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Indoor Climate and Air Quality in a Neonatal Intensive Care Unit

Published Version:
Availability:
This version is available at: https://hdl.handle.net/11585/776539 since: 2022-03-01
Published:
DOI: http://doi.org/10.1159/000508108
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Esempio citazione:

Wolf, M., Diehl, T., Zanni, S., Singer, D., Deindl, P. (2020). Indoor Climate and Air Quality in a Neonatal Intensive Care Unit. *Neonatology*, *117*, 453-459.

Abstract

Introduction and Objective: The skin and respiratory system of premature neonates are in permanent contact with indoor room air. We longitudinally analyzed the room air climate and quality in neonatal intensive care inside and outside an incubator. **Methods:** Sampling was performed in 2 patient rooms and inside a neonatal incubator (Caleo, Draeger Medical, Lübeck, Germany) over 6 weeks with 5-min resolution resulting in 12,090 samples (U-Monitor, U-Earth Biotech, London, UK). Temperature, humidity, and air pollutants, including particulate matter (< 1 µm [PM1] and < 2.5 µm [PM2.5]), volatile organic compounds (VOC), and odorous gases (OG), were recorded. Room air parameters were analyzed using time series analysis. A linear regression model was used to check for statistically significant linear trends. Statistical analysis was performed using decompensation of time series analysis and spectral analysis by fast Fourier transformation. Results: The indoor climate target values of the ward's central ventilation system for temperature and humidity were not always met. Room air parameters (PM, VOC, and OG) showed significant daytime-dependent fluctuations with different oscillation frequencies per day. The daily mean (first quartile – third quartile) concentrations of PM2.5 were significantly higher inside the incubator compared to the surrounding ambient air (2,158 [1,948–2,298] pcs/L vs. 2,018 [1,852–2,058] pcs/L; p < 0.001). OG were significantly lower inside the incubator compared to ambient air. VOC levels inside the incubator were substantially higher during the first 5 days of the observation period compared to VOC levels in the surrounding ambient air. Conclusions: The indoor climate of neonatal intensive care units should be monitored in real time to detect deviations from target parameters quickly. In our neonatal intensive care unit, indoor air quality fluctuated significantly depending on the time of day. We highly suspect that air pollutants are carried into the direct patient environment by visitors and medical staff. The incubator does not protect against PM and VOC exposure but reduces exposure to OG.

Cleaning procedures may lead to substantially higher concentrations of VOC inside the incubator and may represent a potentially harmful factor for premature infants.

Introduction

Premature neonates quickly lose a considerable amount of fluid and temperature in ambient air [1] due to skin immaturity and small subcutaneous fat deposits.

They are cared for in incubators in which temperature and humidity can be adjusted. The air sucked in by incubators is filtered to protect against coarse particles and microbial pathogens. The microclimate thus created can differ significantly from the ambient air [2]. Skin-to-skin care is now standard practice in neonatal intensive care units (NICUs) [3]. Therefore, preterm neonates find themselves either in an incubator or on the chest of the parents. In both cases, the compartment immediately surrounding the patient is air. The quality of the ambient air thus represents an important environmental factor, as air pollutants are proven to damage the human organism [4]. Indoor pollutants can be divided into chemical, biological, and physical substances. Organic air pollutants consist of particle-bound and volatile compounds. Particle pollutants are categorized as particulate matter (PM), artificial mineral fibers, asbestos, and microbial contaminants like fungi, bacteria, and viruses.

Aims

We longitudinally analyzed the indoor air quality in a NICU inside and outside an incubator.

Materials and Methods

Duration and Location of Air Measurements

The ambient air was analyzed over 6 weeks (April 26, 2016, to June 6, 2016) in 2 patient rooms (room A and room B) of our 15- bed NICU of the University Medical Center Hamburg-Eppendorf and inside an intensive care incubator (Caleo, Draeger Medical,

