

Lactobacillus casei strain Shirota (Yakult)

Research Update for Healthcare Professionals

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Lactobacillus casei strain Shirota – Research Update

IMPROVEMENT IN INTESTINAL HEALTH

1. A *Lactobacillus casei* Shirota probiotic drink reduces antibiotic-associated diarrhoea in patients with spinal cord injuries: a randomised controlled trial

Wong S *et al* (2013) *British Journal of Nutrition* 118:1-7.

Abstract

Certain probiotics may prevent the development of antibiotic-associated diarrhoea (AAD) and *Clostridium difficile*-associated diarrhoea (CDAD), but their effectiveness depends on both strain and dose. There are few data on nutritional interventions to control AAD/CDAD in the spinal cord injury (SCI) population. The present study aimed to assess the efficacy of consuming a commercially produced probiotic containing at least 6.5 billion live *Lactobacillus casei* Shirota (LcS) in reducing the incidence of AAD/CDAD, and whether undernutrition and proton pump inhibitors (PPI) are risk factors for AAD/CDAD. A total of 164 SCI patients (50.1 (SD 17.8) years) with a requirement for antibiotics (median 21 d, range 5–366) were randomly allocated to receive LcS (n 76) or no probiotic (n 82). LcS was given once daily for the duration of the antibiotic course and continued for 7 days thereafter. Nutritional risk was assessed by the Spinal Nutrition Screening Tool. The LcS group had a significantly lower incidence of AAD (17.1 v. 54.9%, P 0.001). At baseline, 65% of patients were at undernutrition risk. Undernutrition (64.1 v. 33.3%, P 0.01) and the use of PPI (38.4 v. 12.1%, P 0.022) were found to be associated with AAD. However, no significant difference was observed in nutrient intake between the groups. The multivariate logistic regression analysis identified poor appetite (1/2 meals eaten) (OR 5.04, 95% CI 1.28, 19.84) and no probiotic (OR 8.46, 95% CI 3.22, 22.20) as the independent risk factors for AAD. The present study indicated that LcS could reduce the incidence of AAD in hospitalized SCI patients. A randomised, placebo-controlled study is needed to confirm this apparent therapeutic success in order to translate into improved clinical outcomes.

2. Role of probiotic in preventing acute diarrhoea in children: a community-based, randomized, double-blind placebo-controlled field trial in an urban slum.

Sur D *et al* (2011) *Epidemiology and Infection* 139: 919-926.

Abstract

Acute diarrhoea remains a major public health challenge in developing countries. We examined the role of a probiotic in the prevention of acute diarrhoea to discover if there was an effect directed towards a specific aetiology. A double-blind, randomized, controlled field trial involving 3758 children aged 1-5 years was conducted in an urban slum community in Kolkata, India. Participants were given either a probiotic drink containing *Lactobacillus casei* strain Shirota or a nutrient drink daily for 12 weeks. They were followed up for another 12 weeks. The primary outcome of this study was the occurrence of first episodes of diarrhoea. We assessed this during 12 weeks of intake of study agent and also for 12 weeks of follow-up. There were 608 subjects with diarrhoea in the probiotic group and 674 subjects in the nutrient group during the study period of 24 weeks. The level of protective efficacy for the probiotic was 14% (95% confidence interval 4-23, $P < 0.01$ in adjusted model). The reduced occurrence of acute diarrhoea in the probiotic group compared to nutrient group was not associated with any specific aetiology. No adverse event was observed in children of either probiotic or nutrient groups. The study suggests that daily intake of a probiotic drink can play a role in prevention of acute diarrhoea in young children in a community setting of a developing country.

3. Effect of *Lactobacillus casei* Shirota on colonic transit time in patients with chronic constipation

Krammer HJ *et al* (2011) *Coloproctology* **33**: 109-113.

