Generics Drugs — Are They Really Equivalent to Brands

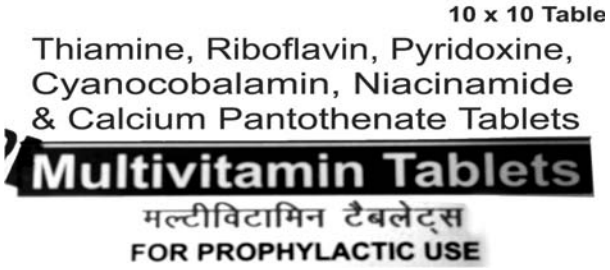

FIG. 1 *Label of a generic drug by the name of 'Multivitamin Tablets'.*

Generic drugs by definition are "the drug products which are comparable to a brand/reference listed drug product in dosage form, strength, quality and performance characteristics, and intended use" [1]. Government of India and several of its States are promoting the use and prescription of generic drugs in public-sector hospitals with the vision of "ensuring availability of quality medicines at affordable prices to all" [2]. Generic drugs, being cheaper, have the potential to reduce the country's healthcare expenditure and ensure affordable healthcare to millions of people.

Even though generic drugs are being promoted, certain issues need to be highlighted. According to the definition and recommendations by WHO and FDA, only those generic drugs which are bioequivalent to the branded counterparts can be approved for marketing [1,3]. They also recommend that a generic drug should have an effectiveness range of between 80-125 percent of the original drug, which, however may be dangerous especially for drugs with narrow therapeutic index. Moreover, the quality control of generic drugs may not be as stringent as that of the brands. The issues related to lack of control over constituents and uncontrolled price of branded products during non-availability of generic drugs have been highlighted in this journal earlier [4].

Recently we encountered another problem while prescribing generic drugs. While treating a child with severe acute malnutrition, we prescribed ''multivitamin tablet'' presuming that it would contain all the vitamins (A, B, C, D, E) in at least the recommended daily allowance. When we checked the constituents of the product being given to the child, it contained only vitamins belonging to B-complex group, yet carried the name 'Multivitamin Tablets' (***Fig.* 1**). Therefore it may not serve the exact purpose which it is supposed to do. As per the definition of generic drugs, their pharmacological effects should exactly be the same as those of their brand-name counterparts [1]. But this problem of quality control over generic drugs remains unchecked due to lack of strict guidelines. The drug should provide what it intends to deliver; the labelling and nomenclature should adhere to ethical standards and not confuse and compromise the recovery of sick patients. Generic drugs need to maintain the quality and not merely serve as a measure of cost-cutting on health care expenses.

SWATI KALRA AND *PIYUSH GUPTA
Department of Pediatrics,
University College of Medical Sciences and GTB Hospital,
Delhi, India.
**prof.piyush.gupta@gmail.com*

REFERENCES

1. Generic drugs. Trade, foreign policy, diplomacy and health. World Health Organization. Available from: *http://www.who.int/trade/glossary/story034/en/*. Accessed July 15, 2014.
2. Generic drugs. Center for Drug Evaluation and Research, U.S. Food and Drug Administration. Available from: *http://www.fda.gov/drugs/resourcesforyou consumers/buyingusingmedicinesafely/understanding genericdrugs/default.htm.* Accessed February 12, 2016.
3. Food & Drug Administration, Generic Drugs: Questions and Answers. Food and Drug Administration. *Available from: http://www.fda.gov/Drugs/ResourcesForYou/Consumers/QuestionsAnswers/ucm100100.htm.* Accessed February 12, 2016.
4. Dabas A, Shah D. Prescription of generic drugs – Is it really a smart initiative? Indian Pediatr. 2014;51:842-3.

Effective Prevention of Parent-to-Child Transmission of HIV

We read the recent article in Indian Pediatrics by Seenivasan, *et al*. [1], with great interest. The authors inferred and suggested that the perinatal transmission detected by polymerase chain reaction (PCR) positivity at 6 weeks in three infants was secondary to intrapartum transmission and could not be attributed to breastfeeding alone. Though risk of transmission increases with duration of breastfeeding, it has been well reported in literature that transmission of human immunodeficiency virus (HIV) through breastmilk can occur even as early as six weeks [2,3]. Moreover, during early stages of breastfeeding, infants may be at increased risk of infectivity due to factors such as immaturity of immune system, increased permeability of gut, or high HIV load in colostrum [4]. In a randomized control study by Nduati, *et al*. [2], there was 10% increase of cumulative risk in breastfed infants for developing HIV infection when compared to formula-fed infants, even at 6 weeks [2]. SAINT trial group inferred that breastfed infants are twice at risk of HIV infection compared to non breastfed infants during the first four weeks [3]. Hence, attributing HIV DNA PCR positivity to intrapartum transmission alone may not be prudent.

