Compliance to Prescription of Routine Vitamin D Supplementation in Infants

We assessed compliance to routine vitamin D supplementation in 330 infants (age 6 wk to 9 mo), who were prescribed supplementation at birth. 137 (41.5%) had received vitamin D supplementation at some point of time till enrolment. Median (IQR) compliance to routine vitamin D supplementation was 66.7% (50%, 83.3%) in those who ever received supplementation. Only 29 (8.8%) were receiving appropriate routine vitamin D supplementation in terms of dose, frequency and duration. There was low level of reinforcement (35%) from healthcare workers and low parental awareness (34%) of the need of supplementation.

Keywords: *Adherence, Guidelines, Prevention, Rickets.*

Routine daily vitamin D supplementation in infants is recommended by the Global consensus on rickets prevention, American Academy of Pediatrics and the Indian Academy of Pediatrics [1-3]. However parental adherence is key to its success, which has been shown to be sub-optional worldwide, resulting in poor outcome of the supplementation [4-8]. There is no relevant Indian data. We conducted this survey to estimate the proportion of infants adhering to prescription of routine vitamin D supplementation between birth and 9 months of age.

This cross-sectional study was conducted in the department of pediatrics of a public medical college-affiliated hospital in Delhi. An approval from the institutional ethics committee was obtained. Considering parental adherence of 68.9% [4], with alpha error of 5%, absolute precision of 5%, and confidence level of 95%, 330 mother-infant pairs were required to be enrolled. Healthy infants between 6 weeks to 9 months of age, who were prescribed vitamin D at birth, were recruited from the immuni-zation clinic, after obtaining written informed consent from the mother. We included only those infants who were born in a health facility and having documents showing prescription of vitamin D at birth. The hospital policy is to prescribe routine vitamin D supplementation at the time of discharge from the health facility at birth. Term and preterm infants are prescribed 400 IU and 800 IU vitamin D, to be given daily till 12 months of age, irrespective of mode of feeding. No specific measures for reinforcement of supplementation are in place on follow-up.

Baseline socio-demographic information was recorded. Mothers were asked whether they are still providing routine vitamin D supplementation to their infant. If not, whether they administered vitamin D to their child at any time and if yes, for how long along with the dose. Compliance was the duration for which supplementation was given as a proportion of the duration of prescription till enrolment. We also ascertained the proportion of infants who had received oral vitamin D supplementation (400 IU) in last 7 days and in previous month, to minimize recall bias.

Parental understanding of the prescription was also assessed for their knowledge regarding total duration for which they needed to give the supplement. Parents were asked whether they were explained verbally by the healthcare worker about routine vitamin D supplementation, the reason for its requirement and method to give it; and whether they received reinforcement for same in their subsequent health visits, if any. They were asked whether they received vitamin D from the health facility, or it incurred out of pocket expenditure. In case of non-compliance of the prescription, the parents were asked for the reason. After the interview, mothers were advised to follow routine supplementation of vitamin D, if they were not giving it earlier. The practices of routine vitamin D supplementation were compared between groups using chi square test. Compliance was compared between groups using the independent samples Mann-Whitney U test. A P value of <0.05 was considered statistically significant.

We interviewed 330 mothers between March and August, 2019. The median (IQR) age of their infants was 3.5 (2.5, 6) months, 190 (57.6%) were <6 months of age, and 180 were boys. Majority of mothers were literate (288, 87.3%) and home-makers (307, 95.5%). Most families (233, 70.6%) belonged to lower socioeconomic strata; 85 (25.8%) were from middle socioeconomic group. Most (300, 91%) infants were born at term, 117 (35.5%) were low birthweight and 36 (10.9%) had required admission in neonatal intensive care unit (NICU) at birth. The study population did not have any infant with active rickets.

