

REFERENCES

1. Singh UK, Sinha RK, Sharma VK. Fulminant hepatitis in Kala-azar. *Indian J Pediatr* 1995; 62: 571-574.
2. di Martino L, Vajro P, Nocerino A, Scotti S, Napolitano G, Vegnente A. Fulminant hepatitis in an Italian infant with visceral leishmaniasis. *Trans R Soc Trop Med Hyg* 1992; 86: 34.
3. El Hag IA, Hashim FA, el Toum IA, Homeida M, el Kalifa M, el Hassan AM. Liver morphology and function in visceral leishmaniasis (Kala-azar). *J Clin Pathol* 1994; 47: 547-551.
4. Hepburn NC, Siddique I, Howie AF, Beckett GJ, Hayes PC. Hepatotoxicity of sodium stibogluconate therapy for American cutaneous leishmaniasis. *Trans R Soc Trop Med Hyg* 1994; 88: 453-455.
5. Carvalho EM, Teixeira R, Johnson WD. Cell-mediated immunity in American visceral leishmaniasis: reversible immune suppression during acute infection. *Infect Immun* 1981; 33: 498-502.

Scientific Letters to the Editor

Bovine Colostrum in Pediatric Respiratory Diseases: A Systematic Review

Sir,

Colostrum is the first natural species-specific food produced by female mammals during the first 24–36 hours after giving birth. Chemically, it is a very complex fluid, rich in nutrients, antibodies and growth factors. The antimicrobial components like lactoferrin, lysozyme and lactoperoxidase¹⁻³ and the immunoglobulins provide passive immunity to the newborn, and the growth factors stimulate the growth of the gut. Whole bovine colostrum and immunoglobulin-enriched colostrum (hyperimmune bovine colostrum; HBC) fractions have been used in infants and immunocompromised adults to treat or prevent enteric infections.^{4,5}

The precise role of bovine colostrum (or HBC) in respiratory infections and other (immune –mediated) diseases like atopy/asthma in children is not well defined. We undertook a systematic review of the literature to look at the potential use in respiratory illnesses in children. We searched PubMed, Cochrane database (Cochrane Central Register of Controlled Trials: CENTRAL)) with key word “bovine colostrum” for studies in human (clinical trials, RCTs, reviews) in children 0-18yr. Comprehensive electronic searches and hand searching of the bibliographies of all the clinical trials were electronically retrieved. The numbers of citations using the key word ‘bovine colostrum’ retrieved with limits applied (humans, age 0- 18 yr, clinical trials/ RCTs/ reviews) were 55. On removing the age limits, 123 citations were retrieved and abstracts were reviewed. Thirty five studies including those in adults, animals and children were reviewed. Cohort studies were also reviewed.

We could not identify any published randomized controlled trials (RCT) evaluating the role of bovine colostrum in respiratory illnesses in children. There

were 3 RCTs on beneficial effect of bovine colostrum in diarrheal diseases including one in immuno-compromised adults⁶, one in children⁷, one in juvenile rheumatoid arthritis.⁸ There was only one study⁹ which partly satisfied the inclusion criteria. In this open, multi-centric, non-comparative, post-marketing study, a total of 605 children of either sex between 1 to 8 yr of age were enrolled. The study was conducted involving 133 pediatricians across India. Children having recurrent episodes of URTI (defined as >6 episodes of URTI during the period 6 months prior to enrollment in the study) or having recurrent episodes of diarrhea were included in the study. Children, having any abnormalities of the respiratory tract, those having >3 episodes of lower respiratory tract and infections requiring hospitalization in the past 6 months or those children receiving corticosteroids (systemic or topical), immunomodulators or when parent/guardian did not give informed consent, were excluded. All children received bovine colostrum (Pedimune®, Mfg. by Merck India Ltd.) 3 g (one teaspoonful) with a glass of water once daily for a period of 12 wk.

Primary outcome measure was reduction in the number of episodes of upper respiratory tract infections (RTI) occurring during the study period (time from enrollment to 12 weeks of bovine colostrum therapy) as compared to the 6 months prior to enrollment in the study. Frequency of hospitalization required for RTI and diarrhea during study period as compared to 6 months prior to enrollment was also compared. The results of 551 patients who completed the study were analyzed. The number of episodes [Mean ± S.D.] of URTIs occurring 6 months prior to bovine colostrum therapy was 5.94 ± 3.88 which reportedly decreased significantly to 1.60 ± 1.74, 0.99 ± 1.20 and 0.52 ± 0.91

Scientific Letters to the Editor

at the end of 4 wks, 8 wks and 12 wks of bovine colostrum therapy respectively ($p < 0.05$). The reduction in the mean number of episodes of URTI was similar in the children of all age groups ($p > 0.05$). After bovine colostrum therapy, the percentage reduction in the number of episodes of URTI from baseline was 73.01 %, 83.25 % and 91.19 % at 4, 8, and 12 wks respectively.

