

Off-label Drug Use in Neonatal Intensive Care Unit

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The research article on off-label use of drugs in neonates [1] brings an important issue of drug safety in neonates into a sharp focus. I request the authors to clarify certain methodological issues.

The authors have stated that the accuracy of dose was checked from standard neonatal formularies, *viz.* British National Formulary 2005 and Neofax 2008, and stated that 75% of medications were not approved by FDA for neonatal use. They have not mentioned the document or the source that they relied upon to classify the drug as off-label or otherwise. It may not be advisable to decide if use of a particular drug constitutes off-label use or not on the basis of information included in a Formulary [2]. Considering USFDA licensing information as a basis to determine off-label status may also not be appropriate, as such a status should be determined on the basis of marketing authorization issued by the Indian licensing authority, the Directorate of Drug Controller General of India (DCGI)/ Central Drug Standards Control Organization (CDSCO).

Unlike in the USA (where the USFDA website provides detailed licensing information), labeling information for drugs approved by DCGI is not easily available. Of late, lay press and judiciary have started paying attention to the issue of off-label drug use [3-5], and some parents expect that such drugs be used in their children only with their knowledge and consent [6]. Under these circumstances, it is imperative that information about the drug license is available in the public domain. This would enable the practitioners and parents to take an informed decision.

Authors' exclusion of inotropes from the analysis has led to lower estimates of off-label use, as dopamine and dobutamine are being used in neonates for several years as off-label drugs. The practitioners may consider their use in neonates as safe and effective on the basis of published data and clinical experience. Nevertheless, such use is considered off-label, as no efforts are made to get the licensing information updated on the basis of evidence generated after the drug is marketed. This 'once off-label; always off-label' situation leads to many time-tested drugs being continued to be classified as off-label. This puts unnecessary onus on the practitioners, and one can only imagine a situation where parents voice their reluctance to use these drugs in their newborn child, because they consider off-label use as experimental or dangerous. Inclusion of these drugs in the analyses could have helped authors flag this important issue.

REFERENCES

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Off-label Drug Use: Author's Reply

The first query is pertaining to use of Neofax and British formulary for checking dosage of various drugs used in newborn. There was no separate neonatal drug formulary available by Indian regulatory body like DCGI at the time when this study was conducted. So, we had to use Neofax and British neonatal drug formulary for bedside consultation of drug dose, route, frequency and duration, and USFDA drug list of approval for neonatal use for the particular indication. Data were cross checked randomly by an independent specialist, who was not the part of this study. Most of the units in India confirm the drug dose, route, frequency and duration from latest Neofax edition or standard text books.

Second query is regarding source/document relied upon to classify the drug as off-label. Definition of off-label used in this study was as per the definition used by Turner, *et al.* [1].

We deliberately did not include inotropes in the list of off-label drugs. Inotropes are used for clinical shock without functional echocardiography and without intra-arterial blood pressure monitoring. This was prospective chart audit, without interfering with practice; so we decided to use only common drugs in this audit.