Lübeck, Germany). Both rooms are designed for the care of 4 patients in incubators and were used throughout the entire measurement period as in routine mode. The incubator was located in room B. The rooms had each a room air volume of 85 m³ and were supplied by a central ventilation system that allows limited regulation of the temperature and humidity with 1 supply air and 1 exhaust air duct per room. The target parameters for the NICU were 23 ° C for room temperature and 50% relative air humidity. The supply air passed through 3 filter stages. The fresh air supply of the building was via the attic and was filtered over an activated carbon filter. The target values of the incubator were 34 ° C air temperature and 60% relative humidity (see suppl. material). We used U-Monitors (U-Earth Biotech Ltd., London, UK) to measure room air quality in both rooms and inside an otherwise empty incubator as described before [5] (online suppl. material). Data were recorded every 5 min and transmitted via Wi-Fi to a software platform. We measured temperature, relative humidity, concentrations of PM fraction with a diameter $< 2.5 \mu m$ (PM2.5) and $< 1 \mu m$ (PM1), volatile organic compounds (VOC), and odorous gases (OG). We used data on outdoor temperature, relative humidity, and sunshine duration from the Hamburg air monitoring network (measuring station: Hamburg-Finkenwerder West).

Statistics

The R software version 3.5.2 (R Core Team, Vienna, Austria) was used for statistical data analysis. Room air parameters were analyzed using time series analysis. A linear regression model was used to check for statistically significant linear trends. Linear trends were tested for correlations with Pearson's product-moment correlation. For further analysis, the time

series were examined with the classical additive component model. If cyclic fluctuations were detected, a spectral analysis was carried out using a fast Fourier transformation (online suppl. material). Differences between groups were calculated using the median test.

Results

Data Acquisition

The data were recorded continuously for 42 days. For room B and the incubator, 12,090 measurements were available for analysis. Due to technical problems, 9 measurements in room A on day 19 were missing, resulting in 12,081 available measurements.

Temperature and Humidity

The average (first quartile – third quartile) temperature was $25.2 \,^{\circ}$ C (25.0–25.0) in room A and $25.9 \,^{\circ}$ C (25.0–25.0) in room B. The average (first quartile – third quartile) temperature measured in the incubator during the study period was $33.5 \,^{\circ}$ C (33.0–34.0). Only slight temperature fluctuations were recorded in both patient rooms as well as inside the incubator (Fig. 1a). There was no correlation between sunshine duration and indoor temperature (room A: r = 0.195, p = 0.22; room B: r = -0.01, p = 0.93). The mean (first quartile – third quartile) relative air humidity was 30.7% (25.0–37.0) in room A and 28.9% (23.0–35.0) in room B, which is significantly below the target value of 50% relative humidity. We detected a gradual increase in the relative humidity values during the measuring period in both rooms. Inside the incubator, the relative mean humidity was 55.3% (52.0–58.0) with no significant fluctuations over time (Fig. 1b).

Volatile Organic Compounds

The VOC concentrations showed short extreme peaks in all locations, which were 30–80 times above the average value. The analysis of the raw data showed that these extremely

short peaks were most likely measurement errors. The daily mean (first quartile – third quartile) VOC values over the entire recording period did not differ significantly between the incubator and the surrounding ambient air in room B (1.1 [0.35–1.3] ppm vs. 0.96 [0.27–1.14] ppm; p = 0.51). However, the concentration of VOC inside the incubator significantly dropped during the first 5 days of the recording (Fig. 2a; p < 0.001). The corrected R^2 estimated the proportion of the clarified variance at 85.2%. In contrast, the VOC concentrations in the ambient air showed no significant decrease (p = 0.24) over the same period (Fig. 2a). Fluctuation analysis showed statistically significant variations for the changes of VOC concentrations depending on the time of day (see suppl. material) with an oscillation frequency of 1 per day in both rooms and the incubator with the highest VOC concentrations at midday.

Odorous Gases

Inside the incubator (4.6 [2.0–5.4] ppm), significantly lower OG concentrations were measured compared to the ambient air in room A (11.3 [5.0–14.7] ppm) and room B (6.7 [3.3–13.2] ppm; p < 0.001) (Fig. 2b). The concentration of the OG fluctuated significantly more in both patient rooms than inside the incubator. Fluctuation analysis showed significant daytime-dependent fluctuations with an oscillation frequency of 1 per day in both rooms and the incubator with the highest OG concentrations at midday.