It is interesting to note that HIV transmission was prevented even in mothers with advanced clinical disease. The important factor, as also stated by the authors, could be the introduction of triple anti-retroviral therapy (ART). However, it may also be important if the authors could furnish the details regarding mode of delivery, associated sexual transmitted infections, and various obstetric factors known to influence HIV transmission among the three groups of HIV positive mothers. It is a well known fact that elective cesarean delivery prior to rupture of membranes reduces the risk of HIV transmission by nearly 50% compared to vaginal delivery [5]. Hence, if those confounding variables are equally distributed among the groups, then ART can be singularly taken as the protective factor.

PANDIARAJAN VIGNESH AND *DEEPTI SURI
Allergy Immunology Unit, Department of Pediatrics, Advanced Pediatrics Center, PGIMER, Chandigarh,India.
**surideepti@gmail.com*

REFERENCES

1. Seenivasan S, Vaitheeswaran N, Seetha V, Anbalagan S, Karunaianantham, *et al.* Outcome of prevention of parent-to-child transmission of HIV in an urban population in Southern India. Indian Pediatr. 2015;52:759-62.
2. Nduati R, John G, Mbori-Ngacha D, Richardson B, Overbaugh J, Mwatha A, *et al*. Effect of breastfeeding and formula feeding on transmission of HIV-1: A randomized clinical trial. JAMA. 2000;283:1167-74.
3. Moodley D, Moodley J, Coovadia H, Gray G, McIntyre J, Hofmyer J, *et al*. A multicenter randomized controlled trial of nevirapine versus a combination of zidovudine and lamivudine to reduce intrapartum and early postpartum mother-to-child transmission of human immunodeficiency virus type 1. J Infect Dis. 2003;187:725-35.
4. Dunn DT, Tess BH, Rodrigues LC, Ades AE. Mother-to-child transmission of HIV: Implications of variation in maternal infectivity. AIDS Lond Engl. 1998;12:2211-6.
5. McGowan JP, Shah SS. Management of HIV infection during pregnancy. Curr Opin Obstet Gynecol. 2000;12:357-67.

Effective Prevention of Parent-to-Child Transmission of HIV: Author's Reply

The publication quoted by author [1] showed the higher risk of breastfeeding-related transmission in early stages of breastfeeding than in the late stages, but the higher risk of mother-to-child transmission was predicted based on the mathematical model developed by them for different sources of epidemiological data. Prior to the 2010 guidelines on HIV and infant feeding [2], avoidance or early cessation of breastfeeding seemed logical or appropriate. However, the repercussions for the health and survival of the infants were serious, with studies showing much higher mortality rate due to diarrhea, malnutrition and other diseases in non-breastfed children. The 2010 recommendations are based on evidence of positive outcomes for HIV-free survival through provision of anti-retrovirals to breastfed HIV-exposed infants. Apart from the above mentioned, there are many publications [3-5] documenting that exclusive breastfeeding at early stage reduces HIV-transmission risk for infants.

In our study, the time of testing (6 weeks of postnatal life) was based on National AIDS Control Organization/ guidelines [6]. Three infants who were exclusively breast fed were HIV-1 DNA PCR positive at 6 weeks of life. Based on the papers [3-5] we quoted above, we may attribute HIV DNA PCR positivity to intrapartum transmission. However, we do agree that intrapartum transmission alone may not be the cause in our study. Breastfeeding is a possible factor for PCR positivity. However, we did not carry out DNA PCR at birth, to rule out intra-uterine transmission. Transmission during delivery would be missed if DNA PCR is taken at birth as viral replication

takes time. Secondly, DNA PCR demonstrated lower sensitivities at birth and 4 weeks of 68.4% and 87.5%, respectively. One infant who was PCR negative at 6 weeks became positive during the second sampling after stopping breast feeds. This we attributed to breast feeding (25 % of total transmission). Moreover, we recommend further studies in Indian setting to assess the effect of formula feeding in HIV transmission, and overall mortality and morbidity.

