

## Short Communication

# Palatability of Vitamin D<sub>3</sub> Preparations Modulates Adherence to the Supplementation in Infancy

Fosca Pronzini<sup>1</sup>, Federica Bartoli<sup>1</sup>, Federica Vanoni<sup>1</sup>, Teresa Corigliano<sup>1</sup>, Monica Ragazzi<sup>1</sup>,  
Piero Balice<sup>1</sup>, Mario G. Bianchetti<sup>1</sup>

<sup>1</sup>Department of Pediatrics, Mendrisio and Bellinzona Hospitals, and University of Bern, Switzerland

### Introduction

The consequences of vitamin D deficiency can be severe. It is therefore recommended that Swiss infants have a minimum intake of 10 µg of vitamin D<sub>3</sub> per day during the first 12 mo of life (1). For this purpose they are prescribed an “alcoholic” preparation that contains vitamin D<sub>3</sub> (1).

Infants given preparations containing vitamin D<sub>3</sub> either dissolved in alcohol or in peanut oil very much prefer the “oily” form (2). As a consequence, beginning on the first of January 2005, we replaced the traditional “alcoholic” vitamin D<sub>3</sub> formulations and replaced it with the peanut oil formulation.

There are conflicting data concerning whether palatability is important for adherence to the recommended regimen of care and persistence with it over time (3, 4). The adherence to the supplementation with vitamin D<sub>3</sub> was therefore compared in Swiss infants prescribed either “alcoholic” or “oily” vitamin D<sub>3</sub>. A preliminary account of the results obtained in infants prescribed “alcoholic” vitamin D<sub>3</sub> has been published elsewhere as a letter (5).

### Subjects and Methods

One hundred forty Swiss infants ranging in age between 4 and 7 mo who presented at our emergency room with minor acute diseases entered the study. The infants were prescribed 10 µg vitamin D<sub>3</sub> per day either as “alcoholic” vitamin D<sub>3</sub> (Vi-De3: Wild AG, Basel, Switzerland; 113 µg/ml [= 2.5 µg/drop] vitamin D<sub>3</sub> dissolved in 65% ethanol) or “oily” vitamin D<sub>3</sub> (Oleovit D3: Fresenius Kabi AG, Bad Homburg, Germany; 450 µg/ml [= 10.0 µg/drop] vitamin D<sub>3</sub> dissolved in peanut oil).

Informed consent from the families and approval of the protocol by our institutional review board were granted for this not commercially sponsored study. The inquiry was performed between October 2003 and March 2004 with 70 infants prescribed four drops daily of “alcoholic” vitamin D<sub>3</sub> (5) and between October 2005 and March 2006 with 70 infants prescribed one drop daily of “oily” vitamin D<sub>3</sub>. The parents of the infants anonymously completed a written questionnaire containing 3 closed-ended questions dealing with the vitamin D<sub>3</sub> supplementation. The questions focused on the adherence to the recommended vitamin D<sub>3</sub> supplementation during the preceding month [possible answers: a) never, i.e. less than once a week, b) 1–3 times a week, c) 4 times a week or more], the recommendations given by health care providers [possible answers: a) adequate recommendation, b) inadequate recommendation],

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Correspondence: Dr. Mario G. Bianchetti, Department of Pediatrics, San Giovanni Hospital, 6500 Bellinzona, Switzerland

E-mail: mario.bianchetti@pediatrician.ch

**Table 1** Demographic characteristics of children enrolled and their families

	“Alcoholic” vitamin D <sub>3</sub> group	“Oily” vitamin D <sub>3</sub> group
N	70	70
Gender, Male : Female	37 : 33	39 : 31
Age*, weeks	22.2 [20.1–28.0]	21.4 [19.8–25.0]
Parental educational level		
Low, N	50	46
Middle, N	13	15
High, N	7	9
Families with at least one older child, N	37	41
Milk nutrient source		
Breast milk, N	25	29
Formula Milk, N	29	26
Breast and formula milk, N	16	15
Parent filling the questionnaire		
Father	5	6
Mother	51	54
Both	14	10

\* Median and interquartile range.

and the taste-elicited reaction of the child to the administration of vitamin D<sub>3</sub> [possible answers: a) favorable, b) unfavorable].

The adherence to the supplementation with vitamin D<sub>3</sub> was considered good in families using vitamin D<sub>3</sub> four times a week or more and poor in families using vitamin D<sub>3</sub> three times a week or less.

Parental educational level was used as an indicator of socioeconomic background and classified as low (pre-primary, primary and lower secondary education), middle (upper secondary education), and high (post-secondary education).

The Mann-Whitney-Wilcoxon test and the  $\chi^2$ -test with the Yates correction for continuity were used for analysis. A P value of <0.05 was regarded as statistically significant.

## Results

Sex ratio, age, the socioeconomic status and the main nutritional source were similar in the “alcoholic” vitamin D<sub>3</sub> group and the “oily”

vitamin D<sub>3</sub> group. More than 90% of the 140 questionnaires were answered by the mother, with or without the father of the child (Table 1).