Abstract

Background. Slow-transit constipation (STC) is caused by a motility disorder of the colon which leads to delayed transit (>72 h). The probiotic strain *Lactobacillus casei* Shirota (LcS) has been shown to improve constipation-related symptoms, such as stool frequency and consistency. A randomized double-blind placebo-controlled trial was performed to determine the effect of LcS on the colonic transit time in patients with STC.

Patients and methods. Colonic transit time of all consecutive outpatients with chronic constipation was determined by the Hinton test using radiopaque markers. Patients with a transit time longer than 72 h were included in the study. A total of 24 patients received either a dairy drink containing 6.5×10^9 colony forming units (cfu) of LcS or a placebo daily for 4 weeks. General gastrointestinal symptoms were evaluated weekly by a questionnaire and the measurement of colonic transit time was repeated after the intervention.

Results. The intake of LcS resulted in a significant acceleration of the total colonic transit time from 95.6 h to 76.5 h ($p=0.05$). This effect was most pronounced in the sigmoid and rectum transit time ($p < 0.007$). no statistically significant change in the total colonic transit time was observed (before: 95.8 h, after: 87.1 h, $p=0.282$) In the placebo group.

Conclusion. The daily intake of a probiotic drink containing LcS significantly reduced the colonic transit time in patients with STC.

4. Probiotic beverage containing *Lactobacillus casei* Shirota improves gastrointestinal symptoms in patients with chronic constipation.

Koebnick C, Wagner I, Leitsmann P, Stern U, Zunfit HJF (2003) *Canadian Journal of Gastroenterology* 17(11): 655-659.

Summary

BACKGROUND:

The aim of the present study was to investigate the effect of a probiotic beverage on gastrointestinal symptoms in patients with chronic constipation.

METHODS:

A double-blind, placebo-controlled, randomized study was conducted over a four-week period in patients with symptoms of chronic constipation (n=70). To all patients, 65 mL/day of a probiotic beverage containing *Lactobacillus casei* Shirota (LcS) or a sensorially identical placebo was administered. Patients completed a questionnaire on gastrointestinal symptoms, well-being and stool habits and underwent a medical examination weekly. Severity of constipation, flatulence and bloating was summarized into four categories (severe, moderately severe, mild and no symptoms).

RESULTS:

The consumption of LcS resulted in a significant improvement in self-reported severity of constipation and stool consistency, starting in the second week of the intervention phase ($P < 0.0001$). Severe and moderately severe constipation was observed less in the LcS group. The occurrence and degree of flatulence or bloating sensation did not change. In the final examination, 89% of the LcS group and 56% of the placebo group showed a positive effect of their beverage on constipation ($P = 0.003$). No adverse reactions were reported.

CONCLUSIONS:

The results indicate a beneficial effect on gastrointestinal symptoms of patients with chronic constipation. The administration of probiotic foodstuffs may be recommended as an adjunctive therapy of chronic constipation.

5. Fermented milk containing *Lactobacillus casei* strain Shirota reduces incidence of hard or lumpy stools in healthy population.

Sakai T *et al* (2011) *Int. J. Food Sci. Nutr.* 62(4): 423-430.

Abstract

The objective of the present study was to investigate the efficacy of fermented milk containing *Lactobacillus casei* strain Shirota (LcS) in a healthy population. Healthy subjects with Bristol Stool Form Scale (BS) score < 3.0 were randomized to fermented milk treatment for 3 weeks or non-intervention control. The primary endpoint was the proportion of subjects that produced hard or lumpy stools (HLS) $\geq 25\%$ of bowel movements (H-HLS). Secondary endpoints included changes in BS score, constipation-related symptom scores and stool parameters. Efficacy was analyzed in 39 subjects. After

3 weeks of treatment the proportion of H-HLS subjects had significantly decreased from 73.7% to 36.8%, whereas in the control group the proportion had increased from 75.0% to 85.0% during the same period ($P = 0.002$). The BS score was significantly improved after the treatment compared with the control ($P < 0.001$). In conclusion, daily consumption of fermented milk containing LcS reduced the incidence of HLS.