Confounding variables like HIV staging of mother, CD 4 counts, mode of delivery, antenatal bleeding per vaginum, prolonged rupture of membrane were comparable as given in ***Table* I** in the study [7]. None of the four women had other sexually transmitted diseases during pregnancy. Hence, ART can be singularly taken as the protective factor.

SEENIVASAN SUBRAMANI
Department of Pediatrics,
Government Kilpauk Medical College,
Chennai, Tamil Nadu, India.
seeni.sholing@gmail.com

REFERENCES

1. Dunn DT, Tess BH, Rodrigues LC, Ades AE. Mother-to-child transmission of HIV: Implications of variation in maternal infectivity. AIDS. 1998;12:2211-6.
2. World Health Organization. Guidelines on HIV and Infant Feeding 2010: Principles and Recommendations for Infant Feeding in the Context of HIV and a Summary of Evidence. Geneva: World Health Organization; 2010. p. 49.
3. Natchu UC, Liu E, Duggan C, Msamanga G, Peterson K, Aboud S, *et al*. Exclusive breastfeeding reduces risk of mortality in infants up to 6 mo of age born to HIV-positive Tanzanian women. Am J Clin Nutr. 2012;96:1071-8.
4. Iliff PJ, Piwoz EG, Tavengwa NV, Zunguza CD, Marinda ET, Nathoo KJ, *et al*. Early exclusive breastfeeding reduces the risk of postnatal HIV-1 transmission and increases HIV-free survival. AIDS. 2005:19:699-708.
5. Rollins NC, Filteau SM, Coutsoudis A, Tomkins AM. Feeding mode, intestinal permeability, and neopterin excretion: a longitudinal study in infants of HIV-infected South African women. J Acq Imm Def Syndrome. 2001;28:132-9.
6. Shah NK, Mamta M, Shah I, Deepak U, Lodha R, Pensi T, *et al*. Guidelines for HIV Care and Treatment in Infants and Children, 1st ed. New Delhi: National AIDS Control Organisation and Indian Academy of Pediatrics, 2006. p. 3-90.
7. Seenivasan S, Vaitheeswaran N, Seetha V, Anbalagan S, Karunaiaanantham, Swaminathan S. Outcome of prevention of parent-to-child transmission of HIV in an urban population in Southern India. Indian Pediatr. 2015;52:759-62.

Nasopharyngeal Carriage of Organisms in Children With Severe Pneumonia

We read with interest the recent article in Indian Pediatrics by Singh, *et al*. [1], and have the following comments to offer:

1. It is not clear why authors excluded children with radiological evidence of consolidation and pleural effusion.
2. Though children with consolidation were excluded, the results state that 63.9% children had infiltrates on chest *X*-ray, which is a bit confusing.
3. The table titled 'Frequency of organisms in nasopharyngeal secretions in children with community acquired severe pneumonia' divides the patients in to 'Home' and 'Hospital'. The basis of such categorization is not clear from the methodology whether they indicate the place of specimen collection or the type of care the patients received.
4. Serotyping of the pneumococcal isolates could have helped in vaccine development.
5. As the conjugate *H. influenzae* vaccine is known to reduce the nasopharyngeal carriage of the organism [2], the data on immunization status of the children would have been interesting as many of these children might have received this vaccine as per latest National Immunization Schedule.
6. Nasopharyngeal carriage of Pneumococcus in children with pneumonia has been used as a surrogate marker for invasive disease [3]. The data on treatment received by the children and their outcome would have enlightened the readers about the clinical utility of the isolates and their antibiotic, susceptibility in the absence of a blood culture.

***ANIRBAN MANDAL AND #PUNEET KAUR SAHI**
Departments of Pediatrics,
All India Institute of Medical Sciences,
and #Lady Hardinge Medical College; New Delhi, India.
**anirban.nrs@gmail.com*

REFERENCES

1. Singh M, Agarwal A, Das RR, Jaiswal N, Ray P.

Nasopharyngeal carriage of organisms in children aged 3 to 59 months diagnosed with severe community acquired pneumonia. Indian Pediatr. 2016;53:125-8.
2. Barbour ML. Conjugate vaccines and the carriage of *Haemophilus influenzae* type b. Emerg Infect Dis. 1996;2:176-82.
3. Greenberg D, Givon-Lavi N, Newman N, Bar-Ziv J, Dagan R. Nasopharyngeal carriage of individual *Streptococcus pneumoniae* serotypes during pediatric pneumonia as a means to estimate serotype disease potential. Pediatr Infect Dis J. 2011;30:227-33.

