Vitamin D depletion in pregnancy decreases survival time, oxygen saturation, lung weight and body weight in preterm rat offspring

Lykkedegn S[1,2], Sorensen GL[3], Beck-Nielsen SS[1,2], Pilecki B[3], Duelund L[4], Marcussen N[5], Christesen HT[1,2*]

[1]Hans Christian Andersen Children's Hospital, Odense University Hospital, Odense, Denmark. [2]Clinical Institute, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark. [3]Institute of Molecular Medicine, Department of Cancer and Inflammation, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark.[4] MEMPHYS, University of Southern Denmark, Odense, Denmark[5]Institute of Pathology, Odense University Hospital, Odense, Denmark.

CONCLUSION

Vitamin D depletion during pregnancy led to a lower SaO_2 and shorter survival-rate in premature rat offspring despite no reduction in lung surfactant constituents. Explanatory factors include reduced lung weight, implying a reduced total lung diffusion area, and decreased birth weight, which may indicate a reduced muscle mass leading to earlier muscular fatigue.

OBJECTIVES

1. To test if vitamin D depletion aggravates respiratory insufficiency in preterm rat offspring.
2. To asses the effects of vitamin D depletion on growth and lung surfactant production.

BACKGROUND

In vivo studies in rodents have shown that vitamin D deficiency during pregnancy causes alterations in lung growth and structure in term offspring. *In vitro* studies of cells from fetal rat lung explants have shown an effect of vitamin D on the embryogenesis and cellular growth and differentiation, including surfactant synthesis and secretion. Laboratory studies on human pulmonary adenocarcinoma-derived cell lines support these findings.

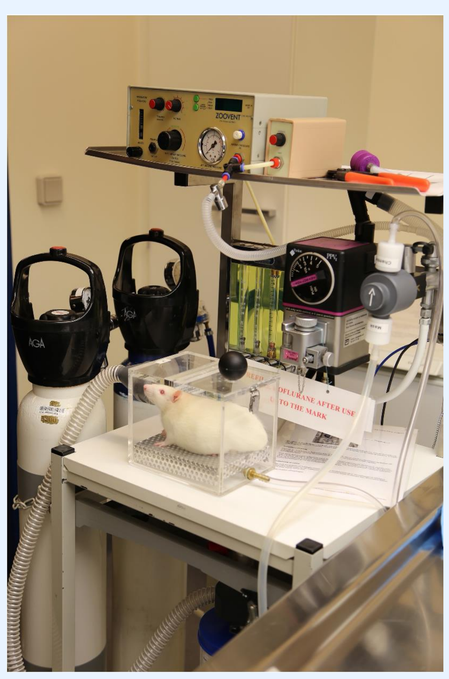
However, *in vivo* studies of the role of vitamin D in lung development in preterm offspring have not been performed.

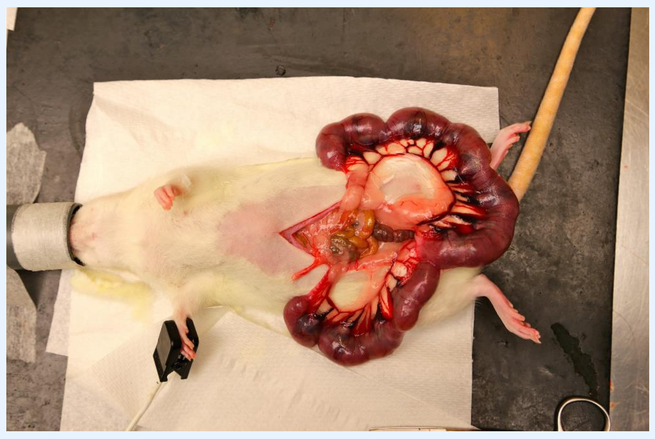
METHODS

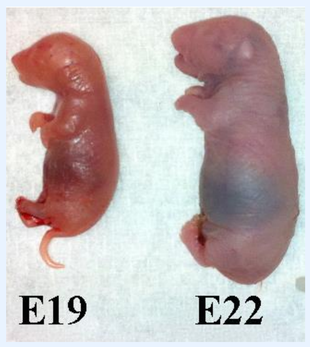
Female Sprague-Dawley rats were randomly assigned low vitamin D (VD_L) or control diet for at least 5 weeks before mating and followed with serum 25-hydroxyvitamin D (s-25(OH)D) measurements.

After cesarean section at gestational day 19 (E19) or day 22 (E22), placental weight (PW), birth weight (BW), crown-rump-length (CRL), oxygenation (SaO_2) at 30 min and survival time were recorded.

The lungs from the pups were analyzed for phospholipid levels, surfactant protein A-D mRNA and the expression of the vitamin D receptor (VDR).







RESULTS

- S-25(OH)D was significantly lower in the VD_L group at cesarean section (12 vs. 30nmol/L, p<0.0001).
- All mother rats achieved a weight gain during the experiment with no significant difference in gestational weight gain between the groups. At the cesarean section, no differences were observed in maternal SaO_2, the duration of maternal anesthesia or in the number of pups in each litter.
- When comparing preterm and term offspring in general, a significant difference was observed in all measurements (lung, birth and placental weights and CRL) as the results of maturation.

RESULTS etd.

