Medication errors in neonatal intensive care unit of a tertiary care hospital in South India: A prospective observational study

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Abstract:
INTRODUCTION: Medication errors (MEs) can prolong hospital stay and are a cause of morbidity and mortality. Studies evaluating MEs and its determinants in Indian neonatal intensive care units (NICUs) are limited. Therefore, this study was done to assess the prevalence, characteristics, determinants, and outcomes of MEs in an Indian NICU setting.

METHODOLOGY: A prospective observational study was conducted over a 1-year period (January–December 2016) among neonates receiving medications in NICU. Systematic random sampling was done, and data were collected using a semi-structured questionnaire after obtaining informed consent from the mother. An ME self-reporting system was also established. Data were analyzed using Chi-squared test and Student’s t-test. Binary logistic regression was used to analyze the determinants of MEs.

RESULTS: Among 269 babies included in the study, 57% (n = 154) were male babies with mean (standard deviation [SD]) birth weight of 2.59 kg (0.701). About 79% (n = 213/269) of the neonates were appropriate for gestational age. The mean (SD) duration of stay in NICU was 7.58 (5.07) days, and 67% of the babies had polypharmacy (use of ≥5 medications). The prevalence of MEs was 22% (95% confidence interval [CI]: 16.96%, 26.84%, n = 108) of all babies, of which only 2% (n = 2) were life threatening. Seventy-seven percent (n = 83) of these errors occurred during administration/preparation and 18% (n = 19) while prescribing. The significant determinants of MEs (adjusted odds ratio [95% CI]) include polypharmacy (4.126 [1.917–8.880]), duration of stay >7 days (1.335 [1.198–1.488]), and babies referred from outside (2.592 [1.217–5.521]).

CONCLUSIONS: MEs were common in NICU setting. The occurrence of life-threatening MEs was minimal. Longer duration of hospital stay, polypharmacy, and babies born outside were significantly associated with occurrence of MEs.

Keywords: Medication error, neonatal intensive care unit, neonates, polypharmacy

Introduction
Medication error (ME) is defined as “a failure in the treatment process that leads to, or has the potential to lead to, harm to the patient.”[1] ME can occur during prescription, transcription, preparation, dispensing, and administration[2] and is an avoidable cause of iatrogenic injury.[3] Preventable MEs accounted for the death of 210,000–400,000 patients in the United States of America (USA) as of 2011.[4] They prolong hospital stay and thereby increase the financial burden to the patient and the health-care system.[5] Data from the USA suggest that the cost of preventable MEs...
is extremely high and can cost anywhere between $17 billion to $29 billion annually.\(^6\)

Patients in critical care units undergo life-saving complex treatment regimens comprising drugs needing careful titration.\(^7\) Neonates are even more vulnerable due to complex dosing calculations against a rapidly changing body surface area, weight, and organ immaturity, especially the liver and kidney.\(^8\) A study done in North India reported that every 19\(^{th}\) prescription from a neonatal intensive care unit (NICU) had a ME which accounted for 5.4% of all prescriptions.\(^8\) Studies done in South American NICUs revealed that 43.5% of all prescribed drugs in Brazil\(^9\) and 42.5% of all prescriptions in Argentina\(^10\) constituted MEs. A multicenter study from Italy reported that 28% of all NICU patients experienced at least one ME\(^11\) and another study from the USA reported 91 MEs per 100 NICU admissions.\(^12\)

To the best of our knowledge, similar studies, especially from South India, are limited as ascertained by a PubMed, Embase, and Scopus database search using keywords medication errors, outcomes, determinants, India, and neonates, 1995–2014. There is a wide variability in the reported prevalence rates from various studies as interinstitutional and national policies and resources to prevent ME differ,\(^13\) and therefore, we aimed to assess the prevalence, characteristics, determinants, and outcomes of MEs in our setting.

### Methodology

This was a prospective observational study conducted from January to December 2016. The NICU where this study was conducted is a 36-bedded facility with an average admission of 100 neonates per month attached to a medical college. Neonates admitted to NICU receiving medications were eligible for the study. Neonates who were discharged or were dead within 24 h of NICU admission were excluded. Assuming the prevalence of ME as 42.5\(^{th}\) and an absolute precision of 5%, the sample size estimated was 263 patients. Systematic random sampling was done, and every 3\(^{rd}\) day, we recruited all eligible neonates in the study. Ethics approval was obtained from the Institutional Ethics Committee of the tertiary care teaching hospital (Ref no: 67/2015). Written informed consent was obtained from the mothers of all eligible neonates.

A ME-reporting system was established for self-reporting by all NICU staff wherein ME-reporting forms and ME-reporting boxes (A drop-box placed in the ward to submit the ME-reporting forms) were made available at the nursing station. The self-reporting forms were anonymized, and the staff were counseled on the importance of reporting ME, thereby providing an opportunity for corrective and preventive action rather than punitive action. Furthermore, the self-reported MEs were analyzed by investigators who were from the Department of Pharmacology, and they were not the reporting authorities for the staff of NICU.