6. Effect of the continuous intake of probiotic-fermented milk containing *Lactobacillus casei* strain Shirota on fever in a mass outbreak of norovirus gastroenteritis and the faecal microflora in a health service facility for the aged.

Nagata S *et al* (2011) *Brit J Nutr* 1(8): 1-8.

Abstract

For conducting effective risk management in long-stay elderly people at a health service facility, an open case-controlled study was performed to evaluate the effect of the intake of probiotic-fermented milk containing *Lactobacillus casei* strain Shirota (LcS-fermented milk) on norovirus gastroenteritis occurring in the winter season during the intake period. A total of seventy-seven elderly people (mean age 84 years) were enrolled in the study. During a 1-month period, there was no significant difference in the incidence of norovirus gastroenteritis between the LcS-fermented milk-administered (n 39) and the non-administered (n 38) groups; however, the mean duration of fever of $>37^{\circ}\text{C}$ after the onset of gastroenteritis was 1.5 (SD 1.7) d in the former and 2.9 (SD 2.3) d in the latter group, showing a significant shortening in the former group ($P < 0.05$). RT-quantitative PCR analysis targeting ribosomal RNA showed both Bifidobacterium and Lactobacillus to be significantly dominant, whereas Enterobacteriaceae decreased in faecal samples from the administered group (n 10, mean age 83 years), with a significant increase in faecal acetic acid concentration. Continuous intake of LcS-fermented milk could positively contribute to the alleviation of fever caused by norovirus gastroenteritis by correcting the imbalance of the intestinal microflora peculiar to the elderly, although such consumption could not protect them from the disease.

7. Probiotic effects on intestinal fermentation patterns in patients with irritable bowel syndrome.

Barrett JS, Canale KEK, Garry RB, Irving PM, Gibson PR (2008) *World Journal of Gastroenterology* 14(32):5020-5024.

Summary

AIM:

To determine whether *Lactobacillus casei* strain Shirota (Yakult) can alter small intestinal bacterial overgrowth (SIBO), as tested by the lactulose breath test, and whether this is associated with changes in symptoms in irritable bowel syndrome (IBS).

METHODS:

18 patients with IBS (Rome II criteria), who showed an early rise in breath hydrogen with lactulose (ERBHAL), consumed 65 mL of Yakult daily for 6 wk. Lactulose breath test was repeated at the end of the treatment period. Symptoms were recorded daily using a 10 cm visual analogue scale.

RESULTS:

14 patients completed the study, 9 (64%) had reversal of ERBHAL, with the median time of first rise in breath hydrogen increasing from 45 to 75 min ($P = 0.03$). There was no significant improvement in the symptom score with probiotic therapy, except for wind ($P = 0.04$). Patients commencing with at least moderate symptoms and who no longer had ERBHAL at the end of treatment, showed improvement in the overall symptoms scores [median final score 5.3 (IQR 3.9-5.9), 55% reduction; $n = 6$] to a greater extent than those who had had persisting ERBHAL [final score 6.9 (5.0-7.0), 12% reduction; $n = 5$; $P = 0.18$].

CONCLUSION:

Yakult is effective in altering fermentation patterns in the small bowel, consistent with reducing SIBO. The loss of ERBHAL was associated with reduced symptoms. The true interpretation of these findings awaits a randomised, controlled trial.

8. Beneficial effects of *Lactobacillus casei* in ulcerative colitis: a pilot study.

Mitsuyama K, Matsumoto S, Yamasaki H, Masuda J, Kuwaki K *et al* (2008) *Journal of Clinical Biochemistry & Nutrition* 43 (Suppl 1):78-81.

Summary

Objective

To investigate the therapeutic effects of *Lactobacillus casei* Shirota (LcS) on patients with ulcerative colitis (UC).