Nasopharyngeal Carriage of Organisms in Children With Severe Pneumonia: Authors' reply

1. The current paper was a part of a multicentric randomized controlled trial for oral amoxicillin administered at hospital *vs*. home [1], published elsewhere. The children with effusion or consolidation were excluded as they required special care and hospitalization for longer durations, and were therefore excluded.
2. The word 'consolidation' has been used to refer end point consolidation which means a significant pathology that means a dense or fluffy opacity that occupies a whole of the lobe or entire lung that may or may not contain air- bronchograms. The term 'infiltrate' was used to define non endpoint infiltrations which include minor patchy infiltrates that are of no sufficient magnitude to constitute primary endpoint consolidation [2,3].
3. The categorization of patients was based on the place of administration of oral amoxicillin *i.e.* whether it has been administered in a hospital setting or at home.
4. Serotyping would have helped definitely but it was beyond the scope of this study as it was focused on treatment of community-acquired pneumonia with oral amoxicillin, and was not directed towards the etiology of the disease [1].
5. The patients were enrolled between 2009 to 2011. Hib vaccination was not a part of national immunization at that time.
6. The pneumococcus isolates and their antibiotic susceptibility has been shown in the manuscript [4].

***MEENU SINGH AND AMIT AGARWAL**
Department Of Pediatrics,
Advanced Pediatrics Centre,
PGIMER, Chandigarh, India.
**meenusingh4@gmail.com*

REFERENCES

1. Patel AB, Bang A, Singh M, Dhande L, Chelliah LR, Malik A, *et al*. A randomized controlled trial of hospital versus home based therapy with oral amoxicillin for severe pneumonia in children aged 3 – 59 months: The IndiaCLEN Severe Pneumonia Oral Therapy (ISPOT) Study. BMC Pediatrics. 2015;15:186.
2. Simbalista R, Araújo M, Nascimento Carvalho CM. Outcome of children hospitalized with community acquired pneumonia treated with aqueous penicillin G. Clinics (Sao Paulo). 2011;66:95-100.
3. Cherian T, Mulholland EK, Carlin JB, Ostensen H, Amin R, de Campo M, *et al*. Standardized interpretation of paediatric chest radiographs for the diagnosis of pneumonia in epidemiological studies. Bull WHO. 2005;83:353-9.
4. Singh M, Agarwal A, Das RR, Jaiswal N, Ray P. Nasopharyngeal carriage of organisms in children aged 3 to 59 months diagnosed with severe community acquired pneumonia. Indian Pediatr. 2016;53:125-8.

Centralized Newborn Hearing screening in Mumbai: Success or Failure?

In India, two children are born with hearing impairment per hour which amounts to 1/2000 to 1/10000 live births. 18000 children with hearing impairment are added to our population every year [1]. Universal newborn hearing screening is mandatory in most developed countries. WHO's Newborn and Infant Screening Report (November 2009) postulates a 1-3-6 rule for newborn hearing screening programs, in which neonates should be ideally screened before 1 month of age, diagnosed by 3 months of age, and intervened by 6 months of age. Presently, Kochi seems to be the only city in India to have centralized new born hearing screening program [2]. The program has screened 1,01,688 babies and identified 162 babies with hearing loss [3].

We started centralized newborn hearing screening in October 2010 and have continued it till date. A two-tier screening approach with oto-acoustic emissions, and brainstem evoked response audiometry (BERA) was followed. A health care worker was identified and trained

to carry out the screening test and documentation. The screener travelled to the identified locations, screened the babies, and provided the provisional reports, following which formal report was mailed to them.

From October 2010 to December 2015, we screened a total of 1716 babies. 809 babies were from well-baby nurseries and 907 babies were from neonatal intensive care unit. 299 babies failed the first screen, but only 66 out of 299 appeared for rescreen. Eighteen babies failed the rescreen and were recommended BERA testing. However, none of the babies turned up for BERA testing or could not be tracked further.

