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Early life exposure to endocrine disrupting chemicals and child health - Summary

Rationale

Children are exposed to chemicals on a daily basis, mostly through everyday products and practices. Exposure starts, however, already as early as before birth, as chemicals present in the body of the mother may pass the placenta to reach the unborn child. Certain chemicals may disrupt the endocrine system (endocrine disrupting chemicals, EDCs), and early life exposure to EDCs may be particularly detrimental due to the vulnerability of the fetus. Hormones are involved in many processes during development, and endocrine disruption during this stage may have long-lasting health effects.

In this thesis an overview is given of literature on early life exposure to EDCs and effects on child growth as well as behavior. Furthermore research is presented on several environmental chemicals determined in a population of newborns in the area of Zwolle. In this population we examined if there were associations between levels of chemicals and growth in early childhood (birth weight, and growth during the first year after birth), as well as with thyroxine levels at birth. The latter was tested to examine the hypothesis that EDCs may affect growth through disruption of thyroid hormones.

What do we know from previous research?

Several studies have looked at the relation between prenatal or early postnatal exposure to EDCs and the prevalence of attention deficit hyperactivity disorder (ADHD) in children. Increased risks for ADHD or positive associations were found for amongst others polychlorinated biphenyls (PCBs), bisphenol A, and polybrominated diphenylethers (PBDEs). Moreover, low molecular weight phthalates were positively associated with externalizing behavior, which is also related to ADHD. Studies looking at autism are scarce, but those that have done so indicate positive associations.

It is also clear that for certain EDCs early life exposure may be associated with weight homeostasis later in life, however not necessarily in an obesogenic direction. Both positive and negative associations are observed between early life exposure and weight or height at various ages, including as early as 14 months, as well as until 20 years of age. In none of the included studies negative associations between perinatal exposure to EDCs and body mass index (BMI) were found and in several studies a positive association was observed.

Previous research also shows that dose-response relations appear to be nonmonotonic, meaning that an increase or decrease in exposure does not necessarily have to be accompanied with a similar in- or decrease in response.

Exposure to chemicals in children of the LINC study

Pregnant women from the area of Zwolle in the Netherlands were asked to participate in a study designed to determine early life exposure to EDCs and associations with child health. Levels of chemicals to which the child was exposed during pregnancy were determined in cord blood and breast milk. Information on lifestyle and various other factors was collected via questionnaires administered during pregnancy and during the first year after the child was born. Data on growth of the child was collected through youth health care centers which were visited by the parents seven times in the first year after birth.

The levels of PCB-153 and dichlorodiphenyldichloroethylene (DDE) observed in the LINC-study are relatively low when compared to other European cohorts, even compared to Belgium and Germany. A previous study also

measured PCB in Dutch children who were born between 1990 and 1992. They reported a sum PCB level of about 13 times higher than the level observed within the LINC-study, and even though we only included PCB-153. This may suggest that PCB levels are decreasing in the Netherlands.

All three of the selected brominated flame retardants could not be detected in cord blood, however they could be measured in some of the breast milk samples. This is similar to what has been observed in cohorts in Spain, Belgium, and France, which also had high percentages (86 – 99%) of samples below the limit of quantification for BFRs in cord blood. Regarding the perfluorinated alkyl acids, levels are lower but in a similar range compared to what has been reported in the large meta-analysis of European cohorts.

EDCs and growth in children

When examining early life EDC exposure and growth in the sample of Dutch participants, effects were observed for weight at birth as well as growth during the first year after birth. High perfluorooctane sulfonate (PFOS) and high DDE exposure were associated with higher birth weight, although this was only observed in female children. Low exposure to mono(2-ethyl-5-carboxypentyl)phthalate (MECPP) was associated with a higher BMI during the first year, both in boys and in girls. Similar effects were observed for low mono(2-ethyl-5-oxohexyl)phthalate (MEOHP) exposure in boys. Moreover, for most compounds boys showed an increase in BMI between six and eleven months of age.

Exposure to DDE, MECPP, and mono(2-ethyl-5-hydroxyhexyl)phthalate (MEHHP) was associated with head circumference during the first year after birth. High exposure to DDE was associated with a greater head circumference in boys, while the opposite was observed for girls. Also high MECPP exposure was related to a greater head circumference in boys. MEHHP exposure on the other hand seemed to mainly affect girls, in particular those with a relatively low exposure, who showed a greater head circumference than others.

Endocrine disruption - thyroxine

As experimental studies have shown that these compounds are endocrine disruptors, we tested whether levels of EDCs were associated with thyroid hormone levels at birth. Thyroid hormones are involved in various processes in the body, including metabolism. At birth, heel prick blood samples are collected from each child in the Netherlands to check for certain congenital disorders. This includes measurement of thyroxine, or T4. Positive associations with T4 were observed for DDE and perfluorooctanoic acid (PFOA) in girls, while for boys PFOS appeared to be of influence. When considering the results for T4 in light of findings for growth, it seems that results for DDE are most consistent. Exposure levels of DDE which were associated with both a relatively high birth weight and BMI later in life, also showed a relatively high T4 level.

Conclusions and future studies

We can conclude that children today are exposed to various chemicals as early as before birth. Even certain pesticides, which have been banned for several decades, can still be detected, although levels do appear to be decreasing. Associations between exposure levels and weight at birth as well as growth during the first year were observed. Moreover, associations were observed with thyroxine, a hormone which is essential for metabolism as well as brain development. Results were sex-specific, and most associations between exposure levels and health outcomes had a non-monotonic dose-response.

Follow-up of these children is essential to see if effects observed during the first year, persist in later childhood. Boys, for example, showed an increase in BMI between six and eleven months of age for exposure to most

compounds. According to growth standards of the WHO, generally a decrease in BMI is observed in this age period, and other studies have furthermore shown that this may be a risk factor for obesity in later childhood. Also regarding behavioral development, follow-up would most certainly be interesting, as previous research has shown that even variations in thyroxine levels within the normal range were associated with outcomes such as ADHD.

Future research should aim to disentangle mixture effects. Currently, most studies report effects compound by compound, which is not an accurate representation of reality. Furthermore awareness needs to be created among the general public as well as policy makers, in order for more strict safety regulations to arise. Scientists should cooperate with industry to improve the safety testing of chemicals.