Methods

In an open-label trial, ten patients with mild to moderately active UC (determined by the Truelove & Witts criteria) consumed a daily probiotic milk drink containing LcS (8 x 10¹⁰) for eight weeks in conjunction with conventional therapy (aminosalicylates and/or prednisolone). Changes in the clinical status of patients were measured by a clinical activity index score at baseline and at two week intervals, which measured several aspects of disease (episodes of diarrhoea, nocturnal diarrhoea, visible faecal blood, abdominal pain or cramping, general wellbeing, abdominal tenderness, need for anti-diarrhoeal medication). The physicians taking these measurements were blinded to the treatment regime of the patients.

The control group consisted of nine previously treated patients with active UC whose baseline characteristics were similar to the study group and had previously received conventional therapy but not a probiotic.

In addition, the effect of heat-treated LcS on IL-6 production was assessed in vitro in samples of lipopolysaccharide stimulated peripheral blood mononuclear cells (PBMC) from patients with active UC.

Results

Compared to the control group, probiotic consumption was associated with significantly improved clinical activity index scores after four weeks ($P = 0.033$), six weeks ($P = 0.026$) and eight weeks ($P = 0.012$). When compared to pre-treatment clinical activity index scores, a trend for improved clinical status was observed in the probiotic group but not in the control group at six weeks ($P = 0.010$) and eight weeks ($P = 0.035$). The probiotic was well tolerated and no adverse effects were reported.

In vitro tests showed that LcS inhibited IL-6 production in PBMC of UC patients.

Conclusions

The data indicate that supplementing conventional UC therapy with *Lactobacillus casei* Shirota is safe and more effective in achieving clinical improvement of active UC compared to conventional treatment alone.

The probiotic mechanism of activity may involve inhibition of IL-6 signalling since this cytokine is thought to promote intestinal inflammation.

These findings need to be confirmed in a larger, randomised controlled trial.

9. Effect of frequent consumption of a *Lactobacillus casei*-containing milk drink in *Helicobacter pylori*-colonized subjects.

Cats A, Kuipers EJ, Bosscherts MAR, Pot RGJ, Vandenbroucke-Grauls CMJE, Kusters JG (2003) *Alimentary Pharmacology and Therapeutics* 17(3):429-435.

Summary

BACKGROUND:

Several studies have reported inhibitory effects of lactic acid bacteria on bacterial pathogens.

AIM:

To test whether a drink containing *Lactobacillus casei* strain Shirota inhibits *Helicobacter pylori* growth.

METHODS:

The in vitro growth inhibition of *H. pylori* was studied when *L. casei* was added to plates previously inoculated with *H. pylori* reference strain NCTC 11637. In an intervention study, 14 *H. pylori*-positive subjects were given Yakult drink (10(8) colony-forming units/mL *L. casei*) thrice daily during meals for 3 weeks. Six untreated *H. pylori*-positive subjects served as controls. *H. pylori* bacterial loads were determined using the 13C-urea breath test, which was performed before and 3 weeks after the start of *L. casei* supplementation.

RESULT:

In vitro, *L. casei* inhibits *H. pylori* growth. This effect was stronger with *L. casei* grown in milk solution than in DeMan-Rogosa-Sharpe medium. No growth inhibition was shown with medium inoculated with lactic acid, *Escherichia coli* strain DH5alpha or uninoculated medium. Filtration of *L. casei* culture before incubation with *H. pylori* completely abolished the inhibitory effect. Urease activity decreased in nine of the 14 (64%) subjects with *L. casei* supplementation and in two of the six (33%) controls (P = 0.22).

CONCLUSIONS:

Viable *L. casei* are required for *H. pylori* growth inhibition. This does not result from changes in lactic acid concentration. In addition, a slight, but non-significant, trend towards a suppressive effect of *L. casei* on *H. pylori* in vivo may exist.