Poor follow-up for rescreening and diagnostic BERA was the greatest challenge to our endeavor. As compared to the experience from Kochi [3], the number of children we screened is much less and follow-up is poor. The dropout of children could possibly be due to lack of effective communication between the screener and the parent, which may be due to lack of background in speech and hearing. We plan to overcome this by introduction of an audiologist to coordinate the patient screening and place audiology interns to carry out the screening. We believe that a centralized two-tier approach is the best and most economically viable approach to neonatal hearing screening, provided adequate communication is established by the screening personnel, so as to ensure a proper follow up.

***JANET VARGHESE AND NEETA NAIK**
EN1 Neuro Services, Kanakia Zillion,
LBS Marg, Kurla (West), Mumbai,
Maharasthra, India.
**janet.en1neuro@gmail.com*

REFERENCES

1. Singh V. Newborn hearing screening: Present scenario.Indian J Community Med. 2015;40:62.
2. Paul AK. Early identification of hearing loss and centralized newborn hearing screening facility-the Cochin experience. Indian Pediatr. 2011;48:355-9.
3. Paul AK. Centralized newborn hearing screening in Ernakulam, Kerala–Experience over a decade. Indian Pediatrics. 2016;53:15-7.

Transfusion-associated Necrotizing Enterocolitis

We read with interest the recently published article on relationship between packed red blood cell (PRBC) transfusion and severe form of necrotizing enterocolitis (NEC) [1].

The association between NEC and blood transfusion has been reported previously in case control studies but no strong evidence is available till now [2]. The authors have concluded that blood transfusion-associated NEC (TANEC) is severe, and is mainly a surgical form of the disease (stage 3a+3b), but number of TANEC cases with this staging and their comparative value in the other NEC group are not reported. Authors also mention that TANEC group was more likely to be of blood type B+ and less likely to be type A+. Data for this inference are not available in the results. Also, in the present study, we feel there are many confounders. The mean birth weight (992.8 g) and gestation age (27.3 weeks) in TANEC group was less compared to other NEC group. A multivariate analysis adjusted with these confounders is important. Significant number of more females in TANEC group is a new finding in the study not reported previously.

The association between NEC and blood transfusion demands a strong evidence of multi-center prospective randomized trial while addressing the confounders.

RAHUL P BHAMKAR
Department of Pediatrics,
Sir HN Reliance Foundation Hospital,
Mumbai, India.
dr.rahulbhamkar@gmail.com

REFERENCES

1. Garg PM Ravisankar S, Bian H, Macgilvray S, Shekhawat PS. Relationship between packed red blood cell transfusion and severe form of necrotizing enterocolitis: A case control study. Indian Pediatr. 2015;52:1041-5.
2. Mohamed A, Shah PS. Transfusion associated necrotizing enterocolitis: A meta-analysis of observational data. Pediatrics. 2012;129:529-40

Transfusion-associated Necrotizing Enterocolitis: Authors' Reply

We agree that association between packed red blood cell (PRBC) transfusion and necrotizing enterocolitis (NEC) has been reported multiple times over the past 20 years but investigators are still hard-pressed to provide a cause-and-effect relationship between the two entities.

During the publication process, several revisions of our data were made, and somehow surgical NEC data and blood group data were omitted from our final published results. In our study, out of 26 transfusion-associated NEC cases, 10 (39%) had stage 2a + 2b NEC and 16 (61%) had stage 3a + 3b cases (P = 0.04), while from control (non-transfusion related NEC) group 45 (61.6%) had stage 2 NEC and 28 cases were of stage 3a + 3b NEC, which was statistically significant. B+ blood group was present in 31% of transfusion-associated NEC and only in 9% of non-transfusion associated NEC cases. This relationship did not reach statistical significance (P=0.07).

The mortality rate mentioned in the abstract section has been adjusted for gestational age, birthweight and gender. After rechecking our data, the number of males in the transfusion associated NEC group were 15 instead of 5, which was not statistically significant. We agree with your contention that association between NEC and blood transfusion should be studied in prospective multi-center randomized trials with control of all confounders.

PARVESH M GARG AND *PREM SHEKHAWAT
Department of Pediatrics, Division of Neonatology,
Metro Health Hospital,
Case Western Reserve University,
2500 Metro Health Drive, Room R 249A, Cleveland,
Ohio 44109, USA.
**pshekhawat@metrohealth.org*