RESEARCH LETTER

Effect of increased protein intake on the risk of female infertility

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Introduction An unbalanced diet and consumption of nutritionally inadequate food may contribute to disease and health disorders.[1] The literature also suggests that the nutritional quality of food, including the amount and type of proteins consumed, may impact female fertility.[2,3] It is possible because the cells present in the ovaries contain insulin-like growth factor-1 (IGF-1) receptors. The IGF-1 level is correlated, among others, with the protein intake.[3-5] Based on these premises, we used epidemiological and clinical data to determine the effect of protein intake on the potential risk of infertility in women.

Patients and methods The study was conducted on a group of 100 women aged 20 to 40 years, who were patients at the Gynaecology and Obstetrics Clinical Hospital of the Poznan University of Medical Sciences, Poznań, Poland. We used simple random sampling (dependant) to ensure research integrity. Participants were divided into 2 groups: group A, including women with infertility disorders (diagnosed by a gynecologist), receiving no pharmacological infertility treatment, and wishing to become pregnant; and group B, including women with no infertility disorders, with no natural or induced miscarriages in history, with successful pregnancies in the past, and wishing to become pregnant.

A nutritional assessment was carried out using a 24-hour dietary recall over 7 days.[6] To ensure the best reliability of the nutritional assessment, all 24-hour dietary recall interviews were conducted face to face. Participants used household measurements or grams. A total of 700 24-hour dietary recall interviews were collected, which described the participants' nutrition during the 7-day period. A database in the MS Access 2011 software (Microsoft Corporation, Redmond, Washington DC, United States) was created to analyze the daily food intake. A qualitative and quantitative analysis of daily food intake was performed using the Dietetyk 2011 computer software (JuMaR, Poznań, Poland), based on the Polish database comprising tables of nutritional value of food.[7] The degree of compliance to nutritional standards for women with moderate physical activity was based on dietary recommendations.[1] Basic anthropometric measurements were performed, which allowed for the evaluation of the nutritional status.

The results were analyzed using the Statistica software, version 10 (StatSoft Polska, Kraków, Poland). For quantitative results, the Shapiro–Wilk test was used to verify normal distribution. The *t* test was used to analyze differences between the variables with equal variance, and the Cochran–Cox test was used for variables with normal distribution and unequal variance. For variables with nonnormal distribution, the Mann–Whitney test was applied. For all variables, a *P* level of 0.05 was considered significant. On the basis of nutritional assessment results, multidimensional logistic regression models were built to correct for factors influencing the inclusion criteria for participation in the study.

The study was approved by the Poznan University of Medical Sciences Bioethical Committee (decision number, 591/09 of June 18, 2009).

Results Except for the waist circumference and waist-to-hip ratio, anthropometric measurements did not show differences in the assessment of the nutritional status between the groups. Additional data are presented in Supplementary material online (*Table S1*).

The analysis of data showed that the energy value of daily food intake was significantly higher in infertile women as compared with control women (1880 cal and 1647 cal, respectively, $P = 0.01$). Infertile women showed a significantly higher mean daily protein intake than the control

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TABLE 1 Effect of protein intake on the risk of female infertility in the raw and adjusted logistic regression models

Variable		Raw model		Adjusted model[a]	
		P value	OR (95% CI)	*P* value	OR (95% CI)
protein	total, g	<0.0001	1.0765 (1.0400–1.1143)	0.0022	1.0750 (1.0264–1.1258)
	plant, g	0.0002	1.1725 (1.0774–1.2761)	0.0446	1.1251 (1.0028–1.2622)
	animal, g	0.0003	1.0804 (1.0361–1.1267)	0.0026	1.0947 (1.0322–1.1610)
	% of energy	NS	1.1404 (0.9643–1.3486)	0.0159	1.3788 (1.0621–1.7900)

a corrected for age, body mass index, waist-to-hip ratio, physical activity, smoking, alcohol and caffeine intake, exposure to harmful chemical and physical factors, and previous use of oral contraceptives

Abbreviations: CI, confidence interval; NS, not significant; OR, odds ratio

group (72.2 ±14.7 g and 57.2 ±14.3 g, respectively, P <0.0001). The energy from protein intake was 15% for infertile women and 14% for fertile women. In both groups, the intake of proteins derived from animal products was higher than that from plant sources. In addition, infertile women showed a significantly higher plant-derived protein consumption than the control group (21.9 g and 18.0 g, respectively, P <0.0001), but they also showed higher animal protein intake than controls (45.9 g and 35.5 g, respectively, P = 0.0001).