The adherence to the recommended supplementation with vitamin D<sub>3</sub> was poor in 36 of the 70 families prescribed the “alcoholic” vitamin D<sub>3</sub> (four drops daily) formulation: 20 never used vitamin D<sub>3</sub> and 16 used it one to three times a week (Table 2). The remaining 34 families used vitamin D<sub>3</sub> four times a week or more. A better ( $P < 0.001$ ) adherence was noted in the “oily” vitamin D<sub>3</sub> group (one drop daily), as indicated by the fact 54 families used vitamin D<sub>3</sub> four times a week or more. Eleven families used “oily” vitamin D<sub>3</sub> one to three times a week, while 5 families never used “oily” vitamin D<sub>3</sub>. A certain number in both the “alcoholic” vitamin D<sub>3</sub> group (18 out of 70 families) and the “oily” vitamin D<sub>3</sub> group (16 out of 70 families) stated that health care providers rarely failed to recommend or encourage the appropriate vitamin D<sub>3</sub> supplementation. Parents of children prescribed “alcoholic” vitamin D<sub>3</sub> more frequently

**Table 2** Adherence to the supplementation with vitamin D<sub>3</sub>, recommendations given by health care providers, and taste-elicited reaction (= "palatability") of the vitamin D<sub>3</sub> formulations

	"Alcoholic" vitamin D <sub>3</sub> group	"Oily" vitamin D <sub>3</sub> group
N	70	70
Adherence to the recommendation		
Never, N	20	5
1–3 times a week, N	16	11
4 times or more a week, N	34	54*
Recommendations by care providers good, N	52	54
"Palatability" poor, N	46	9**

\* P<0.001 respectively \*\* P<0.0001 versus alcoholic vitamin D<sub>3</sub>

(46 versus 9; P<0.001) reported an unpleasant taste-elicited reaction in their children as compared to children prescribed "oily" vitamin D<sub>3</sub>.

The taste-elicited reaction to vitamin D<sub>3</sub> was more often reported as unfavorable (P<0.001) in families with poor (32 out of 52 families) than in those with good adherence (23 out of 88 families) to the supplementation.

Six families of the "alcoholic" vitamin D<sub>3</sub> group with poor adherence to the supplementation spontaneously reported in the footnote of the questionnaire, their concern in relation to the content of ethanol in the vitamin D<sub>3</sub> preparation. On the other hand within the "oily" vitamin D<sub>3</sub> group, 5 families with at least one older child spontaneously reported in the footnote of the questionnaire the preference of their child for the "oily" vitamin D<sub>3</sub> as compared to that of the "alcoholic" vitamin D<sub>3</sub> that had been prescribed in the past for their older infants.

The parental educational level and the milk nutrient source of the children did not affect the results of the inquiry.

## Discussion

Poor adherence to the recommended regimen of care is a recognized problem in the pediatric populations (3, 4, 6). In the present inquiry the

reported non-adherence to the supplementation with vitamin D<sub>3</sub> was less for infants prescribed the "oily" preparation than for those prescribed the "alcoholic" preparation. This result was significantly related to the reaction of the children to the prescribed vitamin D<sub>3</sub> preparation and perhaps even to irrational fears of side-effects related to the toxic potential of ethanol content of some vitamin D<sub>3</sub> preparations.

Understanding the prescribed medication regimen and acceptance of the need for adherence are central issues to enhance adherence to the recommended regimen of care (3, 4, 6). The results of the present inquiry indicate that health care providers very often recommended and appropriately encouraged the supplementation with vitamin D<sub>3</sub>.

There are conflicting data concerning whether children distinguish between different commercial preparations and, thus, whether palatability is important for adherence to the recommended regimen of care. For example in some studies children clearly disliked some suspensions, but adherence was not measured. On the other side some retrospective observations and the present study indicate that the unpleasant taste or rough texture have a negative influence on adherence (3, 4, 6). The problem with palatability studies might be the lack of a "gold standard" for taste. Furthermore the usefulness

of parental reports or facial hedonic scales in young children has been questioned. In our experience, however, simplified facial hedonic scales may be used to assess palatability among newborns and infants (2).

In addition to the unpleasant taste-elicited reaction of the child the poor adherence to the supplementation with the “alcoholic” formulation is also related to the fact that 10  $\mu\text{g}$  of vitamin  $\text{D}_3$  are contained in four drops of the “alcoholic” and in one drop of the “oily” formulation.

“Alcoholic” vitamin  $\text{D}_3$  formulations contain a negligible amount of ethanol (2). Nonetheless, the present data support the assumption that irrational concerns related to the toxic potential of ethanol contribute to poor adherence to the recommended medication. Data from the literature demonstrate an inverse relationship between adverse effects or fears of adverse effects and adherence to the recommended regimen, although this finding is not universal (3, 4, 6).

Approximately 50% and 75% of our parents reported that they were adherent with the prescribed supplementation with “alcoholic” vitamin  $\text{D}_3$  and “oily” vitamin  $\text{D}_3$ , respectively. It is important to stress, however, that parent's reporting of adherence is sometimes overrated, as indicated by the fact that in children with sickle cell disease the adherence with prophylactic penicillin administration reported by the parents was much higher than the effective adherence measured using pharmacy records [7].

In conclusion the causes of poor adherence are poorly understood and sometimes puzzling but the present data suggest that in infants prescribed vitamin  $\text{D}_3$  to prevent nutritional

rickets poor adherence is not related to the parental educational level or to the failure of health care providers to recommend or to appropriately encourage the supplementation. In our experience fears of adverse effects and especially the taste-elicited reaction of the child to the administered vitamin  $\text{D}_3$  influence adherence to the recommended medication.

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