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Review

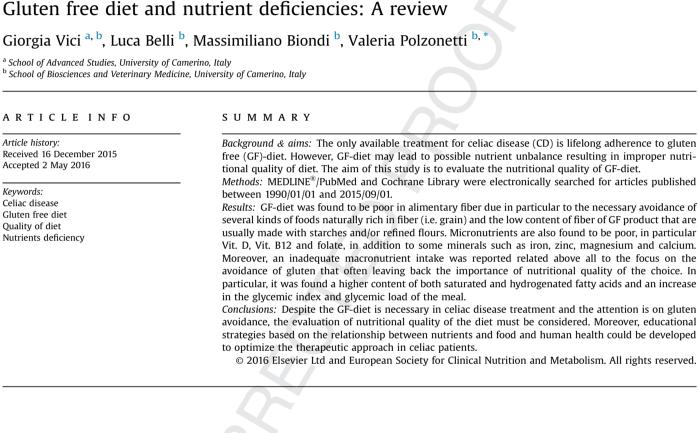
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1. Introduction

Celiac disease (CD) is a chronic enteropathy which affects approximately 1% of the general population [1]. Now, the only treatment is strict lifelong adherence to a gluten-free diet (GF-diet) which leads to disappearance of the signs/symptoms [1,2]. Removing completely gluten from the diet of celiac patients will result, in the majority of patients, in remission in terms of symptoms and serologic and histological aspects [3]. It is reported that many disease complication can be avoided with gluten removal and in children growth and development can return to normal with the adherence to the GF-diet [3,4].

However, it is not always simple for CD patient to strictly follow a GF-diet and to make the right nutritional choices [5].

Moreover, GF-diet may lead to possible nutrient deficiencies (such as fiber and specific micronutrients) or nutrient excess (i.e. saturated fats). Gluten-free products are usually lower in fiber, magnesium and folic acid and gluten-free cereals found in nature have a lower magnesium content compared with gluten-containing ones [6-8].

The aim of this study is to determine and evaluate the nutritional quality of GF-diet and the impact on specific nutrients such as iron, folate, fiber, vitamins (in particular Vit. B12 and Vit. D), zinc, magnesium and calcium.

MEDLINE[®]/PubMed and Cochrane were electronically searched

for articles published between 1990/01/01 and 2015/09/01. A

combination of keywords addressing "gluten", "gluten-free diet",

"gluten free", "gluten free diet" OR "nutritional" OR "quality" were

2 Methods

2.1. Literature search

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2.2. Inclusion criteria

Observation study, controlled clinical trial (CCT), meta-analysis, systematic review, and consensus conferences were included as random controlled trials (RCTs) with randomization at any level. Studies regarding gluten sensitivity were excluded. Papers with information on at least one nutrient of our interest were included.

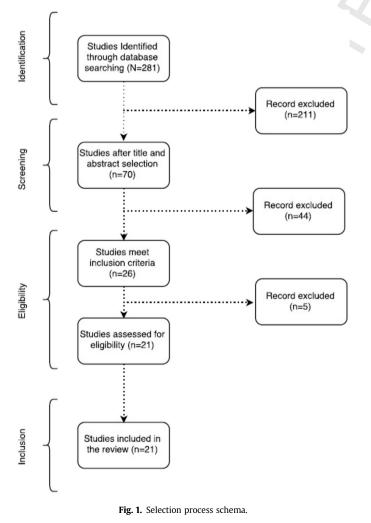
2.3. Data extraction

Data extracted from each eligible study were specifically analyzed in term of nutrition quality of the diet, in particular excess or deficiency of particular nutrients.

Of the 281 identified articles, we excluded 211 on the basis of the title and abstract as they did not fit with our interest. The full text of the remaining 70 articles was extensively reviewed to determine whether the articles met the inclusion or exclusion criteria. 44 articles did not meet our inclusion criteria. We excluded another 5 articles because they did not report data for the use of at least one specific nutrient. The remaining 21 articles were considered for the review (Fig. 1.)

3. Results

As reported in Table 1, several studies reveal different nutrients inadequacies in GF-diet.



3.1. Dietary fiber

As demonstrated by several studies, a GF-diet is often characterized by a lower intake of dietary fiber respect to normal diet containing gluten [9,10].

Fiber deficiency can be encountered both at the diagnosis and during the GF-diet. At the diagnosis, deficiency is related to malabsorption due to villi atrophy. During GF-diet, it could be related to poor quality of GF products, to patients' choice and, of course, to the avoidance of several kinds of foods naturally rich in fiber (i.e. grain).

The composition of GF product can be a reason for the lower intake of fiber. GF product is usually made with starches and or refined flours characterized by low content of fiber. During the production process, in particular the refined process, the outer layer of grains is removed leaving the starchy inner part. As is known, the outer layer containing the most of the fiber so the refined process is related with a decrease of fiber content [9].

Wild and co-workers conducted a study where they compared the nutritional value of GF-diet with data from the National Diet and Nutrition Survey of Adults and the UK Women's Cohort Study (UKWCS).

In particular, they found that there is a significant decrease in fiber content in women diet if compared with UKWCS [11].

Martin and co-workers compared data from 88 German CD patients to the DACH reference value and to the German National Diet and Nutrition Survey (NVSII) data and they observed that the content of fiber in male CD patients was significantly lower than the one of general population [12].

Mariani and co-workers examined the diet of 47 adolescents with CD and 47 healthy aged-matched control subjects. This study showed a lower consumption of carbohydrates and in particular a low content of fiber in the diet of CD adolescents than healthy adolescents [13].

As is known, a consumption of adequate amounts of dietary fiber is related to important health benefits such as prevention of colon cancer, diabetes and cardiovascular disease [9]. Indeed, the *Joint WHO/FAO Expert Consultation on Diet, Nutrition and the Prevention of Chronic Diseases* stated that, by current evidence, an adequate amount of fiber in the diet is related to potential health benefits. In particular, they show their important role for preventing obesity, diabetes, cardiovascular diseases and various cancers [14].

Several studies underline the importance of choosing enrichedfood and the use of pseudocereals [6,10]. Indeed, as underlined by Saturni and co-workers, pseudocereals are good sources of fibers with a fiber content ranges from 7 to 10 g/100 g. Comparing these with other plant foods, it is possible to observe that fiber content is higher in pseudocereal respect to other cereals and also to other plant foods such as fruits and nuts [6].

3.2. Vitamins

Usually, vitamins deficiencies are associated with untreated celiac disease due to malabsorption linked to villi atrophy. However, in some CD patients following a GF-diet, deficiencies of some vitamins may persist and this required a particular attention to the quality of the GF-diet [1,6,9,15].

Martin and co-workers demonstrated that CD patients showed significantly lower level of folic acid, vitamin C and vitamin B12 compared to DACH reference value and to NVSII data [12].

In addition, in a double blind placebo controlled multicentre **Q7** trial, performed on 65 celiac subjects divided into two groups (supplemented with folic acid, cyanocobalamin and pyridoxine vs. no supplemented) the plasma total homocysteine (tHcy) was

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