IMMUNE-MODULATION

1. Immunomodulatory effects of a probiotic drink containing *Lactobacillus casei* Shirota in healthy older volunteers.

Dong H *et al* (2013) *Eur J Nutr* Jan 10.

Abstract

PURPOSE:

There is growing evidence that probiotics confer health benefits to the host by modulating immune function, especially in older people, where immunosenescence is a feature even of healthy ageing. The aim of this study was to investigate the effect of a probiotic drink containing *Lactobacillus casei* Shirota (LcS) on immune function in a healthy non-immunocompromised older population.

METHODS:

Thirty healthy old volunteers were recruited into a randomized placebo-controlled, single-blind crossover study. The volunteers were supplemented with the probiotic drink containing 1.3×10^{10} CFU LcS or skimmed milk per day for 4 weeks, followed by 4 weeks of washout and were crossed over to the other treatment. Peripheral blood and saliva samples were collected at baseline and end of each treatment.

RESULTS:

Probiotic consumption was associated with a significant increase in natural killer (NK) cell activity relative to baseline and a significant decrease in the mean fluorescence intensity of CD25 expression in the resting T cells compared with placebo. Additionally, there was a trend towards an increased ratio of IL-10 to IL-12 relative to baseline after LcS intake.

CONCLUSIONS:

Consumption of a probiotic drink containing LcS improved NK cell activity and tended to produce a more anti-inflammatory cytokine profile in an older population.

2. Daily intake of *Lactobacillus casei* Shirota increases natural killer cell activity in smokers.

Reale M *et al* (2012) *Brit J Nutr* 108(2): 308-14.

Abstract

Dietary probiotics supplementation exerts beneficial health effects. Since cigarette smoking reduces natural killer (NK) activity, we evaluated the effect of *Lactobacillus casei* Shirota (LcS) intake on NK cytotoxic activity in male smokers. The double-blind, placebo-controlled, randomised study was conducted on seventy-two healthy Italian blue-collar male smokers randomly divided for daily intake of LcS powder or placebo. Before and after 3 weeks of intake, peripheral blood mononuclear cells were isolated and NK activity and CD16⁺ cells' number were assessed. Daily LcS intake for 3 weeks significantly increased NK activity ($P < 0.001$). The increase in NK activity was paralleled by an increase in CD16⁺ cells ($P < 0.001$). Before intake, NK cytotoxic activity inversely correlated with the number of cigarettes smoked ($R = -0.064$). LcS intake prevented the smoke-dependent expected NK activity reduction. The analysis of the distribution of changes in smoke-adjusted NK activity demonstrated that the positive variations were significantly associated with LcS intake, while the negative variations were associated with placebo intake (median value of distributions of differences, 20.98 lytic unit (LU)/10⁷ cells for LcS v. - 4.38 LU/10⁷ cells for placebo, $P = 0.039$). In conclusion, 3 weeks of daily LcS intake in Italian male smokers was associated with a higher increase in cytotoxic activity and CD16⁺ cells' number in comparison to the placebo intake group.

3. Daily Probiotic's (*Lactobacillus casei* strain Shirota) Reduction of Infection Incidence in Athletes

Gleeson M *et al* (2011) *International Journal of Sport Nutrition and Exercise Metabolism* 21(1): 55-64.

