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Full Length Research Paper

Relationship between sex hormones in patients with infertility and air pollution

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Recent studies have linked exposure to pollutants with disruptive action on the endocrine system and problems such as infertility, reduced male fertility, abnormal sexual development, among others. Due to extensive evidence indicating that human health may suffer adverse consequences from exposure to pollutants that interact with the endocrine system, this study investigated the effects of pollutants on sex hormone tests from male and female patients who were assisted by reproduction clinic of the specialties of the Faculty of Medicine of ABC. This quantitative, retrospective, descriptive cross-sectional study was done with data obtained from the records of Ambulatory Specialty of the Faculty of Medicine of ABC. Hormone tests such as follicle stimulating hormone (FSH), luteinizing hormone (LH), estrogen, progesterone, testosterone and prolactin were performed and they were evaluated with data of the pollutants: carbon monoxide (CO), ozone (O_3), sulfur dioxide (SO_2), nitrogen dioxide (NO_2) and particulate matter < 10 µg/m^3 (PM_{10}). Our results suggest that PM_{10} was responsible for the observed changes in the hormone prolactin, corroborating the concept that air pollution can have a disruptive action on human reproductive health.

Keywords: Hormones, Infertility and Pollution.

INTRODUCTION

Nowadays, air pollution represents one of the biggest problems of Public Health. It is associated to disorders that affect not only human beings but life of other animals and plants. With the advent of urbanization and growing of the cities, environmental contamination has increased dramatically (Castro et al., 2003).

This concern, however, is not recent. The harmful effects of air pollution have been more clearly discussed since the first half of last century, during episodes of high concentrations of pollutants such as those observed in the Meuse Valley in Belgium in 1930; in Donora, Pennsylvania in 1948; and London, England in the winter of 1952-1953 (Gouveia et al., 2003).

It is possible to consider pollutant as any substance present in the air and related to its concentration may be inappropriate, offensive or harmful to the health, causing inconvenience to the public welfare, damage to materials, fauna and flora or prejudicial to security, use and enjoyment of property and the normal activities of community (CETESB, 2009).

The level of air pollution is measured by the amount of pollutants in the air. National standards were established by IBAMA - Brazilian Institute of Environment and approved by CONAMA - National Environmental Council, through Resolution CONAMA 03/90 (CETESB, 2009).

In the group of pollutants that are broadly used as indicators of air quality, such as PM_{10}, O_3, SO_2, NO_2, CO, in this paper was considered the PM_{10} (particulate matter; diameter < 10 µg/m^3). PM_{10} is a set of pollutants made up of dust, fumes and all sorts of solid and liquid material which remains suspended in the atmosphere because of its small size (CETESB, 2009). The main sources of particle emission to the atmosphere are: vehicles, industrial processes, biomass burning, resuspension of soil dust, among other (CETESB, 2009).

Recent studies have linked exposure to pollutants with disruptive action on the endocrine system and problems such as infertility, reduced male fertility, abnormal sexual

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development, among others. The decline of semen quality observed in the past 50 years and the speed with which these changes have been verified corroborates the hypothesis that attributes the origin of these problems to environmental exposure rather than to the genetic causes (Meyer et al., 1999).

Due to extensive evidence indicating that human health may suffer adverse consequences from exposure to pollutants that interact with the endocrine system, this study investigated the effects of pollutants on sex hormone tests from male and female patients who were assisted by reproduction clinic of the specialties of the Faculty of Medicine of ABC.

METHODS

This quantitative, retrospective, descriptive cross-sectional study was done with data obtained from the records of Ambulatory Specialty of the Faculty of Medicine of ABC.

Thus, between January to December 2007, 1665 individuals seeking assisted reproduction services of Faculty of Medicine of ABC and underwent screening tests in that clinic were selected for this study. Socio-demographic data were also obtained from medical records.

Hormonal tests performed were: follicle stimulating hormone (FSH), luteinizing hormone (LH), estrogen, progesterone, testosterone and prolactin. Exclusion criteria were positive serology for HIV 1 and 2, hepatitis A, B, and C, HTLV, rubella, toxoplasmosis, cytomegalovirus, and CA 125 values equal to or above 35 IU / mL. Data of subjects over the age of 40 years for females and 50 years for males were also excluded resulting in a sample of 380 subjects.

At the same time, data from pollutants (CO, O_3, SO_2, NO_2 and PM_{10}) were obtained from the Environmental Sanitation Agency of the State of São Paulo - SP-CETESB that daily measures the ambient levels of those pollutants. The values of the pollutants were collected from monitoring stations in Santo André (2 stations), São Caetano (1 station), Mauá (1 station), São Bernardo do Campo (1 station), Diadema (1 station) and São Paulo (12 stations) covering areas near the region of Grande ABC.

The pollutants data were evaluated in terms of three, six and twelve months before the date of the hormone tests collection. Daily averages of pollutant for each period were related to the date of sample collection, the city of residence and the city where the pollutant was measured.

Descriptive analysis of all qualitative variables of the study were presented in terms of their absolute and relative values, and quantitative variables were presented in terms of its values of central tendency and dispersion, as well as their values of percentiles. Logistic regression analysis was performed for each pollutant separately. In the models the variables sex hormones (quartiles) were present. Furthermore, each independent variable was analyzed as described above.

RESULTS

Table 1 shows the descriptive analysis of socio-demographic data. Among the 380 subjects eligible for the study, the largest age group was 27-32 years (38.9%), with a mean of 30.24 ± 4.9 years in a group where the majority was female (79.5%).

