Nutrients. 2017 Dec 13;9(12). .

Reduced Educational Outcomes Persist into Adolescence Following Mild Iodine Deficiency in Utero, Despite Adequacy in Childhood: 15-Year Follow-Up of the Gestational Iodine Cohort Investigating Auditory Processing Speed and Working Memory.

Hynes KL[1], Otahal P[2], Burgess JR[3,4], Oddy WH[5], Hay I[6].

Abstract

There is increasing evidence that even mild gestational iodine deficiency (GID) results in adverse neurocognitive impacts on offspring. It's unclear, however, if these persist long-term and whether they can be ameliorated by iodine sufficiency in childhood. We followed a unique cohort (Gestational Iodine Cohort, n = 266) where gestation occurred during a period of mild population iodine deficiency, with children subsequently growing-up in an iodine replete environment. We investigated whether associations between mild GID and reductions in literacy outcomes, observed at age 9-years, persisted into adolescence. Comparisons were made between offspring of mothers with gestational urinary iodine concentrations (UICs) ≥ 150 μg/L and < 150 μg/L. Educational outcomes were measured using Australian National Assessment Program-Literacy and Numeracy (NAPLAN) tests. Children whose mothers had UICs < 150 μg/L exhibited persistent reductions in spelling from Year 3 (10%, -41.4 points (95% Confidence Interval -65.1 to -17.6, p = 0.001)) to Year 9 (5.6%, -31.6 (-57.0 to -6.2, p = 0.015)) compared to children whose mothers had UICs ≥ 150 μg/L. Associations remained after adjustment for biological factors, socioeconomic status and adolescent UIC. Results support the hypothesis that mild GID may impact working memory and auditory processing speed. The findings have important public health implications for management of iodine nutrition in pregnancy.

Thyroid. 2016 Feb;26(2):296-305.

Effects of Maternal Iodine Nutrition and Thyroid Status on Cognitive Development in Offspring: A Pilot Study.

Moleti M[1], Trimarchi F[1], Tortorella G[2], Candia Longo A[2], Giorgianni G[1], Sturniolo G[1], Alibrandi A[3], Vermiglio F[1].

Abstract

BACKGROUND AND OBJECTIVE:

Maternal iodine nutrition and thyroid status may influence neurocognitive development in offspring. This study investigated the effects on the intelligence quotient (IQ) of children born to mothers with different levels of iodine supplementation, with or without the administration of levothyroxine (LT4), prior to and during pregnancy.

PATIENTS AND METHODS:

This pilot, prospective, observational study included four study groups, each comprising 15 mother-child pairs, identified on the basis of maternal histories of iodized salt consumption and LT4 treatment prior to and during pregnancy. The groups were labeled as follows: iodine (I), no iodine (no-I), iodine + LT4 (I + T4), and no iodine + LT4 (no-I + T4). IQ tests were administered to children at 6-12 years of age with the Wechsler Intelligence Scale for Children-3rd Edition (WISC-III), with full-scale IQ (FSIQ), verbal IQ (VIQ), and performance IQ (PIQ) being evaluated.

RESULTS:

Children of I and I + T4 mothers had similar verbal, performance, and FSIQs, which were 14, 10, and 13 points higher, respectively, than children born to no-I and no-I + T4 mothers. A positive association was found between VIQ and maternal urinary iodine ($\beta = 1.023$ [confidence interval (CI) 1.003-1.043]; $p = 0.028$), but not with maternal free thyroxine concentrations at any stage of pregnancy. Overall, the prevalence of borderline or defective cognitive function was more than threefold higher in the children of mothers not using iodized salt than of those mothers using it (76.9% vs. 23.1%, odds ratio 7.667 [CI 2.365-24.856], $\chi 2 = 12.65$; $p = 0.0001$).

CONCLUSIONS:

Neuro-intellectual outcomes in children appear to be more dependent on their mothers' nutritional iodine status than on maternal thyroid function. These results support the growing body of evidence that prenatal, mild-to-moderate iodine deficiency adversely affects cognitive development later in life, with a seemingly greater impact on verbal abilities

Ann Endocrinol (Paris). 2015 Jul;76(3):248-52.

Neurocognitive outcomes of children secondary to mild iodine deficiency in pregnant women.

Caron P[1].

Abstract

Iodine deficiency is the most important preventable cause of brain damage worldwide. During pregnancy, severe iodine deficiency causes endemic cretinism, whereas mild-to-moderate iodine deficiency impairs neurocognitive function of the offspring. Numerous reports demonstrate the impact of iodine supplementation on prevention of cretinism, and recent studies evaluate the effects of iodine prophylaxis on neurocognitive development in children of women with mild-to-moderate iodine deficiency. Iodine prophylaxis is generally well tolerated without side effects for the pregnant women and the offspring. In France, the iodine status was recently considered as satisfactory in children and adult population, but regional studies conducted during the last two decades have shown that healthy women are mild-to-moderately iodine deficient during pregnancy. According to recent World Heath Organization guidelines, systematic iodine prophylaxis is recommended in women planning a pregnancy, during gestation and lactation in order to prevent maternal, neonatal and infantile consequences of mild-to-moderate iodine deficiency.

