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A Fasting and Vegetarian Diet Treatment Trial on Chronic Inflammatory Disorders

Effects on Clinical Condition and Serum Levels of Neutrophil-derived Granule Proteins

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Twenty patients with arthritis and various skin diseases were studied on a metabolic ward during a 2-week period of modified fast followed by a 3-week period of vegetarian diet. During fasting, arthralgia was less intense in many subjects. In some types of skin diseases (pustulosis palmaris et plantaris and atopic eczema) an improvement could be demonstrated during the fast. During the vegan diet, both signs and symptoms returned in most patients, with the exception of some patients with psoriasis who experienced an improvement. The concentrations of lactoferrin in serum reflect the turnover and activity of neutrophil leukocytes. When this protein was initially increased it fell to normal values in most cases. The improvement or impairment of signs and symptoms was related to the lactoferrin levels in serum. *Key words: Psoriasis; Arthritis; Lactoferrin; Vegetarian diet; Fasting.* (Received November 16, 1982.)

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Today, fasting is tried by many Swedish adults for alleged therapeutic purposes. Vegetarian diets are claimed to improve the clinical condition in some disease, e.g. rheumatoid arthritis and various intestinal and cutaneous disorders. A number of Swedish health resorts are advocating fasting periods and lactovegetarian or vegan diets. Reports of improvements during such treatments appear mostly in magazines and the newspaper and only one study seems to have been made under controlled conditions (2).

We therefore decided to investigate the effects of a total vegetarian diet (vegan diet) following a period of 2 weeks of fasting in a group of patients with various cutaneous diseases and to study both the clinical status and laboratory parameters related to inflammatory processes. The schedule we followed is one that is applied at many of the health resorts.

MATERIALS AND METHODS

Subjects

Twenty patients, 15 females (mean age 43 years, range 24–61) and 5 males (mean age 39 years, range 23–55) participated. Two of the patients (one female and one male) deteriorated clinically during the fast and discontinued the treatment. The patients suffered from the following diseases: psoriasis with arthritis (10 patients), pustulosis palmaris et plantaris (4), atopic exzema (3), rosacea (3). No patient experienced an acute exacerbation of the disease at the time for the study. Only one of the patients

was being treated with corticosteroids in a low constant dose, also during the trial. Treatment with other anti-inflammatory drugs was kept constant throughout the trial period. No other treatment than inert softening ointments was allowed for the cutaneous disease. All patients had had their diseases for years and were in a stable condition on admission.

Experimental procedure

During the first day the ordinary hospital diet was given. On the second and third days the patients received the vegetarian diet at a low energy level, 5.0 MJ/day (1200 kcal). They then fasted for 11 days, during which time only vegetarian broths were given, 0.8–0.9 MJ/day (200 kcal).

During the 3 days after the fast was broken, the daily energy intake was gradually increased, to 1.1, 1.7 and 2.6 MJ/day (260, 400 and 620 kcal). It was then adjusted according to the patient's body weight, 150 kJ/kg body weight (35 kcal) for males and 130 kJ/kg (30 kcal) for females, aiming at a stable body weight during the last 2 weeks of the vegan diet, which in 19 patients was given for 3 weeks. One patient was given a vegan diet for 4 weeks, without prior fasting.

Clinical examinations and laboratory tests were performed on the day of admission and on the following day. All analyses done on these days were repeated at the end of the fast and at the end of the period on the vegan diet.

Diets

During the fasting period, vegetarian broths, vegetable drinks, as well as drinks from berries and herbal teas were given every 2–3 hours. These were made from various root vegetables such as beetroot, carrots and potatoes and from bilberries and strawberries.

A 7-day menu was used throughout the vegan diet period. The composition of the food was calculated from food tables. The vegan diet was based on fresh vegetables, root vegetables, millet, lentils and buckwheat. The diet was based on a traditional menu, used at many health resorts and with very little potato or cereal products. Sunflower oil (with a content of 60% of polyunsaturated fatty acids) was used in dressings and a soft margarine (50% polyunsaturated fatty acids) on the bread. The average ratio of polyunsaturated to saturated fatty acids (P/S ratio) was 4.4±0.3 (mean±SD). All animal protein (meat, fish, egg, milk) was excluded, making the protein content of the diet rather low (9% of total energy). The fat content accounted for 42% and carbohydrates for 51% of the total energy. No extra salt or sugar was allowed. The only saccharides were in the berries and fruits, which were included in a controlled and limited amount. The average fibre content was 5.1±0.5 g/1.0 MJ (240 kcal) as calculated from McCance and Widdowson (5).