Particulate Matter

The PM concentration fractions PM1 and PM2.5 were similar in both patient rooms and inside the incubator (Fig. 2c, d). The daily mean (first quartile – third quartile) concentrations of PM1 did not differ significantly between the incubator and the surrounding ambient air (6,211 [5,079–6,864] pcs/L vs. 6,616 [5,009–7,336] pcs/L; p = 0.13). The daily mean (first quartile – third quartile) concentrations of PM2.5 were significantly higher inside the

incubator than in the surrounding ambient air (2,158 [1,948–2,298] pcs/L vs. 2,018 [1,852–2,058) pcs/L; p < 0.001). The PM1 fraction showed more substantial differences between the 2 patient rooms compared to the PM2.5 fraction (Fig. 2c, d). Fluctuation analysis of PM2.5 using a decomposition of time series analyses and fast Fourier transformation showed a statistically significant fluctuation depending on the time of day, both for the patient rooms and in the incubator. The oscillation frequency of PM2.5 in room B and inside the incubator was the same with 1 per day with the highest PM levels at midday. There was no correlation between the parameters PM2.5, PM1, VOC, and OG with temperature and humidity.

Discussion

We present data regarding the indoor air climate and quality in a NICU, which represents an important environmental factor for premature neonates. Our data show that room air parameters, including PM, VOC, and OG, are subject to clear and statistically significant fluctuations depending on the time of day and that the incubator does not protect against most air pollutants. Some of the substances are proven to damage the human organism.

Indoor Room Climate

The average temperature recorded over the recording period of 6 weeks was 25.2 °C in room A and 25.9 °C in room B, which is above the target temperature of 23.0 °C (Fig. 1a). The central ventilation system only allows a limited cooling of the indoor air. We suspected that solar radiation might have elevated the temperature as both patient rooms have large windows facing northwest. However, there was no correlation between sunshine duration and indoor temperature. The relative humidity of the indoor air was significantly below the target value of 50% over a long period (Fig. 1b), especially at the beginning of the recording. We assume that there was a technical problem with the central ventilation system. We conclude

from these observations that it is reasonable to monitor indoor climate parameters in NICUs continuously.

Exposure to VOC and Incubator Cleaning

The VOC concentration inside the incubator showed a remarkable drop during the first days of the recording. We measured values as high as 5 ppm at the beginning of the recording. The VOC concentration then fell within 4 days and persisted at a level of < 2 ppm. Even after adjustment for random effects and cyclical fluctuations, the drop of the VOC values in the incubator during the first 5 days was statistically significant (p < 0.001). We strongly suspect an association with the cleaning of the incubator with disinfectants. From our point of view, the common practice of incubator cleaning should, therefore, be reconsidered. Our data suggest that airing the incubator without a patient inside for a few days can significantly reduce exposure to potentially toxic VOC. Hygiene measures are of particular importance for premature babies due to the immature immune system with high susceptibility to infections [6].

WHO guidelines recommend hygienic hand disinfection before any direct patient contact [7]. In particular premature babies require intensive medical care and nursing, which results in higher consumption of disinfectants than in an intensive care unit for adults [8].

Usually, alcohol-based formulations are used. The Federal Environmental Agency in Germany states that a total concentration of VOC > 25 mg/m3, which corresponds to > 0.4 ppm (based on an assumed mean molecular weight of 150 μmol at 20 ° C and 1,013 mbar), can cause headaches and neurotoxicity [9]. We measured VOC concentrations that significantly exceeded this limit over long periods. Hsieh et al. [10] reported high concentrations of VOC inside the incubator after hand disinfection with an alcohol-based disinfectant solution. The significance of VOC exposure from disinfectants for premature

infants is unclear. Dales et al. [11] report an association of VOC exposure with asthma symptoms and lung function parameters in children. In a German birth cohort study, a high VOC exposure during pregnancy was associated with a changed cytokine profile of T cells in cord blood [12]. Chang et al. [13, 14] found that higher VOC exposure during pregnancy resulted in lower birth weights and a worse neurocognitive outcome of the children. Franck et al. [15] showed a correlation between increased prenatal VOC exposure resulting from renovation work and respiratory symptoms in children during the first 12 months of life.

Daytime-Dependent Fluctuations

We observed significant daytime-dependent fluctuations of indoor air quality with different oscillation frequencies per day. VOC and OG had an oscillation frequency of 1 per day, with the highest values around noon. The PM values showed either 1 or 2 maxima per day, depending on the location. Figure 3 shows the mean concentrations of air pollutants on a typical day and the nurses' shift times. VOC, OG, and PM concentrations visibly increased at the beginning of each shift. In our NICU, medical procedures (rounds, blood sampling, catheterization) and cleaning are mainly performed in the morning.