MEs were also collected by reviewing the inpatient case records by the principal investigator (PI). Sociodemographic data, clinical data including drugs prescribed, and details of the ME were collected using a semi-structured pretested questionnaire by the PI by interviewing the mothers and NICU staff. The outcomes of ME were classified as clinically insignificant if there was no clinically detectable effect due to ME, minor if there was a clinically detectable effect but recovered spontaneously without any intervention once ME was corrected, and life-threatening if an intervention was needed to save life.

Data entry was done in Epi Info\(^{TM}\) version 7 (Publisher: CDC, USA, 2011), and statistical analysis was performed with IBM Statistical Package for the Social Sciences (SPSS) for Windows, version 20.0 (Publisher: IBM Corp., Armonk, New York, USA, 2011). Demographic characteristics and ME prevalence were summarized using descriptive statistics. The determinants of ME were subjected to univariate analysis, followed by a multivariate analysis using binary logistic regression. \(P < 0.05\) was considered as statistically significant.

### Results

Three hundred and twelve neonates were screened, and 269 (86%) were found eligible. The demographic and general characteristics of patients are presented in Table 1. The mean (standard deviation [SD]) birth weight was 2.59 kg (0.701), and the mean (SD) duration of stay was 7.58 days (5.07). Polypharmacy (prescribing >5 drugs) was noted in 67.3% \((n = 181)\), and 71.6% \((n = 192)\) of the babies were inborn (born in the hospital).

The prevalence of ME was 21.9% (95% confidence interval [CI]: 16.96%–26.84%) of all babies. The total number of MEs recorded was 108, among which only 17 (16%) were self-reported. About 14% of these MEs were, however, detected before reaching the patient. The total number of babies affected by at least one ME was 59 (22%), and the number of errors per neonate ranged from one to six.

Figure 1 shows MEs at various stages of medication use. Majority of the MEs (77%, \(n = 83/108)\) occurred during preparation and administration. About 85% \((n = 71/83)\) of those administration errors were related to oral syrups. Figure 2 shows the proportion of different outcomes of MEs during the study duration. There were no deaths recorded due to ME during the study period. About 81.5%
(n = 88/108) of all MEs were attributed to the nurses, followed by 12.0% (n = 13/108) to the junior doctors (interns/residents) and 6.5% (n = 7/108) to the pharmacist.

The hypothesized determinants for MEs [as shown in Table 2] were subjected to univariate analysis. All variables except gender which had a significance value (P value) of <0.2 were considered for multivariate analysis. Place of birth, duration of stay, and number of drugs continued to remain statistically significant.

**Discussion**

Globally, MEs in NICU vary greatly and comparability between studies is difficult as the denominator varies between studies. For example, some studies represented their results as ME per patient, while others represented it as ME per prescription or ME per drug, etc. [8-13] The prevalence of ME in our study was approximately 22%. Studies done in South America described MEs per prescription or per drug prescribed and thus showed a very high rate of approximately 40%. [9,10] Although a vast majority of MEs (90%) reported in our study had clinically no effect, 8% resulted in minor complications. Life-threatening MEs were very minimal (2%), and there were no deaths reported due to ME in our study. This is probably because the most commonly seen serious errors are looked for and picked up by senior consultants and nurses, and there are also certain safety checks in place for avoiding potentially fatal errors. This suggests that an effective ME surveillance system in a NICU setting could be an effective intervention to avoid MEs. Some of the surveillance techniques that have already been evaluated and proven to reduce ME include retrospective chart reviews by two or more experts, Computerized physician order entry (CPOE), or prescriptions using advanced software and clinical audits. [14,15]

Administration errors including preparation errors were the most common MEs (77%) that our study has picked up. Some of the surveillance techniques that have already been evaluated and proven to reduce ME include retrospective chart reviews by two or more experts, Computerized physician order entry (CPOE), or prescriptions using advanced software and clinical audits. [14,15]
up. These errors may be due to inadequate written communication, problems with medicine supply and storage, high perceived workload, patient factors, and staff health status whether they are tired or stressed out.\(^{[16]}\) A vast majority of these errors reported in our study involved the administration of oral syrups. In our setting, in some circumstances, parents are requested to administer oral syrups to their infants, and the parents may fail in providing the correct dose. This highlights the need to educate and motivate patient relatives who could in turn equally take part in the treatment process.

Direct oversight by staff could also prevent such errors but requires more man power which becomes a challenge in low-resource settings or a busy NICU. Another unique challenge in neonates is that they have frequently changing needs of prescription in terms of dose and frequency according to their gestational age and day of life. Thus, wrong dosage and wrong frequency were the two main types of administrative errors noted in our study as caregivers followed previous prescriptions. This could be addressed only by strictly verifying the doctor’s order every time a drug is administered.

Administration errors are more common because a good quantum of patient care provided by any health-care facility involves the administration of some treatment which predominantly involves medications.\(^{[17]}\) This scenario is in contrast to the one which has been reported from developed countries. An analysis of a voluntary, anonymous, internet-based reporting system for medical errors from 54 hospitals in the USA had reported that 47% of the MEs were due to prescription errors whereas administration errors were only 14%.\(^{[18]}\) A similar analysis was not possible in our study as only 16% were voluntary reports.

