## CONTINUING MEDICAL EDUCATION

# LACTOBACILLUS THERAPY

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For years, milk enriched with *Lactobacillus acidophilus* or lactobacillus preparations have been marketed. It was believed that repopulation of colonic bacterial flora with lactobacillus would enhance the digestion of dietary lactose and provide protection against milk intolerance in individuals with lactase deficiency. However, studies have failed to show any reduction in lactose intolerance with the use of sweet acidophilus milk or lactobacillus preparation(1,2). If that be so, is there any justification to consume milk supplemented with lactobacillus or its preparation?

### Characteristic Features of Lactobacillus

Lactobacillus are common commensal parasites of vertebrate and invertebrate animals and also occur widely as saprophytes in fermenting animal and vegetable matter, *e.g.*, souring milk, cheese and silage. The bacilli are Gram positive rod-shaped bacteria (1 to 5 $\mu$m × 1.0 $\mu$m) and commonly occur in pairs inline and in short chains, that are nonsporing, non-motile, either facultatively or strictly anaerobic, strongly acid-producing (acidogenic) by fermentation of carbohydrates, and exceptionally capable of survival and growth under acid conditions (acidure)(3).

Lactobacillus form a major part of the normal commensal flora of the mouth, stomach, small intestine and large intestine and vagina and are present in large number in feces. Within the first 2 to 3 days after birth the alimentary canal of a newborn infant is colonized with lactobacilli, probably derived from its mother's vagina, mouth and intestine. The bacilli are present in the range $10^6$ to $10^{10}$ per ml of fluid contents throughout life except for periods where certain antibiotics are given by mouth. The numbers of lactobacillus are higher when the diet is rich in cereals and sugars than when it is deficient in these and rich in protein. A variety of species are present, the commonest usually being *Lactobacillus acidophilus*. They are responsible for dental caries and subacute bacterial endocarditis in man. But, lactobacillary flora of the intestine and vagina also have a beneficial, protective effect in tending to inhibit colonization by potentially harmful organisms. The lactobacilli have complex nutritional requirements and the different species differ in the range of aminoacids and vitamins required. All species ferment glucose and most ferment lactose, maltose and sucrose. In fermenting glucose and other sugars, all the species form only lactic acid, whilst *Lacto. fermenti* and

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*Lacto. brevis* form acetic acid, formic acid, ethanol, $CO_2$ and other products as well as lactic acid(3). The various species of lactobacilli are *Lacto. acidophilus, Lacto. bulgaricus, Lacto. helveticus, Lacto. lactis, lacto. plantarum, Lacto. fermenti and Lacto. brevis*(3).

Human milk contains a 'growth factor' which facilitates intestinal colonization by *Lactobacillus bifidus*(4). *Lactobacillus bifidus* is therefore, the predominant intestinal commensal organism in breastfed infants, of whose fecal flora it may form as much as 99%. It is associated with a highly acidic reaction in the stools (pH 5.0 to 5.5)(3). The intestinal flora of infants fed human milk may protect them against infections caused by *E. coli*(4). *Lacto. bifidus* is present less regularly and in smaller numbers in the mixed flora of the feces of bottle-fed infants, in which *Lacto. acidophilus* is usually predominant(3). Bifidus which is present in breast fed infants should not be confused with other lactobacillus like *Lacto. acidophilus, Lacto. sporogenes, Lacto. lactis, etc.* Recent studies have suggested that the organism is not a true lactobacillus but is more closely related to the *corynebacterium* group. It has been suggested that the organism (*Lacto. bifidus*) should be called *Bifidobacterium bifidus*(3).

**Claims by the Manufacturers**

Many drug manufacturers have published beneficial activities of lactobacillus preparations, its use as a prophylactic and curative agent and contraindications and side effects(5). Lactobacillus preparations containing *Lacto. acidophilus, Lacto. sporogenes,* and *Lacto. lactis* are available with or without other drugs in the market (*Table I*). It is, therefore, worthwhile to review the role of lactobacillus as a medicine in general practice.

1. *Beneficial Activities*

(*a*) Aids synthesis of B-complex factors, vitamin K and many enzymes, which help in digestion of proteins, carbohydrates and fats.

(*b*) Raises overall immune status of the host bacteria against harmful microorganism.

(*c*) Corrects biological and metabolic alterations in the host as it strengthens the normal intestinal flora.

(*d*) Produces abundant lactic acid and by competitive inhibition prevents the emergence of resistant strains and development of superinfection.

(*e*) Produces abundant lactic acid and lowers the pH which decreases ammonia production in the gut, decreases ammonia absorption from gut and facilitates ammonia excretion from blood into gut in hepatic precoma and coma.

2. *Indications*

(*a*) As an adjuvant to antibiotic therapy.

(*b*) In the treatment of gastrointestinal problems caused by disturbance of normal intestinal flora such as seasonal diarrhea, infantile diarrhea, food intoxication, idiopathic constipation, indigestion, gaseous distension and anocutaneous manifestations.

(*c*) Hypochlorhydria and achlorhydria.

(*d*) After anti-amebic treatment.

(*e*) Aphthous stomatitis.

(*f*) Hepatitis, hepatic precoma and coma.

(*g*) Bowel surgery.

(*h*) Weight stimulation of infants and children.