A more detailed description of the diet and its content of vitamins and minerals will be given elsewhere (3).

Methods

The dermatological status was examined by one and the same clinician (K. L.) on admission, after the fast and after the vegan diet period. For all four dermatological disorders an evaluation was made regarding the location and extent of the lesions, and the degree of erythema, infiltration, scaling and itching. For pustulosis palmaris et plantaris, pain and the number and size of the pustules and for rosacea the number and size of pustules, papules and infiltrates were also noted. In addition, at every examination a subjective evaluation with respect to improvement or impairment was made by the doctor and the patient independently of each other. A five-grade scale for improvement or impairment was used. At every visit, photographs were taken of the efflorescences.

Serum myeloperoxidase and lactoferrin were assayed as described by Olofsson et al. (4) and serum lysozyme as described by Venge et al. (6) using radioimmunosorbent techniques. The normal ranges are 40–200 μg/l and 985–2900 μg/l, respectively. The cortisol concentration in 24 h urine collections was also measured using a radio-immuno assay technique.

Statistics

A three-way analysis of variance was applied for separating effects of therapy, patient characteristics and sex, using the SAS package for an IBM 370/158 computer. In some calculations Student's *t*-test was applied.

RESULTS

Clinical course

Psoriasis. All patients with psoriasis were included because of a complicating arthritis which dominated the clinical picture at the time of the study. In fact, most of these patients

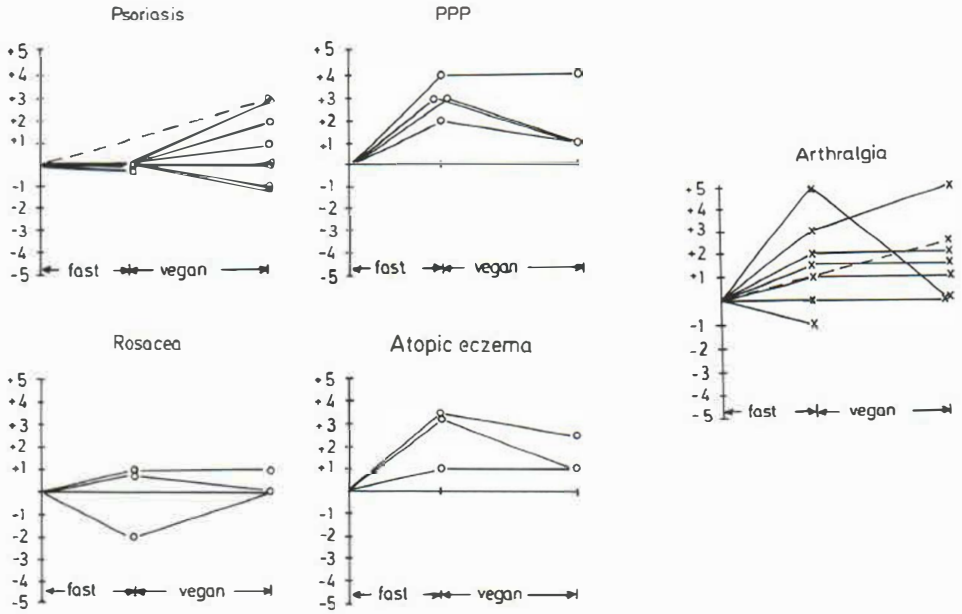

Fig. 1. Comparison of the clinical improvement or impairment at the end of the fast and at the end of the vegan diet, vis-à-vis the state on admission, as evaluated by one clinican (○) according to a five-grade scale for patients with psoriasis, pustulosis palmaris et plantaris (PPP), rosacea, and atopic eczema. The improvement and impairment of the arthralgia as evaluated by the patients are also indicated (X).

had few and small cutaneous efflorescences. With respect to the cutaneous affections, none of the patients improved during fasting, but several showed some improvement after the vegan diet (Fig. 1). One of the patients who improved had decided not to take part in the fast and was thus treated with a vegan diet throughout the trial period. The patients' own grading of the cutaneous affection was close to that of the doctor.

