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Article *in* Journal of Pharmacy and Pharmacology · August 1997

DOI: 10.1111/j.2042-7158.1997.tb06099.x · Source: PubMed

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J. Pharm. Pharmacol. 1997, 49: 721–723
Received January 7, 1997
Accepted March 11, 1997

Effect of Chitosan on Renal Function in Patients with Chronic Renal Failure

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Abstract

The effects of chitosan have been investigated on eighty patients with renal failure undergoing long-term stable haemodialysis treatment.

The patients were tested after a control treatment period of 1 week. Half were fed 30 chitosan tablets (45 mg chitosan/tablet) three times a day. Ingestion of chitosan effectively reduced total serum cholesterol levels (from $10{\cdot}14 \pm 4{\cdot}40$ to $5{\cdot}82 \pm 2{\cdot}19$ mM) and increased serum haemoglobin levels (from $58{\cdot}2 \pm 12{\cdot}1$ to $68 \pm 9{\cdot}0$ g L^{-1}). Significant reductions in urea and creatinine levels in serum were observed after 4 weeks of chitosan ingestion. The feeling of physical strength, the appetite and the sleep of patients in the treatment group had improved significantly after 12 weeks of ingestion, compared with those of patients in the control group. During the treatment period, no clinically problematic symptoms were observed.

These data suggest that chitosan might be effective treatment for renal failure patients, although the mechanism of the effect should be investigated further.

Chitosan is a non-toxic natural polysaccharide of β-1,4-linked D-glucosamine residues. It is produced industrially by deacetylation of chitin obtained from crab and prawn shells (Muzzarelli 1977). Because it has good physiological adaptability it is used as a food additive and in medicinal materials, etc. Because chitosan is not hydrolysable by the digestive enzymes in man, and its chemical structure is similar to that of cellulose, it can be used as a new sort of dietary fibre. However, because it contains one amino group per residue, its cationic character might confer properties quite different from those of other dietary fibres. Most of its chemical functions are attributable to the amino group. Among them, the most noticeable dietary consideration is its adsorption of acidic metabolites such as uric acid and bile acid (Jing & Yamaguchi 1992; Yoshimoto et al 1995a, b). Its hypocholesterolaemic effect on healthy man has also been reported (Sugano et al 1978; Maezaki et al 1993).

This study is a preliminary investigation of the effects of chitosan on renal failure patients undergoing haemodialysis.

Materials and Methods

Test sample

Tablets containing chitosan with an average molecular weight of approximately 27 000 Da and a degree of deacetylation of 89% (Kitosan Shokuhin Kogyo) were administered orally to the test subjects. One chitosan tablet (140 mg) contained 45 mg chitosan and 75 mg dextran and yeast extract. The component-analysis data of the tablet are listed in Table 1.

Test subjects

The subjects of this investigation included 80 long-term stable haemodialysis patients (duration of dialysis > 13 months) consisting of 63 men and 17 women aged from 30 to 72 years. After a control treatment period of 1 week the 80 patients were divided into two groups, the treatment group and the control group, according to sexual distinction, age, dialysis duration and remaining renal function. There was no significant difference between the clinical parameters of the members of the groups (Table 2).

Before the start of the test, all the patients were well informed of the purposes, content and methods of the test, and were independently asked for their agreement to join the project. No patient was administered erythropoietin during the observation period. All of the patients tolerated the regular haemodialysis therapy using dialysate buffered with sodium bicarbonate or acetate.

Study protocol

Patients in the treatment group were administered chitosan orally and received 10 tablets, three times a day, for 12 weeks. Except for the ingestion of chitosan they were given the same therapy as the patients in the control group. All the patients were checked by the doctor at the hospital once every 4 weeks. At every visit their blood pressure, body weight and other nutrition indexes were measured; their blood was also examined for serum creatinine, blood urea nitrogen, serum lipids, haemoglobin, electrolytes, and other clinical parameters.

Statistical analysis

Values are expressed as means $\pm$ s.e.m. All data were analysed by the two-tailed Student t-test. P values of less than 0·05, compared with controls, were taken as indicative of statistical significance.

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Table 1. Composition (%) of chitosan tablet.

Moisture	6·3
Protein*	8·6
Fat	0
Ash	0·1
Chitosan†	31·9
Dextran	53·1

*Component of yeast extract. †MW range 2000–55 000 (average 27 000); viscosity 525 cP; deacetylation 89%.

Table 2. Initial mean parameters of the patients in the two groups.