**TABLE I**-*Various Preparations Available Containing Lactobacillus*

| S. No. | Drug group | Name of drug | Name of company | Indications (as claimed by the manufacturers) |
|---|---|---|---|---|
| 1. | Oral rehyration therapy | Emlyte -S | M.M. Labs. | Electrolyte and glucose imbalance following dehydration and all disturbed ecological balance of intestinal tract. |
| 2. | Vitamins | Vizylac | Unichem | Imbalanced intestinal flora due to antibiotics and chemotherapy |
| | | Vizylac dry powder | Unichem | -do- |
| | | Nutrolin B | Cipla | Bacillus (as adjunct to antibiotic therapy, apthous stomatitis, infantile diarrhea, thrust, acne. |
| | | Lactisyn | Franco-Indian | Aphthous stomatitis, hypochlorhydria, hepatic encephalopathy, adjuvant antibiotic therapy, diarrhea, used both as prophylactic and curative. |
| | | Sporlac | Sankyo Co. Ltd. | Diarrhea, hepatic precoma and coma, aphthous stomatitis, after antiemetic treatment. |
| | | Lacto-bacil | Gujarat Drug and Chemical Ltd. | As an adjuvant to antibiotic therapy, when normal intestinal flora is disturbed due to seasonal diarrhea, food intoxication, idiopathic constipation, *etc.* |
| 3. | Antibiotics | Penplus kid tablets | Systopic Lab. Pvt. Ltd. | A well accepted antibiotic combination with the added advantages of lactobacillus. |
| | | Penplus capsule | Systoptic Lab. Pvt. Ltd. | -do- |
| | | Synthopen kid tablets | Synthiko | Infections susceptible to ampicillin with minimal gastrointestinal side effects. |
| | | Synthopen capsule | Synthiko | Same |

3. *Contraindications*

Individuals allergic to milk or sensitive to lactose

4. *Adverse reactions/Side effects*

Anorexia, nausea, metabolic acidosis, neurological manifestations

**Conditions in which Lactobacillus Preparations Have Been Used Recently**

**Lactose Intolerance**

It is seen that milk treated with lactose enzyme, lactose hydrolysed milk and sweet acidophilic milk results in good carbohydrate absorption and diminishes symptoms of discomfort in lactose malabsorbers(6). If lactose hydrolysis at the brush border is incomplete, the sugar accumulates in the distal intestinal lumen, where lactic acid and hydrogen gas is produced(4). But acidophilus enriched milk did not reduce breath hydrogen production or decrease symptoms in lactose malabsorbers immediately or after a week of daily ingestion. Hence, it is not a suitable milk substitute in patients of lactose intolerance. On the contrary, it is advisable to remove milk from the diet. Adequate nutrition should be maintained using foods such as cereals and meat which are free from lactose(4).

**Diarrhea**

The treatment or prevention of diarrheal diseases by lactobacillus have met with varying degree of success and failures. It is reported that *Lacto. acidophilus* preparation is useful in the treatment of chronic diarrhea as it will promote the growth of saprophytic flora and will alter the intestinal pH(7). Niv *et al.* reported some beneficial results in treating infantile diarrhea with lactobacillus(8). On the other hand Pozo *et al.*(9) concluded that ingestion of lactobacillus for one week did not reduce the duration of acute diarrhea but on the other hand when high doses of lactobacillus was given it caused diarrhea and gastric discomfort.

*Reduction of Bacterial Colonization in Premature Infants*

It was believed that ingestion of lactobacillus can alter bacterial flora of intestinal tract as it normally colonizes in the gastrointestinal tract of breast-fed infants(10). There it can inhibit growth of Gram negative enteric organisms. Reuman *et al.*(11) in their series showed that the facultative Gram negative enteric rods colonization were not decreased by feeding lactobacillus.

*Hepatic Encephalopathy*

It is claimed that it supresses the growth of proteolytic organisms in the intestine of patients having hepatic encephalopathy and also reduces formation of ammonia. Lactobacillus produces lactic acid on coming in contact with nutrients (carbohydrate-glycogen), which lowers the pH making surroundings inhospitable for pathogens and also produce antibiotic like substance called bacteriocin which inhibits the growth of harmful bacteria. However, in actual practice no benefit is seen and no reference of its use has been made in textbooks(4,12). Administration of neomycin and lactulose are reliable drugs in reducing formation of ammonia(12).

*Reduction of Colonic Cancer*

Studies on rats(13) have shown that fecal B glucorinidase, azoreductase and

nitroreductase enzymes can convert indirect acting carcinogens to proximal carcinogens which are responsible for colonic cancer. Feeding of lactobacillus daily reduces fecal $\beta$-glucoronidase and nitroreductase activities, thus reducing the chances of colonic cancer. In human beings, it is difficult to demonstrate the reduction of colonic cancer by feeding lactobacillus.

## Limitations of Lactobacillus Administration

Vitamins especially B-complex groups are needed for the proliferation and metabolism of lactobacillus. As lactobacillus are present in the range $10^6$ to $10^{10}$ per ml of fluid contents throughout life except for periods when certain antibiotics are given by mouth, administration of lactobacillus preparations have no added advantage. They are responsible for dental caries and subacute bacterial endocarditis. In higher doses, lactobacillus preparations cause diarrhea. Lactobacillus has no role in hepatitis, hepatic precoma and coma and does not prevent colonization of bacteria by facultative Gram-negative organisms. However, there is increase in the cost of treatment without advantage.

## Conclusions

The drug manufacturers claim various advantages of adding lactobacillus to the treatment regimens of antibiotics, oral rehydration solutions *etc.* However, a review of the pertinent literature reveals that lactobacillus have no role to play in the management of above disorders. In fact, there is evidence to show that they can be harmful and unnecessarily increase the cost of treatment. Hence, it is recommended that pediatricians must discourage the use of those products which contain lactobacilli.

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