Arthralgia. The evaluation of the arthritic condition was based solely on the patient's own judgements. The symptoms were less pronounced during the fasting period (except in 2 patients, who became worse). However, in almost all cases the symptoms gradually returned during the vegan diet period, but after the trial the condition was still regarded as slightly better than on admission by most patients (Fig. 1).

Pustulosis palmaris et plantaris. There was a considerable improvement during fasting in all 4 patients. The number of pustules decreased (from several hundred per foot to fewer than ten in one case). The blush became less intense and the skin less swollen. Deterioration again occurred during the vegan diet period, except in one patient (Fig. 1), but all patients still showed some improvement on leaving the clinic. The clinical course later continued towards the state that was seen on admission in all cases. The patients' judgements were in good agreement with those of the doctor.

Rosacea. The changes that occurred in this group of patients were small and inconsistent (Fig. 1). The patients who felt they had improved reported a higher rating of improvement than did the doctor, noticing a less 'tense' skin.

Atopic eczema. One patient was considered to be definitely improved after the whole treatment period, the improvement starting already during the fasting (Fig. 1). This patient had a previously known intolerance to some food consitutents, positive antibody titres against peanut protein, and elevated IgE levels.

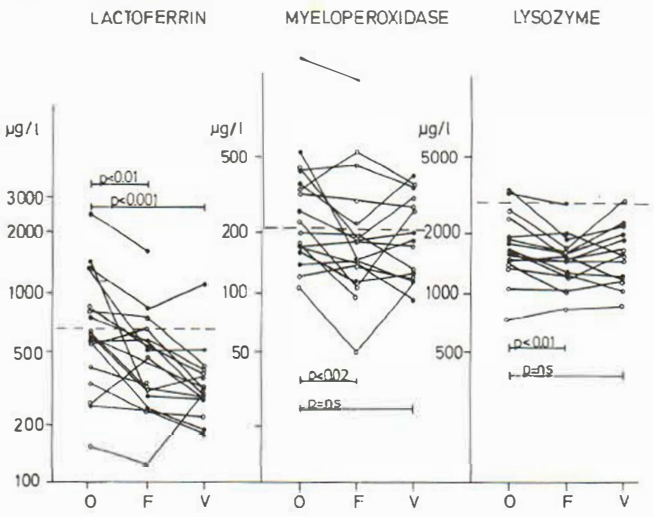

Fig. 2. The serum concentrations of lactoferrin, of myeloperoxidase and of lysozyme are indicated on admission (*O*), after the fast (*F*) and after the vegan diet (*V*). Filled symbols indicate patients wtih psoriasis with arthritis, x indicates patiens with PPP, rosacea, and atopic eczema. The statistical significances between the differences in protein concentrations on the three occasions are indicated on the figure, as evaluated by means of paired *t*-test. The horizontal line indicates the upper 95 % confidence limit of a normal population of the respective protein.

Laboratory tests related to the inflammatory process

The erythrocyte sedimentation rate was not significantly lower after the fast or the vegan diet period, but the haptoglobin concentration decreased during fasting and then increased again, though remaining at a lower level than before treatment (Table I). The increase in haptoglobin concentration from the end of the fast to the end of the vegan diet period was significant in females ($p<0.001$).