Parameter group	Treatment group	Control
Age (years)	38	38
Amount of dialysis (months)	32	33
Lipid levels (mM)	10·14	8·50
Urea (mM)	7·5	8·2
Creatinine (mM)	100·1	119·0

Results

Effects of administration of chitosan on general clinical situation

After 12 weeks of chitosan ingestion, the proportions of the patients with improved appetite and sleep pattern in the treatment and control groups were 68% and 43%, respectively, and the proportions of the patients with improved physical strength were 80% and 13%, respectively. Patients who initially suffered from halitosis or itching reported improvements. During the period of ingestion of chitosan, three patients reported throat irritation and one reported bad itching all over. No other clinically problematic symptoms such as diarrhoea and constipation were observed.

Observation of the patients and the patients' reports indicated that chitosan ingestion alleviated uremic symptoms of patients in the treatment group during the test period.

Effects of the chitosan ingestion on the serum lipid levels

The values obtained for serum lipid concentrations during the test period are shown in Table 3.

After ingestion of chitosan for 12 weeks, the average total serum cholesterol level of the patients in the treatment group decreased significantly to $5{\cdot}82 \pm 2{\cdot}19$ mM from $10{\cdot}14 \pm 4{\cdot}40$ mM. A significant decrease in average serum lipoprotein level was also observed after 4 weeks of chitosan ingestion by the patients in the treatment group. Practically no change was observed in the serum high-density lipoprotein levels of patients in both groups. The triglyceride values tended to shift to a slightly lower level in the treatment group throughout the test period, however the differences were not significant between the two groups.

Effect of chitosan ingestion on serum haemoglobin level

The ingestion of chitosan resulted in a significant increase in the serum haemoglobin levels of patients in the treatment group after 4 weeks compared with patients in the control group. Serum haemoglobin levels for the treatment group increased from $58{\cdot}2 \pm 12{\cdot}1$ to $69{\cdot}3 \pm 11{\cdot}3$ g L^{-1} whereas the corresponding values for the control group were $59{\cdot}2 \pm 8{\cdot}4$ and $58{\cdot}4 \pm 9{\cdot}3$ g L^{-1}. The increased haemoglobin levels in the treatment group were maintained throughout the remainder of the test (Table 4).

Table 3. Effect of chitosan on lipid levels in serum.

Week	Treatment group	Control group	P*
Total cholesterol (mM)			
0	$10{\cdot}14 \pm 4{\cdot}40$	$8{\cdot}50 \pm 3{\cdot}05$	N.S.
4	$7{\cdot}31 \pm 2{\cdot}55$	$8{\cdot}95 \pm 3{\cdot}52$	N.S.
8	$7{\cdot}13 \pm 1{\cdot}65$	$9{\cdot}08 \pm 3{\cdot}28$	$<0{\cdot}05$
12	$5{\cdot}82 \pm 2{\cdot}19$	$7{\cdot}25 \pm 2{\cdot}63$	$<0{\cdot}05$
Lipoprotein a (mg L^{-1})			
0	1020 ± 334	1026 ± 408	N.S.
4	593 ± 410	796 ± 374	N.S.
8	335 ± 326	665 ± 411	$<0{\cdot}05$
12	377 ± 361	607 ± 464	$<0{\cdot}05$
High-density lipoprotein (mM)			
0	$1{\cdot}53 \pm 0{\cdot}52$	$1{\cdot}65 \pm 0{\cdot}60$	N.S.
4	$1{\cdot}83 \pm 0{\cdot}50$	$1{\cdot}72 \pm 0{\cdot}68$	N.S.
8	$1{\cdot}91 \pm 0{\cdot}61$	$1{\cdot}94 \pm 0{\cdot}40$	N.S.
12	$2{\cdot}02 \pm 0{\cdot}57$	$1{\cdot}81 \pm 0{\cdot}39$	N.S.
Triglyceride (mM)			
0	$3{\cdot}24 \pm 1{\cdot}82$	$3{\cdot}00 \pm 1{\cdot}95$	N.S.
4	$2{\cdot}95 \pm 2{\cdot}16$	$3{\cdot}35 \pm 1{\cdot}75$	N.S.
8	$2{\cdot}85 \pm 1{\cdot}79$	$2{\cdot}34 \pm 1{\cdot}15$	N.S.
12	$2{\cdot}06 \pm 0{\cdot}71$	$2{\cdot}22 \pm 0{\cdot}66$	N.S.

*$P < 0{\cdot}05$ indicates significant difference (n = 40). N.S. = not significant.

Table 4. Effect of chitosan on levels of haemoglobin and nitrogen metabolites in serum.

