Risiken erkennen – Gesundheit schützen

Folate Status of the Population in the European Community and Strategies for Change

Minutes of BfR for 11/12 January 2007

In January 2007 an European expert meeting on “Folate Status in Europe and strategies for change” was held at the Federal Institute for Risk Assessment (BfR). 31 experts from 15 European countries participated in the meeting. They discussed ways of improving the folic acid intake of the population in Europe and means of reducing the risk of neural tube defects in newborn babies.

The experts agreed that more targeted awareness-raising campaigns are needed in order to draw women’s attention to the importance of folic acid intake prior to and during the first three months of pregnancy. The results of the meeting are summed up in the following report.

Further information on this subject can be accessed on the BfR website: http://www.bfr.bund.de/cm/208/folsaeurestatus_in_europa_und_moeglichkeiten_der_intervention.pdf.

The intake of folate from foods and the folate status of (parts of) the European population are below the dietary recommendation and also below the doses necessary for the prevention of neural tube defects (NTDs). At the same time, the prevalence of NTD in Europe is about 1 case per 1,000 live-births. Earlier studies have shown a preventive effect of folic acid on the occurrence of NTDs. Therefore, to increase the intake of folate/folic acid is a major public health objective in Europe.

Up to now, women of childbearing age were advised to take supplements of 400 µg folic acid from 4 weeks before to 2 to 3 months after conception. However, only about 10 % of women (in one country because of intensive information campaigns up to 50 %) follow this advice. Therefore, in many European countries fortification of flour or another staple food with folic acid is considered an alternative strategy.

Against this background, the Advisory Forum of EFSA proposed at its September meeting in 2006 to convene a discussion forum on this issue in order to reflect on current practice and discuss opportunities for a common European strategy to tackle the problem.

31 participants from 14 EU member states and from Switzerland attended the meeting, which was hosted by the Federal Institute for Risk Assessment in Berlin.

The participants of the forum recognised that:

- with respect to the intake of folate from normal foods . . .
  - there is not a single reference value for folate intake by the general population in Europe (e.g.: Italy, UK: 200 µg, Ireland: 300 µg, and Germany, Austria, Switzerland, Poland and Slovakia: 400 µg folate (equivalents) per day). The same occurs with regard to the reference values for women in childbearing age (e.g.: Germany: 600 µg; Italy: 400 µg folate equivalents per day). This makes it difficult to compare the actual intake situation when this is expressed as a percentage of the recommended intake.
  - the average dietary folate intake of women in Europe is around 200 µg per day;
  - status data are either not available or not comparable, because different methods

have been used for assessment;
- dietary surveys, however, often underestimate the real intake of food items and consequently of nutrient amounts;
- dietary surveys do not always include the contribution of folic acid from fortified foods and from folic acid supplements.

- with respect to the prevalence of NTDs . . .

  - according to EUROCAT, the NTD prevalence in Europe has been stable over the past decade (about 1 case per 1,000 live-births), although the rate per live-births declined (about 2/3 of cases are terminated);
  - there is significant variation in the prevalence between European countries although some of this may be due to differences in how these data are collected;
  - one of the reasons for the variation in NTD rates per live-births is the differing practice of terminating pregnancies in European countries (while in Ireland abortion is illegal, up to 80 % of diagnosed cases of NTD are aborted in other countries);
  - passive[1] NTD registers are likely to underestimate the rates (the register in Mainz and the Hungarian Congenital Abnormality Registry are the only active registers in Europe);
  - it is crucial to have a reliable database of NTD rates for monitoring the impact of folic acid supplementation or fortification measures;
  - efforts should be made at the local and national level to improve the reliability of NTD registers;
  - passive case registers in European countries should be validated against the data of at least one active register per country.

- with respect to the advice to supplement folic acid . . .

  - only about 50 % of pregnancies in Europe are planned;
  - only a minority of women of childbearing age who plan their pregnancy does follow the advice to take folic acid supplements both with respect to the dose (400 µg/d) and to the right time (from four weeks before to two to three months after conception);
  - the compliance of women seems not to be influenced by either knowledge of the preventive effect of folic acid (e.g. in countries where 75-80 % of women stated that they were well aware about the issue, the compliance was still not satisfactory), or other factors such as costs for the individual (e.g. in Italy where folic acid is free of charge, only a small number of women follows the recommendation);
  - in the Netherlands a big campaign on promotion of supplement intake achieved that about 50 % of women took folic acid supplements, however, without any demonstrable effect on the reduction of NTD occurrence;
  - as to the effective dose of additional folic acid intake, no dose-response-studies have been conducted;
  - in the majority of European countries a dose of 400 µg folic acid per day is recommended to women of child-bearing age in addition to their dietary folate intake. In some countries 800 µg folic acid per day as a supplement is recommended for both primary and secondary prevention);

[1] Passive registers rely on spontaneous reporting of cases by doctors or hospitals while active registers collect complete data of prenatal diagnosed cases by e.g. ultrasound, cases diagnosed by post-mortem investigation of (aborted) foetuses and of live-born cases with NTD.

- a recent publication[2] indicates that it might be necessary to extend the recommended period for preconceptional folic acid supplementation to > 4 weeks for maximal prevention of NTDs based on folate concentrations.

- with respect to voluntary fortification of foods with folic acid . . .