Multidimensional logistic regression models were built (TABLE 1) to correct for other factors that may cause infertility and allow a reliable interpretation of the effect of nutrition on infertility. As opposed to the raw model, the adjusted model took into account nutrition corrected for factors that could falsify the results and influence the inclusion into the infertile group. These factors included age, body mass index, waist-to-hip ratio, physical activity, smoking, alcohol and caffeine consumption, exposure to chemical and physical agents in the workplace, and the use of oral contraceptives in the past. In both the raw and adjusted models, the protein intake had a strong effect on the risk of infertility (odds ratio [OR] >1; P <0.05), which increased with a higher total protein, vegetable protein, as well as animal protein intake. Interestingly, in the raw regression model, the proportion of energy intake from protein was not linked to an increased risk of infertility (OR >1; P >0.05); however, in the adjusted model, the proportion of energy intake from protein that exceeded the recommended amount had an effect on women's infertility (OR >1; P <0.05).

Discussion The amount of energy from protein intake in our study was consistent with the official recommendations; however, there were significant differences between the groups in the amount of protein intake. Infertile women exceeded the official recommendations by about 30%, which indicates that they ate too much protein. This might have had a negative effect on their fertility. In fertile women, the average protein intake was compliant with the recommendations. A recent study by Chavarro et al[4] indicated that the quantity and type of protein contribute to ovulation disorders in women and thus increase the risk of infertility, because IGF-1, which regulates blood glucose levels, may impede ovulation. The authors showed that women with increased protein intake (about 115 g) had a 41% increased probability of developing ovulation disorders, which, in turn, resulted in a longer time for women to become pregnant. Moreover, Chavarro et al[4] found that increased animal protein consumption contributed to the risk of ovulation infertility. The effect was also present when 5% of the plant protein energy was used to substitute carbohydrates, which decreased the risk by 43%. Conversely, when 5% of the animal protein energy was used to substitute carbohydrates, it resulted in a 20% higher risk of infertility. Investigators showed that, among animal proteins, those from red meat and poultry had the most "negative" effect on fertility, while egg and fish protein did not show a similar negative influence.[3,4] Chavarro et al[4] noted an increased percentage of protein energy intake (15.4%–23.1%), which depended on the quartile of food intake.

In a study investigating the eating habits of Polish women of childbearing age, Hamułka et al[8] showed a similar protein energy intake of 14.8%. A similar amount was also demonstrated for women with a history of natural miscarriage: 15.4%, of which plant protein constituted 55% of the recommended intake and animal protein—109%.[9] The mean daily protein intake in this group ranged from 49.0 to ±25.4 g, which constituted 80% of the official recommendation and was lower than that found in our study.[9] Gogojewicz et al[10] observed similar protein consumption in a group of fertile women who participated in fitness classes.

A study by Stefańska et al[11] reported a large excess of protein intake. The authors found that the protein intake was 66 ±23 g/d, 70 ±32 g/d, and 71 ±27 g/d in normal-weight, overweight, and obese women, respectively. In all these groups, the protein energy share was 18% and they consumed more animal protein.[11] The recommended proportion between these 2 protein sources should be two-thirds of plant and one-third of animal protein.[1] In the cited research, the daily nutrition of women showed an opposite pattern, which was significantly higher in the infertile group. This relationship can be explained by the positive influence of plant proteins on reducing the risk of insulin resistance and decreasing IGF-1 levels, which, when increased, may play an important

role in polycystic ovary syndrome and are linked to ovulation disorders.[4,12] Chavarro et al[3] indicated that high levels of IGF-1 and insulin were related to high animal protein intake. The researchers concluded that IGF-1 has a possible inhibitory effect on ovulation and increases the production of male hormones, which, in turn, prevents ovarian follicle maturation. Another possibility explaining the effect of protein intake on fertility is related to the fact that plant proteins contain large amounts of arginine, a substrate used for nitric oxide synthesis. Nitric oxide has vasodilation properties that improve blood circulation and flow in the sex organs, resulting in oocyte development and embryo implantation.[13]

In conclusion, our study showed that both the increased protein intake and the proportion of energy obtained from protein were associated with an increased risk of infertility.

Supplementary material online Supplementary material is available with the online version of the article at www.pamw.pl.

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