Outcome of Biliary Atresia After Kasai's Portoenterostomy: Few Concerns

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We read with interest the recent article by Redkar, *et al*. [1] highlighting the surgical outcomes of biliary atresia after Kasai's Portoenterostomy (KPE). Authors reported their experience from a large retrospective cohort reconfirming the utility of jaundice clearance at 3 months post-surgery as a valid indicator of long-term outcome.

There are several points that need to be clarified. In the 'Methods' section, authors mentioned utilizing Hepatobiliary iminodiacetic acid (HIDA) scan, rather than liver biopsy, for diagnostic purpose. All of their patients presented with pale stools. HIDA scan itself has limited use in patients presenting with pale stools considering its low specificity (as low as 45-70%) [2-4]. It adds little to diagnostic evaluation in a cholestatic infant, and is of value only in excluding (and not in diagnosing) billary atresia by documenting patency of biliary tree [1]. On the other hand, sensitivity, specificity and diagnostic accuracy of liver biopsy for diagnosis of billary atresia exceeds 90% [1,4]. Other causes of cholestasis such as bile duct paucity and idiopathic neonatal hepatitis can also have non-excretory HIDA scan, but can be diagnosed reliably on liver biopsy avoiding unnecessary exploratory laparatomy [2].

Authors also tested for 'TORCH' serology in all patients with suspected biliary atresia [1]. Out of the 78 patients tested for TORCH infection, 39 had CMV IgM positive and were treated with gancicyclovir. Routinely doing 'TORCH' serology in these patients is of very limited use as there is still no definite link between 'TORCH' infections and causation of billiary atresia. Investigation for 'TORCH' infections and their subsequent treatment based on only serology (rather than on confirmatory liver tissue histology and polymerase chain reaction based methods) only delays the optimum management, and may even adversely affect the outcomes [5].

In the present study, 14% patients had clinical ascites on admission. This suggests an already advanced liver disease. Though there is no definite upper age limit of KPE, attempting surgery in decompensated liver disease patients is unheard of in literature and is likely associated with extremely poor outcomes. Follow-up of only one year also limits drawing of any definite conclusions from the study, as biliary atresia is a progressive fibro-inflammatory disease even post-KPE.

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AUTHOR'S REPLY

The points raised by these readers include utilization of liver biopsy rather than HIDA scan for diagnosis of biliary atresia. We would like to clarify that as mentioned in our methods, all patients underwent clinical examination, stool color examination, liver function tests and ultrasonography of abdomen. While TORCH serology and a HIDA scan were done in most patients [1], we have relied on intra-operative cholangiogram as the diagnostic test for BA, which is still considered the gold-standard for its diagnosis [2]. In addition, the interpretation of a biopsy can be difficult and needs an experienced pathologist as there is a lot of overlap in the histological findings of biliary atresia and neonatal hepatitis [3]. Infact, lack of expertise in histopathology has also refrained us from incorporating histological findings in our study report. We have accepted that as one of the limitations in our study [1].

The reviewer also pointed on testing for TORCH serology and treatment for the same. As mentioned above, TORCH serology was done in most (n=78/121) patients as a part of workup for neonatal cholestasis. Ganciclovir was started after a CMV-PCR confirmation

(not mentioned in the article), without alteration or delay in the usual workup and management of biliary atresia. CMV positive biliary atresia patients have poorer outcome with reduced jaundice clearance, native liver survival and increased mortality [4]. We usually treat patients of BA associated with CMV with ganciclovir.

In our study, although 14% of patients presented with clinical ascites, most of them (*n*= 11/14, 78.6%) had normal or borderline albumin levels with normal bleeding parameters. Out of these, four patients had jaundice clearance, and were alive at 1 year. This cannot be considered as a poor outcome, especially considering the non-feasibility of primary liver transplantation in our country. Factors like scarcity of organs and centers offering pediatric liver transplant programs, financial constraints and need for lifelong immunosuppression, make Kasai's Portoenterostomy as the initial procedure of choice, even for patients with late presentations [1,5].

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Some Problems Associated with Generic Drugs

Ministries of Health and Family Welfare of Government of India and the states, and Medical Council of India (MCI) have mandated that doctors shall prescribe generic drugs only and no branded drug should be prescribed. It is presumed that reputed pharmaceutical companies maintain stringent quality control of their products as their reputation is at stake. The same may also be true of unbranded products, but the market is currently flooded with spurious or sub-standard drugs [1]. It should be presumed that the Government machinery must have put in some mechanism to ensure that no spurious or sub-standard drug is manufactured any where in the country, so as to provide high quality drugs at low cost. I would like to bring to notice of the concerned authorities some of the problems that doctors could face:

1. The issue of different doses of drug (*e.g.*, dextromethorphan, paracetamol) in formulations from different companies has been raised in past [2-4].
2. Phenylephrine is not available as single salt for oral consumption, but is available in majority of cases in combination with Chlorpheniramine maleate, cetrizine or levocetrizine. The combination of phenylephrine with other molecules manufactured by different pharmaceutical companies have different quantities of different ingredients. Interchange of brands may result in up to 100% lower or higher dose of drug that may be ineffective in one case or very high dose resulting in toxicity in other case. Doctors usually know the composition of the brand of drugs they prescribe, and it may be difficult to write names and quantity of all the ingredients needed for a particular patient, and would not be possible for the pharmacist to identify the required products.
3. Dicyclomine is not recommended for children below six months of age. For infantile colic in children below six months of age, Simethicon, Dil oil and Fennel oil are often prescribed. Some manufacturers market products containing dicyclomine in addition to the other ingredients meant for use in children aged <6 months; clinicians may face difficulty in prescribing these drugs.
4. *Saccharomyces boulardii* is recommended for antibiotic-associated diarrhea, and recommended dose is 5 billion spores once or twice a day. There are few preparations of *S. boulardii* with 5 billion spores in each dose. If the doctors are not permitted to prescribe *S. boulardii* as a brand preparation, they will have to write probiotic *S. boulardii*, 5 billion spores once or twice a day. As on date, no generic preparation has 5 billion spores of *S. boulardii*. Pharmacist can hand over any probiotic or pre-