Abstract

The purpose of this study was to examine the effects of a probiotic supplement during 4 mo of winter training in men and women engaged in endurance-based physical activities on incidence of upper respiratory-tract infections (URTIs) and immune markers. Eighty-four highly active individuals were randomized to probiotic ($n = 42$) or placebo ($n = 42$) groups and, under double-blind procedures, received probiotic (PRO: *Lactobacillus casei* Shirota [LcS]) or placebo (PLA) daily for 16 wk. Resting blood and saliva samples were collected at baseline and after 8 and 16 wk. Weekly training and illness logs were kept. Fifty-eight subjects completed the study ($n = 32$ PRO, $n = 26$ PLA). The proportion of subjects on PLA who experienced 1 or more weeks with URTI symptoms was 36% higher than those on PRO (PLA 0.90, PRO 0.66; $p = .021$). The number of URTI episodes was significantly higher ($p < .01$) in the PLA group (2.1 ± 1.2) than in the PRO group (1.2 ± 1.0). Severity and duration of symptoms were not significantly different between treatments. Saliva IgA concentration was higher on PRO than PLA, significant treatment effect $F(1, 54) = 5.1$, $p = .03$; this difference was not evident at baseline but was significant after 8 and 16 wk of supplementation. Regular ingestion of LcS appears to be beneficial in reducing the frequency of URTI in an athletic cohort, which may be

related to better maintenance of saliva IgA levels during a winter period of training and competition.

4. Effects of a fermented milk drink containing *Lactobacillus casei* strain Shirota on the human NK- cell activity.

Takeda K and Okumura K (2007) *The Journal of Nutrition* Suppl 137:791S–793S.

Abstract

Nine healthy middle-aged and 10 elderly volunteers drank fermented milk containing 4 x 10¹⁰(10) live cells of *Lactobacillus casei* strain Shirota daily for 3 wk, and their natural killer (NK) activity and other immunological functions were examined. In the experiments with middle-aged volunteers, NK activity significantly increased (P<0.01) 3 wk after the start of intake, elevated NK cell activity remained for the next 3 wk, and this effect was particularly prominent in the low-NK-activity individuals. In the experiments with elderly volunteers, NK activity significantly decreased (P<0.01) in the control group 3 wk after the start of intake; however, the intake of *Lactobacillus casei* strain Shirota maintained the NK activity. These results suggest that daily intake of *Lactobacillus casei* strain Shirota provides a positive effect on NK-cell activity.

CANCER

1. Probiotics as efficient immunopotentiators: Translational role in cancer prevention

Shida K and Nomoto K (2013) *Indian J Med Res* 139:808-819.

Abstract

Accumulating evidences indicate that some diseases are triggered by abnormalities of the gut microbiota. Among these, immune-related diseases can be the promising targets for probiotics. Several studies have proved the efficacy of probiotics for preventing such diseases including cancers, infections, allergies, inflammatory bowel diseases and autoimmune diseases. *Lactobacillus casei* strain Shirota (LcS) is one of the most popular probiotics, benefits of which in health maintenance and disease control have been supported by several science-based evidences. This review summarizes human clinical trials with this probiotic against cancer development and also discusses the possible immunomodulatory mechanisms by which LcS exerts anti-cancer activity.

2. Probiotic Beverage with Soy Isoflavone Consumption for Breast Cancer Prevention: A Case-control Study

Toi M et al (2013) *Curr Nutr Food Sci* 9(3):194-200.

Abstract

The purpose of this study is to evaluate how beverages containing *Lactobacillus casei* Shirota (BLS) and soy isoflavone consumption since adolescence affected the incidence of breast cancer. In a population-based case-control study, three hundred and six cases with breast cancer and 662 controls aged 40 to 55 were matched for age and residential

area and included in the analyses. Diet, lifestyle and other breast cancer risk factors were investigated using the self-administered questionnaire and interview. Odds ratios (ORs) of BLS and soy isoflavone consumption for breast cancer incidence were independently and jointly estimated using a conditional logistic regression. The ORs of BLS consumption (\geq four times a week against $<$ four times a week) was 0.65 and statistically significant ($p = 0.048$). The analysis of association between soy consumption and breast cancer incidence showed the more the isoflavone consumption is, the lower the odds of breast cancer becomes. Adjusted ORs for breast cancer in the second, the third and the fourth quartiles of soy consumption against the first quartile were 0.76, 0.53 and 0.48, respectively (trend test, $p = 0.0002$). The BLS-isoflavone interaction was not statistically significant; however, a biological interaction was suggested. Regular consumption of BLS and isoflavones since adolescence was inversely associated with the incidence of breast cancer in Japanese women.

