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Influence of air quality on the results of in vitro fertilization attempts: A retrospective study

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ABSTRACT

Objective: To assess the influence of air quality on the results of IVF.
Study design: We performed a retrospective study on 292 patients who have undergone an IVF attempt from April 2012 to December 2015 in our French university hospital. Patients were included in the study if data on the air quality at home and at work were available and if they haven't been gone for more than 4 days in a month. Data were recorded during the 3 months before oocyte collection and 1 month after embryo transfer. Air quality measurements were obtained from the Observatoire Régional de l'Air en Midi-Pyrénées (ORAMIP) and concerned the levels of nitrogen dioxide (NO_2), ozone (O_3), particulate matter PM10 and SO_2 measured every day.
Results: Acute exposures to high levels NO_2 or PM10 were associated with lower results of IVF (ovarian response to stimulation, number of top embryos) while these parameters were enhanced when patients were exposed to high levels of O_3 during the first 2 months of folliculogenesis. These effects were found even for a short exposure (1 day).
Conclusions: Air quality has an impact on global health and also on the reproductive function and public and authorities must be aware of environmental protection.

Introduction

Air pollution is highly suspected to have a deleterious effect on human health at several levels. It has been implicated in cardiovascular diseases [1], strokes [2], respiratory diseases [3,4] such as lung cancer [5], childhood asthma [6] and atopic dermatitis [7]. Furthermore, perinatal exposure to polycyclic aromatic hydrocarbons (PAH), nitrogen dioxide (NO_2) and particulate matter (PM) has been demonstrated to have a negative impact on neuropsychological development in children [8].

Exposure to air pollution negatively impacts spontaneous fertility in animals [9,10]. Mohallem et al. found a significant decrease in the number of newborns and a significant increase in embryo implantation failure for in mice exposed to air pollution from the start of life [11]. Veras et al. reported a significant increase in the mating time and a significant decrease in the fertility index (number of pregnant females/total number of females) in mice exposed to pollution from automobile traffic [12].

In human Slama et al. and Nieuwenhuijsen et al. observed a significant link between a decrease in the fertility rate and an exposure to PM2.5 and NO_2 [13,14]. Dejmek et al. found a significantly negative association between fertility rates and SO_2 exposure [15]. Recently, a report from the Nurses' Health Study II cohort, a prospective from 116 430 female nurses, showed that the risk of infertility significantly increased for women living within 199 m of a major road compared to women living more away and that every 10 mg/m^3 increased in cumulative PM 2.5–10 increased the risk of infertility of 10% [16].

In assisted reproductive technologies (ART), Legro et al. have reported a deleterious effect of NO_2 on the live birth rate, mainly when the exposure took place during the implantation period [17]. Perin et al. found an increase in the miscarriage rate when women were exposed to high PM10 levels during the follicular phase [18,19]. However in these studies, exposure evaluation did not encompass the entire period of human follicular growth (about 2.5 months) but only the follicular phase [17–19] and did only take home address into account when measuring the exposure levels [17].

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The present study aimed to evaluate the impact of air pollutants both at home and work addresses throughout the entire folliculogenesis process (from initiation to ovulation) and the first steps of embryogenesis, using the human in vitro fertilization (IVF) model.

Materials and methods

Participants

Two hundred and ninety two couples undergoing an IVF attempt from April 2012 to December 2015 were included only once in the study, whatever the cause of infertility (mean age of women: 34.4 ± 4.4). Exclusion criteria were as follows: use of frozen gametes or embryos, absence from the usual workplace or place of residence more than 4 days in one month, and residence or workplace without air quality measurement. Only 292 out of 703 patients were therefore able to be included in the study.

Air quality measurements

Data were obtained from the Observatoire Régional de l'Air en Midi-Pyrénées (ORAMIP) and concerned the levels of NO_2, O_3, PM10 and SO_2 measured every day. Since the SO_2 levels were always lower than the detectable dose, they were not included in the study. PM2.5 measurements were not available.

Since in this area there are very few toxic industries, the main sources of pollutants are street and road traffic and house heating.

Since the effects of some pollutants have been reported biphasic [17], we have studied the results of air quality measurements during 4 periods as a function of the day of oocyte collection in order to cover the complete folliculogenesis and the implantation window: period 1: from 90 to 60 days before, period 2: from 60 to 30 days before, period 3: from 30 to 1 day before, period 4: from collection day to 30 days after. Exposure to pollutants during periods 1–3 were used to evaluate their effects on ovarian response, fertilization rate and the number of top embryos. Exposure during period 4 aimed to evaluate the effects of pollutants on ongoing pregnancy and implantation rates.