  - presently, there is a wide range of products voluntarily fortified with folic acid on the European market;
  - voluntary fortification may lead to an unequal and unpredictable intake of folic acid and does not necessarily reach those who are particularly in need;
  - to increase awareness within the target population the availability of fortified food products would need to be promoted (this would require approval of a special health claim);
  - due to the wide range of fortified products with varying folic acid levels and due to the rapid shifts of the market, monitoring of folic acid intake via voluntarily fortified foods is both important and very difficult;
  - for a reliable intake assessment, accurate information on the consumption of folate rich foods, the range of folate rich foods on the market and their relative contribution to dietary intakes would be required, and continuous updates of food composition tables would be necessary;
  - to limit the number of foods fortified with folic acid and restrict the levels of fortification requires combined effort because the *EC* Regulation 1925/2006 *on the addition of vitamins and minerals and of certain other substances to foods* foresees no such restrictions;
  - the decisions on the regulation of maximum levels for addition of nutrients to foods will be taken by the Standing Committee on the Food Chain and Animal Health (SCFCAH) and the European Commission. Advice by the EFSA in this matter is not foreseen.

- with respect to mandatory fortification of foods with folic acid . . .

  - mandatory folic acid fortification would be the most effective way of increasing the intake of folic acid in all groups of the population, including that of the target group;
  - the benefit of this measure to a relatively small group of women needs to be balanced against the exposure to folic acid of the whole population;
  - estimations on the potential impact on the intake of folic acid via fortified flour/bread by various population groups have been made in several countries. On the basis of these estimates the scientific advisory bodies of Ireland and the UK proposed mandatory folic acid fortification of bread or flour, respectively;
  - the UK committee has also recommended controls on folic acid intake via voluntarily fortified foods as an accompanying measure of mandatory fortification;
  - consumers' choice should be accommodated by excluding certain kinds of flour/breads from the programme;
  - the experience from other countries and the consumption habits of the European population confirm that bread/flour is the most appropriate staple food to be fortified;
  - careful monitoring of effects – both intended and undesirable – is necessary.

- with respect to the safety of additional folic acid intake . . .

[2] Lamers Y, Prinz-Langenohl R, Bramswig S, Pietrzik K (2006). Red blood cell folate concentrations increase more after supplementation with [6S]-5-methyltetrahydrofolate than with folic acid in women of childbearing age. Am J Clin Nutr. 84:156-61.

- the risk of masking symptoms of an undiagnosed vitamin B12 deficiency by additional intake of folic acid should be assessed in the elderly population of different countries;
- an additional fortification with vitamin B12 could be taken into consideration;
- data on vitamin B12 status need to be assessed regularly;
- the scientific basis for an association between folic acid and cancer is incomplete;
- presently the benefit of folic acid in preventing cancer is as uncertain as the risk of promoting it;
- in persons free of (pre-)cancerous lesions and with low folate status, an increase in folic acid intake may decrease the risk of cancer, while it may promote the progression of already existing pre-cancerous lesions in the gut;
- there are no data on a safe level of folic acid with regard to the risk of cancer promotion;
- there appears at present to be no increase of cancer rates in countries with folic acid fortification programmes.

- with respect to technical and legal preconditions . . .

  - by using fortified flour for baking bread, up to a 25–30 % loss of folic acid will have to be taken into account during the baking process, depending on the type of bread and conditions of baking;
  - there are no problems of homogeneity of fortified flour;
  - Article 11 of the Regulation 1925/2006 requests member states to inform the Commission of existing national provisions on the mandatory addition of vitamins and minerals to foods by 19 July 2007 and to notify the Commission if it considers it necessary to adopt new legislation on the mandatory addition of vitamins and minerals to specified foods;
  - different fortification levels may impede free trade of products between European countries. Therefore, industry and manufacturers need to be partners in the discussion about harmonisation;
  - European population reference intakes for folate/folic acid should be defined by the EFSA with priority.

The following research needs were identified:

- Why has the advice to take supplements not been successful, and how could the situation be improved?
- Molecular mechanism for folate/folic acid-induced prevention of NTDs;
- Experimental and epidemiological studies to assess the role of folates/folic acid in birth defects and developmental disorders other than NTDs;
- Molecular mechanism by which folic acid might prevent or promote cancer (in order to identify biomarkers and risk markers).

The participants of the forum concluded that

- National NTD registers should be improved and strengthened, taking into account regional differences. This would make EUROCAT more reliable.

- In many European countries primary prevention of NTDs is more acceptable. It should be differentiated from secondary “prevention” by prenatal diagnosis of NTD and termination of pregnancies.

- Targeted and continuous public health campaigns are necessary to promote periconceptional supplement intake of folic acid, regardless of any fortification measures taken.

- While considering the implementation of (mandatory or voluntary) folic acid fortification as a public health measure, fortification levels should be kept as low as possible (effective but safe).

- Independent from the kind of intervention chosen, regular monitoring of impact and effectiveness in all groups of the population is essential. Possible parameters are: folic acid intake, red cell folate and vitamin B12 status, homocysteine levels, prevalence of NTDs, prevalence of other malformations.

- With respect to the open questions on the safety of folic acid, another meeting especially on the issue of cancer promotion is desirable.

- The results of this Discussion Forum will be presented to the EFSA Advisory Forum.