- At E19, VD_L pups had a lower birth weight (2.13 vs. 2.29g, p<0.001), lung weight (0.09 vs. 0.10g, p=0.002), SaO_2 (54% vs. 69%, p=0.002) as well as reduced survival time (0.50 vs. 1.25h, p<0.0001) compared to the controls (fig. 1 and 2).
- At E22, the VD_L-induced pulmonary differences were leveled out, but VD_L pups had lower CRL (4.0 vs. 4.5cm, p<0.0001).
- The phospholipid levels and the surfactant protein mRNA expression did not differ between the dietary groups, nor did the expression of the VDR.

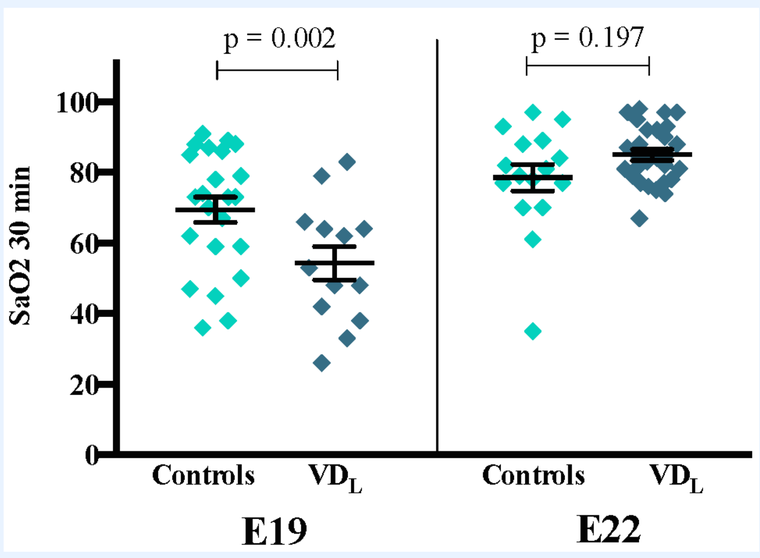


Fig. 1. SaO_2 measured in rat pups 30 minutes after birth. SaO_2 was measured 30 minutes after birth at E19 (VD_L group (n = 13); control group (n = 23)) and E22 (VD_L group (n = 28); control group (n = 16)). Within 2 minutes 3-5 measurements were made and the highest value of SaO_2 was used for analysis. Each measurement was finished within 10-15 seconds to avoid desaturation secondary to prolonged measurement.

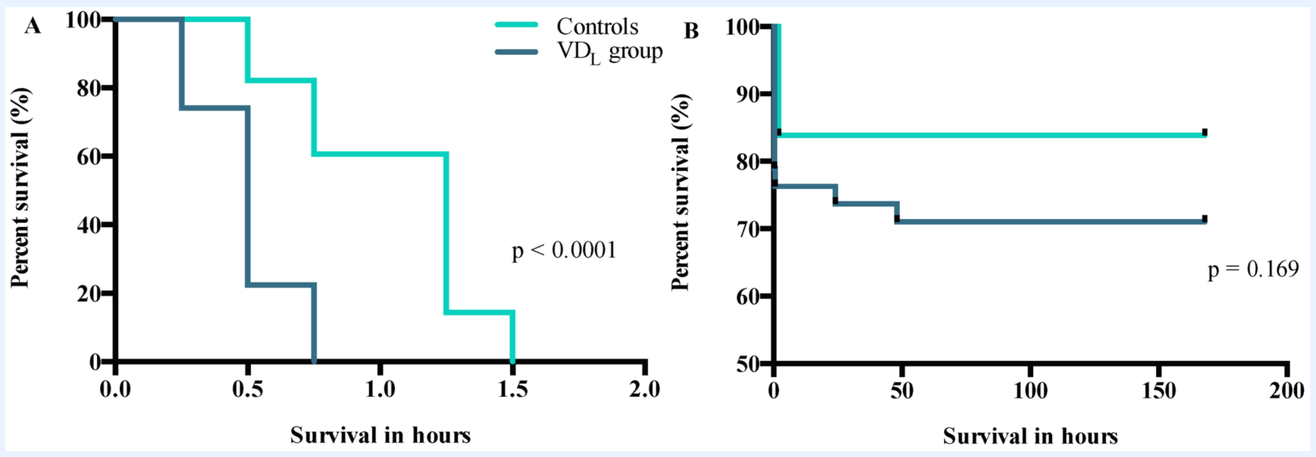


Fig. 2 Survival-rate in hours after birth. Kaplan-Meier survival analysis of both
A)E19 (VD_L group (n = 58); control group (n = 28)) and
B)E22 (VD_L group (n = 38); control group (n =31)) pups.

PERSPECTIVES

Our study emphasizes the value of animal models to study the effects of vitamin D on the lungs. Aggravation of respiratory failure may occur due to reduced lung and birth weight as the result of severe vitamin D depletion. However, we were unable to show a direct effect of vitamin D deficiency on surfactant measures or VDR expression.

Future studies should pursue to evaluate our results using an optimized version of our model with animals assigned to the diets immediately after weaning.

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HCA Research HANS CHRISTIAN ANDERSEN CHILDREN'S HOSPITAL

OUH Odense University Hospital

Region of Southern Denmark

UNIVERSITY OF SOUTHERN DENMARK.DK

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Sine Lykkedegn

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