3. Randomized trial of dietary fiber and *Lactobacillus casei* administration for prevention of colorectal tumours.

Ishikawa H, Akedo I, Otani T, Suzuki T, Nakamura T *et al* (2005) *International Journal of Cancer* 116:762-767.

Abstract

The epidemiologic evidence that dietary fiber protects against colorectal cancer is equivocal. No large-scale clinical study of the administration of *Lactobacillus casei* has been reported. We examined whether dietary fiber and *L. casei* prevented the occurrence of colorectal tumors. Subjects were 398 men and women presently free from tumor who had at least 2 colorectal tumors removed. Subjects were randomly assigned to 4 groups administered wheat bran, *L. casei*, both or neither. The primary end point was the presence or absence of new colorectal tumor(s) diagnosed by colonoscopy after 2 and 4 years. Among 380 subjects who completed the study, 95, 96, 96 and 93 were assigned to the wheat bran, *L. casei*, both and no treatment groups, respectively. Multivariate adjusted ORs for occurrence of tumors were 1.31 (95% CI 0.87-1.98) in the wheat bran group and 0.76 (0.50-1.15) in the *L. casei* group compared to the control group. There was a significantly higher number of large tumors after 4 years in the wheat bran group. The occurrence rate of tumors with a grade of moderate atypia or higher was significantly lower in the group administered *L. casei*. No significant difference in the development of new colorectal tumors was observed with administration of either wheat bran or *L. casei*. However, our results suggest that *L. casei* prevented atypia of colorectal tumors.

4. *Lactobacillus casei* strain Shirota and prevention of recurrence of bladder cancer.

Naito S (2008) *International Journal of Probiotics and Prebiotics* 3(3):163-164.

Abstract

Although superficial bladder cancer can be successfully treated by a transurethral resection (TUR), the high frequency of intravesical recurrence remains a concern. *Lactobacillus casei* (LC) preparation, a powdered preparation containing about 1×10^{10} cells of LC strain Shirota per gram, has been safely used as a probiotic agent for more than 30

years in Japan. When orally administered, LC preparation has been reported to act as an immunomodulator and to potentiate antitumor responses in mice. Based on these reports, two randomized, controlled clinical trials have been conducted, and the oral administration of LC preparation has shown to be a safe and effective modality not only as monotherapy, but also as a combination therapy with intravesical instillation chemotherapy, for preventing recurrence after TUR of superficial bladder cancer. Furthermore, a case-control study has also been conducted and the habitual intake of LC preparation was shown to reduce the risk of bladder cancer. Thus, LC preparation is considered to be effective for preventing not only the occurrence, but also recurrence after TUR of superficial bladder cancer.

5. Preventive effect of a *Lactobacillus casei* preparation on the recurrence of superficial bladder cancer in a double blind trial.

Aso Y, Akaza H, Kotake T, Tsukamoto T, Imai K *et al* (1995) *European Urology* 27:104-109.

Abstract

A double-blind trial was conducted in 138 patients with superficial transitional cell carcinoma of the bladder following transurethral resection to evaluate the prophylaxis of recurrence by an oral *Lactobacillus casei* preparation (BLP). Patients were stratified into the following 3 subgroups: (A) with primary multiple tumors; (B) with recurrent single tumors, and (C) with recurrent multiple tumors. In each group, patients were randomly allocated to receive BLP or placebo. BLP showed a better prophylactic effect in subgroups A and B than placebo, whereas no significant difference was observed in subgroup C. Cox multivariate analysis showed that the outcome with BLP was significantly better than with placebo ($p = 0.01$). Slight and tolerable adverse reactions occurred in 3 patients receiving BLP and in 3 of the placebo-treated patients. Oral administration of BLP was thus safe and effective for preventing recurrence of superficial bladder cancer.