Lactoferrin in serum was raised in 8 of 19 patients and the myeloperoxidase concentration was raised in 10 of 18 patients. After fasting there was a significant drop in the serum lactoferrin ($p<0.01$) and serum myeloperoxidase ($p<0.01$) levels. Lysozyme in serum was only elevated initially in 2 of 17 patients and only a slight although significant ($p<0.01$) decrease was seen after fasting, with a tendency towards restoration of the levels after the vegan diet (Fig. 2). The polymorphonuclear blood cell (PMN) count also showed a tendency to drop after fasting (Table I). However, after the period of vegan diet the PMN

Table I. *Values for erythrocyte sedimentation rate, polymorphonuclear blood cell count, and haptoglobin concentration in serum and cortisol excretion in urine are given before treatment, after the fasting period, and after the vegan diet period*

	ESR (mm/h)	PMN blood cell count (10^9/l)	Haptoglobulin (g/l)	Cortisol nmol/24 h urine
Before treatment	26±4 (7–56)	4.26±0.37 (2.00–7.80)	2.08±0.22	279±35 (72–610)
After treatment	21±4 (3–67)	3.69±0.44 (1.7–7.7)	1.49±0.23 [aaa]	185±20 (71–350)
After vegan diet	22±4 (2–61)	2.70±0.25 [bb] (1.6–5.1)	1.69±0.22 [b]	211±27 (120–470)

[a]Indicates the degree of significance for the changes during the fasting period; [b]during the whole treatment period; [c]during the vegan diet only. One symbol indicates $p<0.05$, two symbols $p<0.01$ and three symbols $p<0.001$.

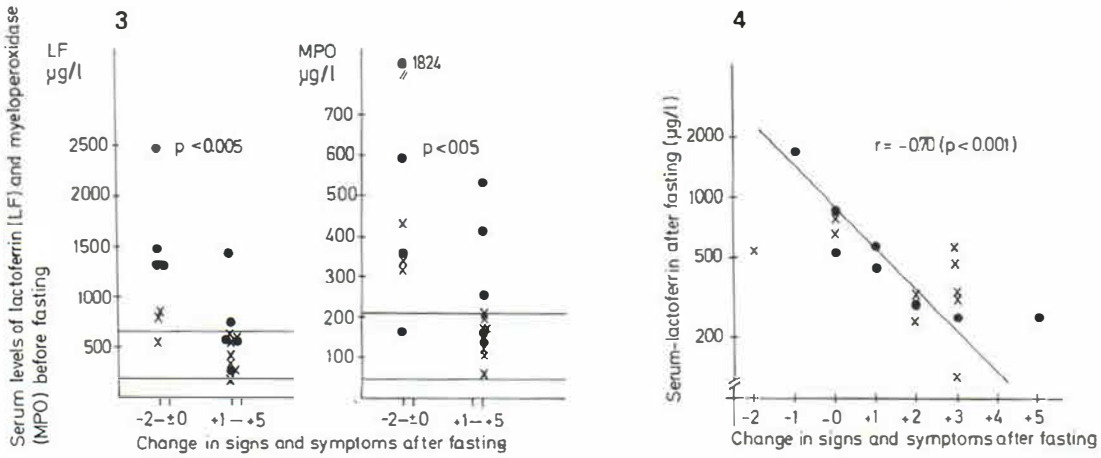

Fig. 3. Serum levels of lactoferrin and myeloperoxidase before fasting in the two subgroups who showed an improvement or an impairment of signs and symptoms (i.e. for the psoriasis patients with respect to subjective joint symptoms and for the other patients with respect to objective cutaneous symptoms). Filled symbols indicate patients with psoriasis with arthritis, x indicates patients with pustulosis palmaris et plantaris, rosacea, and atopic eczema. Statistical differences between the improved (+1 to +5) and impaired (−2 to ±0) subgroups are given in the figure.

Fig. 4. Serum lactoferrin concentrations after fasting as related to the degree of improved or impairment after 2 weeks of fasting in patients with psoriasis with arthritis (filled symbols) and in patients with cutaneous disease (x; see text to Fig. 3). The coefficient of correlation is given in the figure and the solid line indicates the linear regression line.

count had dropped to an even lower level and was significantly different ($p<0.01$) from the value before fasting.

The patients were allocated to one of two groups according to their type of reaction during the fast. In this allocation the arthritis was regarded as the predominant feature in the patients with psoriasis and the subjective evaluation of the arthritic condition was therefore used for these patients. For the other patients the objective evaluation of the cutaneous signs was used as a basis. The group of patients with improvement had lower pretreatment levels of lactoferrin and myeloperoxidase than those who were unchanged or worsened (Fig. 3). There was also a significant ($r=-0.70$, $p<0.001$) correlation between the serum lactoferrin levels after fasting and the alteration in signs and symptoms, which was most evident for patients with psoriatric arthritis (Fig. 4). No relationship between symptoms and the serum levels of the respective granulocyte-protein was discernible after the vegan diet.