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J Clin Endocrinol Metab. 2013 May;98(5):1954-62.

Mild iodine deficiency during pregnancy is associated with reduced educational outcomes in the offspring: 9-year follow-up of the gestational iodine cohort.

Hynes KL[1], Otahal P, Hay I, Burgess JR.

Abstract

CONTEXT:

Severe iodine deficiency (ID) during gestation is associated with neurocognitive sequelae. The long-term impact of mild ID, however, has not been well characterized.

OBJECTIVE:

The purpose of this study was to determine whether children born to mothers with urinary iodine concentrations (UICs) <150 μg/L during pregnancy have poorer educational outcomes in primary school than peers whose mothers did not have gestational ID (UIC ≥150 μg/L).

DESIGN:

This was a longitudinal follow-up (at 9 years old) of the Gestational Iodine Cohort. Pregnancy occurred during a period of mild ID in the population, with the children subsequently growing up in an iodine-replete environment.

SETTING AND PARTICIPANTS:

Participants were children whose mothers attended The Royal Hobart Hospital (Tasmania) antenatal clinics between 1999 and 2001.

MAIN OUTCOME MEASURES:

Australian national curriculum and Tasmanian state curriculum educational assessment data for children in year 3 were analyzed.

RESULTS:

Children whose mothers had UIC <150 μg/L had reductions of 10.0% in spelling (-41.1 points, 95% confidence interval [CI], -68.0 to -14.3, P = .003), 7.6% in grammar (-30.9 points, 95% CI, -60.2 to -1.7, P = .038), and 5.7% in English-literacy (-0.33 points, 95% CI, -0.63 to -0.03, P = .034) performance compared with children whose mothers' UICs were ≥150 μg/L. These associations remained significant after adjustment for a range of biological factors (maternal age at birth of child, gestational length at time of birth, gestational age at time of urinary iodine collection, birth weight, and sex). Differences in spelling remained significant after further adjustment for socioeconomic factors (maternal occupation and education).

CONCLUSIONS:

This study provides preliminary evidence that even mild iodine deficiency during pregnancy can have long-term adverse impacts on fetal neurocognition that are not ameliorated by iodine sufficiency during childhood.

Lancet. 2013 Jul 27;382(9889):331-7.

Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC).

Bath SC[1], Steer CD, Golding J, Emmett P, Rayman MP

Abstract

BACKGROUND:

As a component of thyroid hormones, iodine is essential for fetal brain development. Although the UK has long been considered iodine replete, increasing evidence suggests that it might now

be mildly iodine deficient. We assessed whether mild iodine deficiency during early pregnancy was associated with an adverse effect on child cognitive development.

METHODS:

We analysed mother-child pairs from the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort by measuring urinary iodine concentration (and creatinine to correct for urine volume) in stored samples from 1040 first-trimester pregnant women. We selected women on the basis of a singleton pregnancy and availability of both a urine sample from the first trimester (defined as ≤13 weeks' gestation; median 10 weeks [IQR 9-12]) and a measure of intelligence quotient (IQ) in the offspring at age 8 years. Women's results for iodine-to-creatinine ratio were dichotomised to less than 150 μg/g or 150 μg/g or more on the basis of WHO criteria for iodine deficiency or sufficiency in pregnancy. We assessed the association between maternal iodine status and child IQ at age 8 years and reading ability at age 9 years. We included 21 socioeconomic, parental, and child factors as confounders.

FINDINGS:

The group was classified as having mild-to-moderate iodine deficiency on the basis of a median urinary iodine concentration of 91·1 μg/L (IQR 53·8-143; iodine-to-creatinine ratio 110 μg/g, IQR 74-170). After adjustment for confounders, children of women with an iodine-to-creatinine ratio of less than 150 μg/g were more likely to have scores in the lowest quartile for verbal IQ (odds ratio 1·58, 95% CI 1·09-2·30; p=0·02), reading accuracy (1·69, 1·15-2·49; p=0·007), and reading comprehension (1·54, 1·06-2·23; p=0·02) than were those of mothers with ratios of 150 μg/g or more. When the less than 150 μg/g group was subdivided, scores worsened ongoing from 150 μg/g or more, to 50-150 μg/g, to less than 50 μg/g.