Overall, 137/330 (41.5%) infants received vitamin D supplementation at some point of time till enrolment; median (IQR) duration of vitamin D supplementation in 137 infants was 60 (30, 105) days. Only 52 (15.8%) children were receiving vitamin D continuously for 7 days in the last week. Thirty-six (26.3%) of those practicing routine supplementation (n=137) did not receive vitamin D in last 7 days, and 25 (18.3%) did not receive it anytime over last one month. Median (IQR) compliance to routine vitamin D supplementation in these 137 infants was 66.7% (50%, 83.3%). Only 29 (8.8%) infants were receiving appropriate routine vitamin D supplementation in terms of dose, frequency and duration. A significantly higher proportion of preterm infants and NICU graduates received vitamin D supplementation (ever, within 7 days and within 4 weeks) as compared to term and those not requiring NICU care, respectively (***Table* I**). The compliance was also significantly higher in preterm and NICU graduates. There were no significant differences in supplementation practices or compliance according to gender or feeding status.

Table I Adherence to Routine Vitamin D Supplementation in Infants (*n*=330)

Category	*Ever received vitamin D*	*Received vitamin D in last 7 days*	*Received vitamin D in last 4 weeks*	*Compliance (%) Median (IQR)*
Gender				
Male (*n*=180)	71 (39.4)	50 (27.8)	57 (31.7)	66.7% (60.0%, 77.5%)
Female (*n*=150)	66 (44.0)	51 (34.4)	55 (36.7)	66.7% (66.7%, 81.5%)
P value	0.47	0.27	0.34	0.71
Gestation				
Preterm (*n*=30)	25 (83.3)	20 (66.7)	19 (63.3)	83.3% (66.7%, 85.7%)
Term (*n*=300)	112 (37.3)	81 (27.0)	94 (31.3)	66.7% (50%, 82.2%)
P value	<0.001	<0.001	<0.001	0.026
Admission history				
NICU (*n*=36)	31 (86.1)	26 (72.2)	27 (75.0)	80% (66.7%, 86.6%)
Non-NICU (*n*=294)	106 (36.1)	75 (25.5)	86 (29.3)	66.7% (50%, 83%)
P value	<0.001	<0.001	<0.001	0.020
Mode of feeding				
*Exclusively breastfed (*n*=190)	94 (49.5)	72 (37.9)	83 (43.7)	66.7% (50%, 85%)
Mixed fed (*n*=65)	24 (36.9)	20 (30.8)	20 (30.8)	66.7% (65.7%, 84.4%)
P value	0.08	0.30	0.07	0.43

*Values in no (%) except where stated otherwise; Compliance is calculated for infants who have ever received vitamin D supplementation (n=137). *Mode of feeding is depicted for infants <6 months age; compliance in this category is calculated for infants <6 months who ever received vitamin D supplementation (n=118).*

Of the 137 mothers who administered vitamin D to their infants, only 67 (49%) had understanding of correct duration of supplementation requirement. Verbal explanation regarding routine vitamin D supplementation at initial discharge after institutional delivery was reported by 115 (35%) mothers. Reinforcement during previous follow-up healthcare visits was reported by 74 (22.4%) mothers. Overall, 111 (33.6%) mothers were aware about routine supplementation. Most parents (98%) incurred out-of-pocket expenditure for supplementation.

Perrine, *et al*. [5] reported that even the educated parents from USA fared poorly in adherence, which was 10.5% in exclusively breastfed and 8.5% in mixed-fed younger infants. In another study from USA, only 15.9% of breastfed infants received routine supplementation [6]. Overall, 27.1% of US infants in 2009-2016 met vitamin D intake guidelines and there was no increase in proportion of infants who meet the guidelines over 5 years [7]. In 2011, a study in Poland showed 82.1% and 60.2% of infants aged 6 and 12 months, respectively, received daily vitamin D supplementation [8]. In 2017, a study in 29 European countries collectively reported good (≥80% of infants), and low adherence (<50%) by 59% and 10% (3/29) countries, respectively [9].

