Maternal dietary B vitamin intake, other than folate, and the association with orofacial cleft in the offspring

Introduction

Orofacial clefts (OFCs) are common congenital abnormalities in humans occurring in 1–2 per 1000 Caucasian new-borns. Its prevalence varies with geographic region, ethnic background and socio-economic status [1, 2]. The majority of OFCs are isolated malformations. The aetiology of nonsyndromic OFC is multifactorial, in which both genetic and environmental aspects, such as nutrition are involved. The pathogenesis of OFC though still remains unravelled due to its complexity and heterogeneity [3, 4].

Evidence is accumulating that inadequate maternal nutrition during pregnancy, in particular of vitamins, could be a risk factor for the occurrence of congenital...
Materials and methods

We performed a case-control study in the Netherlands in the period 1998–2001 of which the design has been described in detail by Van Rooij et al. [10]. Two hundred and six mothers of a child with nonsyndromic OFC were recruited in collaboration with the nine largest cleft palate centres at around 14 months after the delivery of the child. The control mothers were women with a non-affected child of the same age, recruited in the population domain of the case group, through acquaintances from mothers of an OFC child (59 %) or nurseries and infant welfare centres (41 %). Known pregnant and lactating mothers as those mothers who altered their diet compared to the periconceptional period were excluded. Incidental folic acid supplement users were also excluded from our calculations through which 182 OFC mothers and 172 control mothers revealed for analysis. All mothers were Dutch Caucasians. The Medical Ethical Committees of all participating hospitals approved the study protocol and a written informed consent was obtained from every participant.

All mothers filled out a general questionnaire from which data such as age, education level, pregnancy nausea, maternal periconceptional alcohol consumption, smoking and the periconceptional use of vitamins were extracted. From the mothers who visited the hospital for the study, maternal length and weight was recorded. Their body mass index was defined as weight divided by the quadrate of the length. Educational level was categorised into low education (primary/ lower vocational/intermediate/intermediate vocational education) and high education (higher secondary/higher vocational or university education). Nausea was characterised by duration, period, and seriousness. Because of the potential influence on the diet, extreme nausea is defined as nausea starting after the first week of pregnancy with excessive vomiting or nausea resulting in a changed or decreased food intake. Women were considered to be drinking alcohol or smokers when any alcohol consumption or smoking was reported in the periconceptional period. Data on vitamin supplements comprised the dosage, contents of the tablets (folic acid only or multivitamins containing folic acid, thiamine, riboflavin, niacin, pyridoxine and cobalamin), frequency of intake and specification in which weeks the supplements were taken before and during pregnancy. Periconceptional use of vitamin supplements was defined as daily intake from four weeks before through eight weeks after conception.

Furthermore, all participants filled out a validated Food Frequency Questionnaire (FFQ), developed for the Dutch cohorts of the European Prospective Investigation into Cancer and Nutrition study (EPIC) which provided information on the dietary intake of the B vitamins, thiamine, riboflavin, niacin, pyridoxine and cobalamin [20]. The FFQ was mailed to the subjects and filled out at home. During a hospital visit scheduled for this study or through a telephone interview we checked the FFQ in a standard way for completeness and consistency. The FFQ accounted for at least 90 % of the population mean intake of food groups and nutrients of interest. In the FFQ, subjects could indicate their answers in frequency per day, per week, month, year or never. For