Week	Treatment group	Control group	P*
Haemoglobin (g L^{-1})			
0	$58{\cdot}2 \pm 12{\cdot}1$	$59{\cdot}2 \pm 8{\cdot}4$	N.S.
4	$69{\cdot}3 \pm 11{\cdot}3$	$58{\cdot}4 \pm 9{\cdot}3$	$<0{\cdot}05$
8	$67{\cdot}1 \pm 9{\cdot}4$	$59{\cdot}2 \pm 13{\cdot}5$	$<0{\cdot}05$
12	$68{\cdot}1 \pm 9{\cdot}0$	$58{\cdot}0 \pm 9{\cdot}0$	$<0{\cdot}05$
Urea (mM)			
0	75 ± 51	82 ± 82	N.S.
4	54 ± 19	79 ± 19	$<0{\cdot}05$
8	49 ± 20	78 ± 32	$<0{\cdot}05$
12	45 ± 19	75 ± 66	$<0{\cdot}05$
Creatinine (mM)			
0	$1{\cdot}001 \pm 0{\cdot}509$	$1{\cdot}198 \pm 0{\cdot}70$	N.S.
4	$0{\cdot}867 \pm 0{\cdot}261$	$1{\cdot}049 \pm 0{\cdot}565$	$<0{\cdot}05$
8	$0{\cdot}870 \pm 0{\cdot}223$	$1{\cdot}019 \pm 0{\cdot}462$	$<0{\cdot}05$
12	$0{\cdot}875 \pm 0{\cdot}227$	$1{\cdot}015 \pm 0{\cdot}283$	$<0{\cdot}05$

*$P < 0{\cdot}05$ indicates significant difference (n = 40). N.S. = not significant.

Effects of the chitosan ingestion on serum nitrogen metabolites

Compared with those of the control group, the average serum levels of urea and creatinine of the treatment group had decreased significantly after 4 weeks. In the succeeding period these levels were maintained until the end of the test period (Table 4).

During the investigation no differences were observed between the levels of serum electrolytes (Na, K, Cl, Ca and P), white blood corpuscles or serum uric acids of the two groups.

Furthermore, the mean body weights of each group did not change noticeably throughout the test period (data not shown).

Discussion

When 30 tablets/day containing 45 mg chitosan/tablet were given in the diet, the total serum cholesterol and lipoprotein levels of the patients were significantly reduced. Similar hypocholesterolaemic effects of chitosan on healthy bodies have been reported by Maezaki et al (1993) and Sugano et al (1978). In animal experiments many reports (Nagyvary et al 1978; Jeening et al 1988; Muzzarelli et al 1989; Maezaki et al 1993) confirm the cholesterol-lowering effect. According to these reports, it is clear that chitosan combines with bile acid in the digestive tract and that the product is excreted in the faeces, thereby reducing the body's cholesterol level. It is well known that hypercholesterolaemia often occurs in renal failure patients. As anti-lipid drugs, which reduce serum cholesterol, can induce side effects, aggressive treatment of hypercholesterolaemia patients with nephrotic syndrome has not yet been attempted. The effect of chitosan ingestion on serum cholesterol levels shown by the current study might be of great significance for the treatment of hypercholesterolaemia patients with nephrotic syndrome.

The ingestion of chitosan reduced serum urea and creatinine levels in patients in the treatment group. There are two possible explanations of this reduction of the levels of nitrogen metabolites: activation of remaining renal function for clearance of nitrogen metabolites, resulting in the depletion of urea and creatinine levels in the body; and combination of chitosan with nitrogen metabolites in the digestive tract then excretion of the products, thus reducing serum levels of nitrogen metabolites. The binding of urea, ammonium, and some acidic substances with chitosan have been reported (Nagyvary et al 1978; Jeening et al 1988; Muzzarelli et al 1989; Maezaki et al 1993), however, it is also reported that creatinine would not bind with chitosan in the in-vitro experiment. Reduction of serum creatinine levels could not be explained solely by binding with chitosan. It has been reported (Yoshimoto et al 1995a) that chitosan combines with some acidic substances suspected as uraemia toxins resulting in their excretion from the body and an improvement of remaining renal function. Because serum levels of urea and creatinine are important indicators of renal function, the lowering of these levels means that renal function has improved.

Another expression of improvement of renal function observed in the treatment group was the significant increase in serum haemoglobin levels without administration of human erythropoietin. The nephrotic syndrome is often associated with anaemia, reduction of the serum haemoglobin value. This form of anaemia is difficult to cure. Usually human erythropoietin is used for treatment of patients with anaemia nephrotic syndrome undergoing haemodialysis, but its administration must continue long-term with risks of many side-effects. The current results indicate a favourable effect on elevation of the level of serum haemoglobin.

For preventive and conservative treatment, the administration of chitosan might be a beneficial dietary supplement for renal failure patients.

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