Two patients discontinued treatment, out of which one discontinued due to skin rash and the other discontinued due to poor acceptability of taste. Total incidence of adverse effect was found to be 2.97%, and was mild to moderate in nature and resolved after appropriate therapy. No detail of the type of URTI is provided.

On critical appraisal of the study, there appear to be significant limitations. There is lack of clarity on the number of episodes in different time periods of observation, used for comparison. The baseline is number of episodes in over 6 months. This data should have been converted to monthly episodes and then compared to the number of episodes at 4 weeks, 8 weeks and 12 wks. Otherwise the number of episodes over 6 month cannot be compared with those in 4 weeks. Also, it is not clear if only children with more than 6 episodes of URTI were included as the range of episodes reported in the paper range from 0- 20.

To conclude, our review highlights that there is no strong scientific evidence to support use of colostrum in respiratory illnesses. There is need for further research to evaluate the role of bovine colostrum in children with various respiratory illnesses.

P. Ramesh Menon, Rakesh Lodha and S.K. Kabra

*Department of Pediatrics
All India Institute of Medical Sciences
Ansari Nagar, New Delhi-110029, India.
E-mail: skkabra@hotmail.com
[DOI-10.1007/s12098-009-0257-0]*

REFERENCES

1. Sanchez L, Clavo M, Brock JH. Biological role of lactoferrin. *Arch Dis Child* 1992; 67: 657-661.
2. Levay PF, Viljoen M. Lactoferrin: a general review. *Haematologica* 1995; 80: 252-267.
3. Lonnerdal B, Lyer S. Lactoferrin: molecular structure and biological function. *Annl Rev Nutr* 1995; 15: 93-110.
4. Pakkanen R, Aalto J. Growth factors and antimicrobial factors of bovine colostrum. *International Dairy J* 1997; 7: 285-297.
5. Huppertz HI, Rutkowski S, Busch DH, Eisebit R, Lissner R, Karch H. Bovine colostrum ameliorates diarrhea in infection with diarrheagenic *Escherichia coli*, Shiga toxin-producing *E. coli*, and *E. coli* expressing intimin and hemolysin. *J Pediatr Gastroenterol Nutr* 1999; 29: 452-456.
6. Abubakar I, Aliyu SH, Arumugam C, Usman NK, Hunter PR. Treatment of cryptosporidiosis in immuno-compromised individuals: systematic review and meta-analysis. *Br J Clin Pharmacol* 2007; 63: 387-393.
7. Ashraf H, Mahalanabis D, Mitra AK, Tzipori S, Fuchs GJ. Hyperimmune bovine colostrum in the treatment of shigellosis in children: a double-blind, randomized, controlled trial. *Acta Paediatr* 2001; 90: 1373-1378.
8. Malin M, Verronen P, Korhonen H, Syvaaja E-L, Salminen S, Mykkanen H *et al*. Dietary therapy with *Lactobacillus GG*, bovine colostrum or bovine immune colostrum in patients with juvenile chronic arthritis: Evaluation of effect on gut defense mechanisms: *Inflammopharmacology* 1997; 5:219-236.
9. Patel K, Rana R. Pedimune in recurrent respiratory infection and diarrhoea—the Indian experience—the pride study. *Indian J Pediatr* 2006; 73: 585-591.

Scientific Letters to the Editor

Melamine-tainted Milk: When China Sneezes, Hong Kong Catches Cold

Sir,

Pride among the Chinese following the successful August Beijing Olympic Games was rapidly changed to shame when news broke in September that many young children had developed kidney problems after consuming melamine-tainted milk products.¹ The company that produced the infant formula, Sanlu Group Co., was China's biggest producer of powdered milk and was 43 percent owned by a New Zealand dairy farmers' cooperative, Fonterra. The incident was failure for China's product safety system, which had been overhauled in an attempt to restore consumer

confidence after a string of recalls and warnings abroad over tainted toothpaste and other goods.

On 22 September 2008, China's Ministry of Health reported that nearly 40,000 children had sought medical treatment related to the consumption of melamine-contaminated powdered infant formula. Almost 12,900 were hospitalized and three deaths had been confirmed as being related to contamination of infant formula.²

Melamine is a nitrogen-rich organic base chemical widely used in plastics, adhesives, countertops,