers with treated and untreated hypothyroidism were compared with controls. Hypothyroidism is not uncommon in pregnancy; the prevalence of newly diagnosed hypothyroidism in pregnancy is 2% to 4%. In addition, the incidence of hypothyroidism diagnosed in pregnancy in women undergoing L-T₄ therapy antedating pregnancy has been reported to be between 20% and 40% at the first obstetrical visit (3). Therefore, it has been recommended to advise women on L-T₄ therapy to add two extra tablets per week of the usual L-T₄ dose when pregnancy is confirmed (4), or as an alternative, to have a serum TSH <1.2 mIU/L before planning pregnancy (5). Since the placental transfer of maternal thyroid hormones to the embryo in early pregnancy is very well accepted (6), the question of diagnosing hypothyroidism via universal screening in early pregnancy became a heated argument in the medical community, although recent guidelines by the ATA (7) and the Endocrine Society (8) recommend

selective screening in women considered to be at risk, supporting early statements by the American College of Obstetricians and Gynecologists (9). As mentioned by Downing et al., every health care professional caring for pregnant women affected by hypothyroidism had the experience of a patient requesting an early termination of pregnancy. Several publications in the past few months brought some good news for children from mothers with hypothyroidism. Lazarus et al., in a large study of mothers with subclinical hypothyroidism, in which half of them received L-T₄ replacement therapy and the other half served as controls, concluded that antenatal screening (at a median gestational age of 12 weeks 3 days) with treatment of the women for hypothyroidism did not result in improved cognitive function in children at 3 years of age (10). In other studies from Japan, the children of mothers with hypothyroidism whose L-T₄ treatment was started after the second half of pregnancy had neurodevelopment cognitive scores similar to their siblings who were born when their mothers were euthyroid throughout pregnancy (11, 12). As stated by Downing et al., "Although further data are required to exclude a more subtle impact on cognitive function, the present findings, together with other studies in the medical literature, do not support widespread concern that affected infants whose mothers are treated after the first trimester of pregnancy will have significant intellectual delay as long as maternal thyroid function is normalized before the third trimester. Larger randomized control trials of patients with early MH are necessary to exclude a more subtle impact on neurocognitive function."

- Jorge H. Mestman, MD

Neuropsychological Development in Children of Mothers with Hypothyroidism Is Normal When Euthyroidism Is Achieved after Conception

References

- Pharoah PO, Connolly KJ, Ekins RP, Harding AG. Maternal thyroid hormone levels in pregnancy and the subsequent cognitive and motor performance of the children. Clin Endocrinol (Oxf) 1984;21:265-70.
- 2. Haddow JE, Palomaki GE, Allan WC, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med 1999;341:549-55.
- Cleary-Goldman J. Malone FD, Lambert-Messerlian G, Sullivan L, Canick J, Porter TF, Luthy D, Gross S, Bianchi DW, D'Alton ME. Maternal thyroid hypofunction and pregnancy outcome. Obstet Gynecol 2008;112:85-92.
- 4. Yassa L, Marqusee E, Fawcett R, et al. Thyroid hormone early adjustment in pregnancy (the THERAPY) trial. J Clin Endocrinol Metab 2010; 95:3234-41. Epub May 12, 2010.
- 5. Abalovich M, Alcaraz G, Kleiman-Rubinsztein J, et al. The relationship of preconception thyrotropin levels to requirements for increasing the levothyroxine dose during pregnancy in women with primary hypothyroidism. Thyroid 2010;20:1175-8.
- Calvo RM, Jauniaux E, Gulbis B, et al. Fetal tissues are exposed to biologically relevant free thyroxine concentrations during early phases of development. J Clin Endocrinol Metab 2002;87:1768-77.

- Stagnaro-Green A, Abalovich M, Alexander E, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid 2011;21:1081-125. Epub July 25, 2011.
- 8. De Groot LJ, Abalovich M, Alexander E, et al. Endocrine Society guidelines on management of thyroid disease during pregnancy and postpartum. J Clin Endocrinol Metab. in press.
- Committee on Patient Safety and Quality Improvement, Committee on Professional Liability. ACOG Committee Opinion No. 381: subclinical hypothyroidism in pregnancy. Obstet Gynecol 2007;110:959-60.
- 10. Lazarus JH, Bestwick JP, Channon S, et al. Antenatal thyroid screening and childhood cognitive function. N Engl J Med 2012;366:493-501.
- 11. Liu H, Momotani N, Noh JY, Ishikawa N, Takebe K, Ito K. Maternal hypothyroidism during early pregnancy and intellectual development of the progeny. Arch Intern Med 1994;154:785-7.
- 12. Momotani N, Iwama S, Momotani K. 2012 Neurodevelopment in children born to hypothyroid mothers restored to normal thyroxine (T₄) concentration by late pregnancy in Japan: no apparent influence of maternal T₄ deficiency. J Clin Endocrinol Metab 2012;97:1104-8. Epub February 8, 2012.