Since patients were excluded from the study if they were absent from the usual workplace or place of residence more than 4 days in one month, not all patients could be evaluated for all periods.

Evaluation of chronic exposure

To evaluate the effect of chronic exposure, the mean concentrations of NO_2, O_3 and PM10 was calculated for each period. Then patients were divided into 4 groups as a function of the 25th, 50th and 75th percentiles of the concentration of each pollutant.

Evaluation of acute exposure

Each day, air quality was classified as follows according to WHO recommendations [20]

For NO_2: good if $< 110\ \mu g/m^3$, medium to poor if $< 200\ \mu g/m^3$, bad if $\geq 200\ \mu g/m^3$,

For O_3: good if $< 105\ \mu g/m^3$, medium to poor if $< 180\ \mu g/m^3$, bad if $\geq 180\ \mu g/m^3$,

For PM10: good if $< 28\ \mu g/m^3$, medium to poor if $< 50\ \mu g/m^3$, bad if $\geq 50\ \mu g/m^3$,

Since the number of days with bad levels was low for NO_2 and O_3 (fewer than 5 days for each period), we have grouped the bad and medium levels into poor groups for the analyses.

The number of days per month of exposure to a specific level of a pollutant widely varied from a patient to another. For instance, the number of days with an exposure to PM10 levels between 28 and 34 $\mu g/m^3$ was 0 for 52 patients, 1 for 28, 2 for 24, 3 for 32, 4 for 17, 5 for 14, 6 for 8 and >6 for 19.

To evaluate acute exposure, patients were classified in the worst group if they had at least one day of exposure to high levels of pollutants during the period. Indeed, as shown in the results section, we found similar effects of pollution whatever the duration of exposure.

IVF procedures

The ovarian stimulation protocol was a long agonist protocol in 11% of cases and an antagonist protocol in 89%. ICSI was performed in 71% of cases. We found no difference in results as a function of stimulation protocols or fertilization method (IVF or ICSI).The number of embryos transferred was chosen as previously described [21].

The ovarian response was evaluated through the ratio of the number of oocytes collected to the mean number of FSH units administered daily [22].

The top embryos were defined as score 4 and 3 according to the classification of Giorgetti et al. [23].

Statistical analysis

Clinical data were extracted from the patient database used in the ART center.

Statistical analyses were performed using Statview software (SAS Institute, Cary NC, USA). Data are means ± SD in the text and means ± SEM in the figures. Comparison of percentages used χ^2 test and comparison of means the Student *t*-test or the Mann-Whitney test (2 groups) or the Kruskall-Wallis test (more than 2 groups), depending on the normality of data distribution.

The study was approved by Toulouse University Hospital's Clinical Research Ethics Committee (no 01bis-0516).

Results

The ovarian response to stimulation was sensitive to the level of chronic exposure to O_3 only during period 1 (90 –60 days before oocyte collection) (Fig. 1). This effect was not dose-dependent since women in the highest quartile of concentrations for chronic exposure to O_3 in period 1 had a similar ovarian response than women with a low chronic exposure while women in the 50–75 quartile of concentrations had a significantly higher ovarian response. In fact, the effect of O_3 appeared to be related to an acute exposure independently of the length of exposure. For instance, during period 2, a 1-day exposure had the same effect on ovarian response as a more than 7 days of exposure (respectively 0.063 ± 0.41 and 0.064 ± 0.050; NS). This was also true during period 2 although the level of chronic exposure to O_3 during period 2 did not affect ovarian response. Ovarian response was not influenced by chronic or acute O_3 exposure during period 3. It must be noted that the basal parameters (age, BMI, FSH, AMH, AFC, tobacco consumption, infertility duration, type of infertility) did not differ between the different groups of patients (Supplementary file 1). The number of top embryos was sensitive to the level of chronic exposure to O_3 only during period 1. Within period 1, the women in the 2 highest quartiles of chronic exposure to O_3 concentrations have more top embryos than those in the 2 lowest quartiles. Here again it seems than an acute exposure is involved since about one more top embryo is available in those acutely exposed to O_3 during period 1 ($p < 0.01$) or period 2 ($p < 0.05$). Top embryos number was not influenced by chronic or acute O_3 exposure during period 3.