The visiting hours are mainly in the afternoon. Our results suggest that air quality fluctuations are highly probable due to the changing number of persons in the room. The different times of the daily maximum values of PM, VOC, and OG suggest that these substances enter the patient rooms by different routes (Fig. 3). Our results are in line with a study by Licina et al. [16] that also reports significant PM fluctuations in an NICU depending on the time of day.

The Incubator as a Protective Environment

The incubator is often perceived as a protective shield that shelters the premature baby from stressors and harmful environmental influences. The spatial separation as well as the filtering of sucked-in air support this perception. Unfortunately, our data show that this perception

does not apply to essential air pollutants. Only the concentration of OG was significantly lower inside the incubator than in the ambient air. The PM concentrations in the incubator were the same (PM1) or even higher (PM2.5) compared to ambient air. Further studies should address the distribution of air pollutants inside and outside incubators to improve technical solutions for filtering. Our data strongly suggest that air pollutants are brought into the immediate environment of premature neonates by staff and visitors and raise the question of whether exposure to air pollutants is causally related to the number of visitors in a NICU. PM pollution inside the incubator could potentially be due to an insufficient filter technology of the incubator. After cleaning the incubator with disinfectant agents, sufficient time should be allowed for aeration to reduce the exposure of premature infants to VOC. Given the high relevance of indoor air quality for the health of staff and patients, the technical implementation of indoor air monitoring should be considered when planning new NICUs or renovating existing buildings.

Limitations

We analyzed indoor air pollutants in a NICU in 2 different patient rooms and inside an incubator over 6 weeks. We did not perform comparative measurements in adjacent rooms, the corridor, and in the outside air. Also, we did not measure the density of staff and visitors. Due to the size of the measuring instrument and to protect patients from potential harm, we performed the measurements in an empty incubator. During the study period, the opening flaps of the incubator remained closed, whereas, under real conditions, the flaps are opened several times a day during nursing or medical procedures. The data were collected in only one NICU and, therefore, only allow limited conclusions for other settings. The standard for measuring fine dust in the outside air is the gravimetric measurement, which yields the

particle mass concentration in $\mu g/m3$ and for which EU limit values are available. We measured fine dust as particle measurements yielding the particle number concentration in pcs/L. Unfortunately, there are no standardized conversion algorithms between the units pcs/L and $\mu g/m3$. The definition of the total VOC exposure has so far been used very heterogeneously in the literature so that comparisons to other study results remain difficult

Conclusions

The indoor climate of a NICU should be monitored in real time to detect deviations from target parameters quickly.

In a NICU, indoor room air quality is subject to significant fluctuations depending on the time of day. Air pollutants are most likely introduced into the direct patient environment by visitors and medical staff. The incubator does not protect against exposure to PM and VOC; however, it reduces the exposure to OG. Cleaning procedures can lead to substantial concentrations of VOC inside the incubator.

Acknowledgments

We thank Sebastian Runge for the statistical analysis of the data and the entire NICU team for their support of the study.

Statement of Ethics

The ethics vote was waived because the ambient air measurements did not affect the care and treatment of the patients. None of the patients had any contact with the measuring device.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

Funding Sources

There was no funding for this study.

Author Contributions

M.W. carried out the indoor air measurements, helped discuss the data, and critically revised the draft manuscript. T.D. helped design the study, carried out the indoor air measurements, and gave substantial input for the manuscript draft. S.Z. advised and monitored the technical aspects of indoor air measurements and helped to discuss the data. D.S. had the idea for this study, developed the study design, and critically revised the manuscript draft.

P.D. analyzed and discussed the data, created the illustrations, and wrote the manuscript draft.

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- **Fig. 1**. Indoor and outdoor temperature, sunshine duration (a) and humidity (b) in both rooms and inside the incubator (placed in room B).
- **Fig. 2**. Volatile organic compounds (VOC) (a), odorous gases (OG) (b), particulate matter fraction $\leq 1 \mu m$ (PM1) (c), particulate matter fraction $\leq 2.5 \mu m$ (PM2.5) (d) over time in both rooms and inside the incubator (located in room B).
- **Fig. 3**. Daytime-dependent fluctuations on a typical day of volatile organic compounds (VOC) (a), odorous gases (OG) (b), particulate matter fraction < 1 μ m (PM1) (c), particulate matter fraction < 2.5 μ m (PM2.5) (d) in both rooms and inside the incubator. The values for a typical day were calculated by averaging all measurements at a particular hour of all days. The vertical lines mark the beginning of each nurse's shift.