Cortisol excretion in 24-h collections of urine tended to be lower after the fast (significant in women) and then increased somewhat to the end of the vegan diet period, but did not reach the admission values (Table I).

DISCUSSION

In this study, fasting undoubtedly relieved the pain in many patients with arthritis, and was also associated wtih a decrease in measurable signs of some dermatological diseases. In most cases the effect was temporary and as a rule the relief and improvement regressed during the vegan diet following fasting. There were some interesting exceptions, however. One patient with psoriasis and one with eczema were definitely improved after the whole

treatment period. In the patient with psoriasis this may have been due to the change to vegan diet, as she was the only subject who did not fast. It is of course less surprising that a patient with atopic eczema may improve after an change of diet, and such experience has been reported for children on an egg and milk exclusion diet (4).

Lactoferrin and possibly also myeloperoxidase is a protein which may serve as a specific marker of neutrophil turnover and/or activity in the blood. Lysozyme levels, however, probably reflect the activity and turnover of monocytes and macrophages and only to a lesser extent the turnover of neutrophil granulocytes. Our finding of high levels of neutrophil-derived proteins thus suggests an increased turnover and/or activity of neutrophils in many of the patients. The normal serum lysozyme levels indicate that the monocyte–macrophage activity was unaltered.

The decrease in neutrophil-derived proteins and in particular in lactoferrin levels in serum after fasting might suggest an altered neutrophil activity. However, a tendency towards a parallel drop in PMN counts during the same period suggests a more complex effect, probably also including effects on the turnover of neutrophils. Whatever the cause, there were some interesting relationships between the serum levels of lactoferrin and myeloperoxidase and the change in signs and symptoms after fasting. In those patients with initially high levels of neutrophil-proteins only a few experienced an improvement after fasting, in contrast to those patients with normal protein levels, in whom with few exceptions arthralgia was releived or cutaneous manifestations improved in connection with the period of fasting. The possible relationship between the degree of inflammation and the benefit of fasting was further emphasized by the highly significant correlation between the lactoferrin levels after fasting and the alteration in signs and symptoms. The results suggest that the possible beneficial effect of fasting is dependent on the degree of inflammation—in this study reflected by the neutrophil activity—involved in the patients disease process and that it might be possible to predict the outcome of such therapeutic regimes as fasting in the individual case. The average drop in lactoferrin levels during fasting was large. Hospitalization does not give rise to this type of change (unpublished results) and we therefore suggest that it is attributable to fasting.

Other variables reflecting inflammatory activity, such as the haptoglobin concentration in the serum, were also decreased as a consequence of fasting, but in contrast to lactoferrin they showed a tendency to return to pre-fast levels after the vegan diet. Thus fasting seems to have a fairly potent anti-inflammatory effect. The mechanism underlying the observed changes remains enigmatic, since it could not be explained by an increased cortisol production. In fact the cortisol excretion was significantly reduced among women during fasting.

The vegan menu was similar to one used at a popular Swedish health resort. Most patients, however, experienced the vegan diet used in this study as being too different from their habitual diet and very few tried to continue with any type of vegetarian diet after the end of the trial. During long-term studies it will be necessary to use a modified diet which will enable the patients to continue the regimen at home.

In conclusion, this pilot study has shown that many signs and symptoms are affected during a fast and that these changes are related to neutrophil leukocyte turnover as reflected in serum lactoferrin and myeloperoxidase. Clinical improvements seen during the fast vanished in most cases during treatment with the vegan diet. However, there were some patients who clearly seemed to benefit from the latter diet. Further studies should aim at defining the subgroups of patients, e.g. what patients with psoriasis and atopic eczema, who may be suited for this type of treatment. It is also important to investigate whether less pronounced dietary modifications than were applied in this study may change the clinical course of such disorders.

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