It is important to identify factors contributing to non-compliance. It appears that providing the drug and information, and monitoring adherence at surveillance visits could be important factors. Previous studies have suggested to reinforce parental education regarding supplementation and methods for reducing forgetfulness in mother; and identification of risk factors for poor compliance in the subsequent health visits to improve the outcome of routine supplementation [4,9]. It is possible that better supplementation practices and better compliance in infants born preterm and NICU graduates in our study were the result of reinforcements they received through more frequent follow-up in dedicated high-risk neonatal clinics.

This had limitation of being a single center study, with probability of recall bias. Further research on identifying the factors and finding remedies thereof are needed to improve adherence to routine daily supplementation of vitamin D to infants. It is important to note that this low compliance may offset the projected gains, based on 70% prescription rate by the pediatricians in the same setup [10]. Results from different regions, and preferably cohort studies, will provide more robust date to guide practice and policy.

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Olanzapine for the Treatment of Breakthrough Vomiting in Children Receiving Moderate and High Emetogenic Chemotherapy

The efficacy of olanzapine (mean dose 0.09 mg/kg/dose) was evaluated in 31 children 2-18 years of age, for chemotherapy induced breakthrough vomiting. Among 42 chemotherapy blocks with emesis, complete and partial responses were observed in 34 (80.9%) and 6 (14.3%) blocks, respectively, while 1/31(2.4%) patient had refractory vomiting. Mild sedation and transient transaminitis were the observed side effects.

Keywords: *Anti-emetic, Emesis, Malignancy, Vomiting.*

Chemotherapy induced vomiting (CIV) has been shown to have a detrimental influence on quality of life and treatment compliance of patients [1]. Despite the use of novel anti-emetics, breakthrough CIV can occur in 30-40% of children receiving moderate or highly emetogenic chemotherapy (MEC/HEC) [2,3]. There is paucity of data regarding choice of optimum agent and management of breakthrough CIV in children [3]. The present study was planned to demonstrate efficacy and safety of olanzapine in the treatment of breakthrough vomiting in children receiving MEC or HEC.

This observational study was conducted over a period of 6 months in children aged 2-18 years, receiving MEC or HEC who developed breakthrough emesis on protocol-defined prophylaxis, as described previously [4]. Institutional ethics committee approval and written informed consent from parents were obtained. The dose of oral olanzapine was 0.05-0.1 mg/kg/dose (maximum 5 mg/dose) once in every 24-hour period for 3 days, regardless of duration of chemotherapy block or subsequent response. The dose was rounded off to the closest half or full tablet of commercially available preparations of 2.5 mg and 5 mg strengths. Laboratory investigations included complete blood count, liver and kidney function at screening and before each cycle. Each episode of vomiting and treatment related adverse events like sedation and transaminitis were recorded as per the Common terminology criteria for adverse events ver 4.03, for atleast 5 days [5].

The primary outcome was an assessment of response for 5 days from the first dose of olanzapine. Complete response (CR) was defined as no emetic episode and use of no other rescue medications. Partial response (PR) was if patient had 1-2 emetic episodes with no use of rescue medications, and failure (refractory) if patient had more than 2 emetic episodes and/or use of rescue medications. Rescue drugs were permitted as per physician's discretion (commonly metoclopramide). Data were analyzed using IBM SPSS version 23.0, using standard physician's statistical methods.

During the study period, 108 (median age 9.2 years) pediatric cancer patients received 412 blocks of MEC and HEC. A total of 31 (31.8%) patients and 42 (10.1%) chemotherapy blocks were associated with breakthrough emesis. Eleven patients had breakthrough emesis in more than one block. Demographic data of patients is shown in ***Table* I**. The mean (range) olanzapine dose was 0.09 (0.04-0.15) mg/kg/dose.

Complete and partial responses were observed in 34 (80.9%) and 6 (14.3%) chemotherapy blocks, while 1 (2.4%) patient had refractory vomiting. One patient did not receive the