Lack of sophisticated Health Information Technology (HIT) systems in our setting such as e-prescribing systems, CPOE, and bar-coded electronic Medication Administration Record has resulted in the majority of the error being at the level of drug administration,\(^{[19–21]}\) and in our system, it is mostly the nursing staff who administer the drugs. It is said that nurses spend 40% of their time in medication administration.\(^{[22]}\) It is because of these compelling reasons; our study invariably shows that majority of the MEs (81.6%) were caused at the level of nurses. However, none of the errors reported in our study were due to administration of a medication to a wrong baby though misidentification errors are more common in NICU.\(^{[23]}\) Administration errors could be best checked by direct observation when compared to chart reviews or anonymous ME-reporting systems. A trained nurse practitioner present in the NICU would be ideal for direct observation, but the challenge lies in training them adequately and the costs involved in doing so.\(^{[19]}\) Further research is warranted in an Indian setting whether HIT would do any good in reducing MEs. However, costs to set up HIT are a major limiting factor, especially in small- and medium-sized hospitals or not-for-profit hospitals as it involves high initial setup costs, followed by recurring coordination costs, monitoring costs, and governance costs.\(^{[24]}\) A study conducted in 24 hospitals in Tamil Nadu, India, has reported that hospital management information systems have high cost and high effectiveness with an incremental cost-effectiveness ratio of 3301.33.\(^{[25]}\)

The next common erring steps after administration errors in our study were prescribing errors (18%) and dispensing errors (4%), both of which can be averted with the help of a trained pharmacist attending the rounds. The MEs by pharmacists were quite low as it is difficult to pick them by chart review, and the nurses would proceed to give the wrongly dispensed drug without realizing. Furthermore, pharmacists in India have a small role to play by merely supplying commercially available medicines without having the need to prepare and dispense. However, a pharmacist trained in pharmacotherapy would be able to recommend medication doses, their frequency, and monitoring parameters for the patient.\(^{[19]}\) A study done in the USA evaluating the efficacy of a full-time clinical pharmacist attending rounds with physicians in an ICU brought down the number of preventable adverse events by 66%, suggesting their beneficial role in ICUs.\(^{[26]}\)

With regard to the determinants of ME in our setting, we found that place of birth whether inborn (born in the hospital attached to the NICU) or referred from outside, duration of stay more than a week, and polypharmacy (≥5 drugs per prescription) were significantly associated with ME. Hospitalization

### Table 2: Determinants of medication error in neonatal intensive care unit

| Variable                              | Univariate analysis | Multivariate analysis* |
|---------------------------------------|---------------------|------------------------|
|                                       | Unadjusted OR       | P                      | Adjusted OR (95% CI)   | P          |
| Gender                                | 0.855               | 0.597                  | 1.013 (0.600–1.709)    | 0.962      |
| Birth weight                          | 1.773               | 0.007                  | 2.592 (1.217–5.521)    | 0.014      |
| Inborn/out born                       | 1.789               | 0.055                  | 1.335 (1.198–1.488)    | <0.001     |
| Duration of stay (>7 days)            | 1.397               | <0.001                 | 4.126 (1.917–8.880)    | <0.001     |
| Polypharmacy (>5 drugs/prescription)  | 8.808               | 0.014                  |                        |            |

*Variables with \(P<0.20\) in univariate analysis were only considered. \(OR=\) Odds ratio, \(CI=\) Confidence interval
of more than 1 week in NICU increases the odds of experiencing a ME by nearly 34% (95% CI: 20%–49%), and polypharmacy almost quadruples the chance of ME occurrence (adjusted odds ratio: 4.126, 95% CI: 1.917–8.880). We also found that babies born elsewhere being referred to our institution were at a higher risk of experiencing a ME. This is probably due to other factors such as maturity of the baby with regard to its gestational age and the severity of illness that come into play[27] which were not accounted for in our study.

Limitations of our study include MEs being assessed only on 3–4 days a week. The work experience of the health-care personnel in an NICU as a determinant for ME was not evaluated as anonymity of erring person was strictly maintained to promote self-reporting of MEs. Due to the same reason, we were also not able to assess the workload of various cadres of staff which is another strong risk factor for occurrence of ME. The role of Hawthorne effect cannot be ruled out as the staff were aware that the study on ME was ongoing.

Conclusion

The prevalence of ME in our setting was moderately high, with 22% of all babies evaluated having experienced at least one ME though only 2% were life threatening. MEs occurred mostly during drug administration (77%). Longer duration of stay and polypharmacy were significantly associated with occurrence of ME. Despite the availability of a multistage check system comprising the senior consultants, head nurse, and the pharmacists, it is challenging to maintain a good quality of care in an NICU setup warranting for more interventions to reduce ME in order to enhance the quality of care. HIT has proved to be very efficient in the west. However, the feasibility and affordability of such technology in a developing country like India is questionable. Therefore, till more efficient systems are set up, awareness and education of ME along with a ME surveillance program is the need of the hour.

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Conflicts of interest
There are no conflicts of interest.

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