INTERPRETATION:

Our results show the importance of adequate iodine status during early gestation and emphasise the risk that iodine deficiency can pose to the developing infant, even in a country classified as only mildly iodine deficient. Iodine deficiency in pregnant women in the UK should be treated as an important public health issue that needs attention

Environ Geochem Health. 2015 Aug;37(4):619-29.

A review of the iodine status of UK pregnant women and its implications for the offspring.

Bath SC[1], Rayman MP.

Abstract

Iodine, as a component of the thyroid hormones, is crucial for brain development and is therefore especially important during pregnancy when the brain is developing most rapidly. While randomised controlled trials of pregnant women in regions of severe iodine deficiency have shown that prenatal iodine deficiency causes impaired cognition, less is known of the effects in regions of mild deficiency. This is relevant to the UK as the World Health Organisation now classifies the UK as mildly iodine deficient, based on a national study of 14-15 year old schoolgirls in 2011. We have previously published a study using samples and data from the UK-based Avon Longitudinal Study of Parents and Children (ALSPAC) that found an association between low iodine status in early pregnancy (urinary iodine-to-creatinine ratio <150 μg/g) and lower verbal IQ and reading scores in the offspring. Though the women in ALSPAC were recruited in the early 1990s, the results of the study are still relevant as their iodine status was similar to that reported in recent studies of UK pregnant women. This review discusses the evidence that mild-to-moderate iodine deficiency during pregnancy has deleterious effects on child neurodevelopment and relates that evidence to the data on iodine status in the UK. It has highlighted a need for nationwide data on iodine status of pregnant women and that a randomised controlled trial of iodine supplementation in pregnant women in a region of mild-to-moderate iodine deficiency with child outcomes as the primary endpoint is required.

Cochrane Database Syst Rev. 2017 Mar 5;3:CD011761. .

Iodine supplementation for women during the preconception, pregnancy and postpartum period.

Harding KB[1], Peña-Rosas JP[2], Webster AC[3], Yap CM[4], Payne BA[5], Ota E[6], De-Regil LM[1].

Abstract

BACKGROUND:

Iodine is an essential nutrient required for the biosynthesis of thyroid hormones, which are responsible for regulating growth, development and metabolism. Iodine requirements increase substantially during pregnancy and breastfeeding. If requirements are not met during these periods, the production of thyroid hormones may decrease and be inadequate for maternal, fetal and infant needs. The provision of iodine supplements may help meet the increased iodine needs during pregnancy and the postpartum period and prevent or correct iodine deficiency and its consequences.

OBJECTIVES:

To assess the benefits and harms of supplementation with iodine, alone or in combination with other vitamins and minerals, for women in the preconceptional, pregnancy or postpartum period on their and their children's outcomes.

SEARCH METHODS:

We searched Cochrane Pregnancy and Childbirth's Trials Register (14 November 2016), and the WHO International Clinical Trials Registry Platform (ICTRP) (17 November 2016), contacted experts in the field and searched the reference lists of retrieved studies and other relevant papers.

SELECTION CRITERIA:

Randomized and quasi-randomized controlled trials with randomisation at either the individual or cluster level comparing injected or oral iodine supplementation (such as tablets, capsules, drops) during preconception, pregnancy or the postpartum period irrespective of iodine compound, dose, frequency or duration.

DATA COLLECTION AND ANALYSIS:

Two review authors independently assessed trial eligibility, risk of bias, extracted data and conducted checks for accuracy. We used the GRADE approach to assess the quality of the

evidence for primary outcomes.We anticipated high heterogeneity among trials, and we pooled trial results using random-effects models and were cautious in our interpretation of the pooled results.

MAIN RESULTS:

We included 14 studies and excluded 48 studies. We identified five ongoing or unpublished studies and two studies are awaiting classification. Eleven trials involving over 2700 women contributed data for the comparisons in this review (in three trials, the primary or secondary outcomes were not reported). Maternal primary outcomesIodine supplementation decreased the likelihood of the adverse effect of postpartum hyperthyroidism by 68% (average risk ratio (RR) 0.32; 95% confidence interval (CI) 0.11 to 0.91, three trials in mild to moderate iodine deficiency settings, 543 women, no statistical heterogeneity, low-quality evidence) and increased the likelihood of the adverse effect of digestive intolerance in pregnancy by 15 times (average RR 15.33; 95% CI 2.07 to 113.70, one trial in a mild-deficiency setting, 76 women, very low-quality evidence).There were no clear differences between groups for hypothyroidism in pregnancy or postpartum (pregnancy: average RR 1.90; 95% CI 0.57 to 6.38, one trial, 365 women, low-quality evidence, and postpartum: average RR 0.44; 95% CI 0.06 to 3.42, three trials, 540 women, no statistical heterogeneity, low-quality evidence), preterm birth (average RR 0.71; 95% CI 0.30 to 1.66, two trials, 376 women, statistical heterogeneity, low-quality evidence) or the maternal adverse effects of elevated thyroid peroxidase antibodies (TPO-ab) in pregnancy or postpartum (average RR 0.95; 95% CI 0.44 to 2.07, one trial, 359 women, low-quality evidence, average RR 1.01; 95% CI 0.78 to 1.30, three trials, 397 women, no statistical heterogeneity, low-quality evidence), or hyperthyroidism in pregnancy (average RR 1.90; 95% CI 0.57 to 6.38, one trial, 365 women, low-quality evidence). All of the trials contributing data to these outcomes took place in settings with mild to moderate iodine deficiency. Infant/child primary outcomesCompared with those who did not receive iodine, those who received iodine supplements had a 34% lower likelihood of perinatal mortality, however this difference was not statistically significant (average RR 0.66; 95% CI 0.42 to 1.03, two trials, 457 assessments, low-quality evidence). All of the perinatal deaths occurred in one trial conducted in a severely iodine-deficient setting. There were no clear differences between groups for low birthweight (average RR 0.56; 95% CI 0.26 to 1.23, two trials, 377 infants, no statistical heterogeneity, low-quality evidence), neonatal hypothyroidism/elevated thyroid-stimulating hormone (TSH) (average RR 0.58; 95% CI 0.11 to 3.12, two trials, 260 infants, very low-quality evidence) or the adverse effect of elevated neonatal thyroid peroxidase antibodies (TPO-ab) (average RR 0.61; 95% CI 0.07 to 5.70, one trial, 108 infants, very low-quality evidence). All of the trials contributing data to these outcomes took place in areas with mild to moderate iodine deficiency. No trials reported on hypothyroidism/elevated TSH or any adverse effect beyond the neonatal period.

AUTHORS' CONCLUSIONS:

There were insufficient data to reach any meaningful conclusions on the benefits and harms of routine iodine supplementation in women before, during or after pregnancy. The available evidence suggested that iodine supplementation decreases the likelihood of postpartum hyperthyroidism and increases the likelihood of the adverse effect of digestive intolerance in pregnancy - both considered potential adverse effects. We considered evidence for these

outcomes low or very low quality, however, because of study design limitations and wide confidence intervals. In addition, due to the small number of trials and included women in our meta-analyses, these findings must be interpreted with caution. There were no clear effects on other important maternal or child outcomes though these findings must also be interpreted cautiously due to limited data and low-quality trials. Additionally, almost all of the evidence came from settings with mild or moderate iodine deficiency and therefore may not be applicable to settings with severe deficiency.More high-quality randomised controlled trials are needed on iodine supplementation before, during and after pregnancy on maternal and infant/child outcomes. However, it may be unethical to compare iodine to placebo or no treatment in severe deficiency settings. Trials may also be unfeasible in settings where pregnant and lactating women commonly take prenatal supplements with iodine. Information is needed on optimal timing of initiation as well as supplementation regimen and dose. Future trials should consider the outcomes in this review and follow children beyond the neonatal period. Future trials should employ adequate sample sizes, assess potential adverse effects (including the nature and extent of digestive intolerance), and be reported in a way that allows assessment of risk of bias, full data extraction and analysis by the subgroups specified in this review

Ann Clin Biochem. 2015 Nov;52(Pt 6):705-8.

The new emergence of iodine deficiency in the UK: consequences for child neurodevelopment.

Rayman MP[1], Bath SC

Abstract

Adequate iodine intake is important during pregnancy as it is a component of the thyroid hormones that are crucial for fetal brain and neurological development. While randomized controlled trials in severe iodine deficiency have shown that iodine deficiency in pregnancy causes impaired offspring cognition, less is known of the effects in regions of mild/mild-to-moderate deficiency. The United Kingdom is now classified as mildly iodine deficient by the World Health Organization, based on a 2011 national study of 14-15-year-old schoolgirls. As pregnancy is the most critical time for brain development, we evaluated iodine status in pregnant women in Surrey (n = 100) and Oxford (n = 230). The median urinary iodine concentration was 85.3 μg/L in Surrey women, considerably lower than the WHO/United Nations Children's Fund/International Council for the Control of Iodine Deficiency Disorders cut-off of 150 μg/L. Oxford women had similarly low status. We investigated whether that level of iodine deficiency was associated with adverse child cognitive effects using stored samples and data from the Avon Longitudinal Study of Parents and Children cohort. In adjusted analyses, we found a significant association between low maternal iodine status in early pregnancy (urinary iodine-to-creatinine ratio <150 μg/g) such that children had an approximately 60% greater risk of being in the bottom quartile of scores for verbal intelligence quotient, reading accuracy and comprehension. UK women who might become pregnant should ensure they have adequate iodine status to avoid compromising their children's brain development