As seen in table 1, 37.6% subjects lived in Santo André, 21.8% in São Paulo, 12.6% in São Bernardo do Campo, 10.5% in Mauá, 6.6% in Diadema, 2.4% in São Caetano do Sul and 8.4% in other cities with less than 1.1%.

Table 2 shows the descriptive analysis of hormone tests performed. Concerning the results of not normal hormone tests, the following percentages were observed: 45.0% for FSH, 6.7% for LH, 57.4% for estrogen, 84.7% for progesterone, 19.5% for testosterone and 14.3% for prolactin.

Table 3 presents retroactive data for the pollutant PM_{10} in relation to the date of the hormone tests collection. It was observed that the pollutant concentration remained constant over 12 months.

Logistic regression analysis was performed for each hormone tests with each measured period of the pollutant PM_{10} divided into quartiles. In this analysis no significant difference was observed.

In order to verify the relationship between air pollution and hormone tests, final multiple logistic regression model was used, and it was considered a significant level of 5% ($p < 0.05$, $p < 0.005$ and $p < 0.005$) for prolactin hormone test. Variables considered were the averages of the pollutant PM_{10} at 3, 6 and 12 months retroactive to the date of the examination, according to Table 4.

DISCUSSION

This is the first study that has evaluated the effects of exposure to pollutants in sex hormone levels in subjects who were assisted by reproduction clinic in the Grande ABC region.

It is a fact that pollutants affect human health. In our study we found that concentrations of prolactin were altered when related to particulate matter PM_{10}.

Maybe impact of climate change on air quality results in higher morbidy (Kristie et al., 2009). Such morbidities (pneumonia and influenza) have been reported as disease-related quality of air (Meyer et al., 1999; Nascimento et al., 2006; Kristie et al., 2009; martins et al., 2002).

Table 1: Descriptive analysis of socio-demographic data

PARAMETERS	N	%
Age (years)		
< 27	109	28.7
27 - 32	148	38.9
33 - 40	121	31.8
41 - 50	2	0.5
Gender		
Female	302	79.5
Male	78	20.5
City		
Santo André	143	37.6
São Paulo	83	21.8
São Bernardo do Campo	48	12.6
Mauá	40	10.5
Diadema	25	6.6
São Caetano do Sul	9	2.4
Other cities	32	8.4

Table 2: Descriptive analysis of sex hormones tests

TESTS	N	Not	Nor /Nor	% *	M	SD	Median	R.V. (F/M)**
FSH (mIU/mL)	329	148/109	45.00	9.76	6.53	5.90 [5.80–21.00] / [0.70 –1.00]	[F]/[M]	
LH (mIU/mL)	312	21/291	6.70	6.08	5.94	4.90 [0.00–17.00] / [0.80 –7.60]	[F]/[M]	
Estrogen (ng/dL)	61	35/26	57.40	48.57	63.44	36.50 [< 84.00] / [< 84.00]	[F]/[M]	
Progesterone (mIU/mL)	195	166/30	84.70	6.29	5.96	5.20 [0.48–1.72] / [0.27 –0.90]	[F/[M]	
Testosterone (ng/dL)	128	25/103	19.50	296.72	287.53	234.00 [< 81.00] / [> 245.00]	[F]/[M]	
Prolactin (ng/dL)	240	34/206	14.30	16.58	13.05	15.39 [1.90–25.00]/[2.50–17.00]	[F]/[M]	

* Percentage of not normal tests, **References values adopted in this study.

Table 3: Descriptive analysis of PM_{10} pollutant (particulate matter < 10 μg/m^3) related to the period measured (3, 6, 12 months)

Pollutant	Period	N	M	Median	SD
PM10 (μg/m^3)	3 M	380	40.87	40.79	11.78
PM10 (μg/m^3)	6 M	380	38.29	36.06	9.68
PM10 (μg/m^3)	12 M	380	37.31	36.07	4.54

Even checking other pollutants O_3, CO, NO_2, PM_{10}, SO_2, our results suggest that PM_{10} was responsible for the observed changes in the hormone prolactin.

Prolactin seems to play an important role in the physiology of human reproduction. Increased serum concentration of prolactin in the follicular and mid-cycle was demonstrated in humans, suggesting that the hormone has mentioned an important role in ovarian physiology. In humans undergoing *in vitro* fertilization, high concentrations of prolactin in follicular fluid were associated with the maturation of cumulus-oocyte complex, successful fertilization and pregnancy (Franco and Sala, 2004).

Recently, many studies characterize pollutants as endocrine disruptors or interfering. Endocrine disruptors are defined as exogenous chemicals, natural or synthetic, which cause adverse health effects on an organism or its progeny, affecting the endocrine system and other

Table 4: Prolactin and PM_{10} regression

Test – Period	Quartil	OR	IC MIN/MAX
Prolactin – 3 M	1st Q	1.00	-
	2nd Q	4.11	0,81 - 20,94
	3rd Q	21.17	2.79 - 160.58
	4th Q	4.22	0.49 - 36.01
Prolactin - 6 M	1st Q	-	-
	2nd Q	0,27	0.050 – 1.64
	3rd Q	0,04	0.005 - 0.45
	4th Q	0,08	0.005 – 1.38
Prolactin – 12 M	1st Q	-	-
	2nd Q	1.36	0.35 - 5.33
	3rd Q	1.56	0.36 - 6.78
	4th Q	1.08	0.23 - 5.12

adverse effects (Ghiseli and Jardim, 2007; Alves et al., 2007; Goloubkova and Spritzer, 2000; Queiroz and Waissmann, 2006; Multigner and Oliva, 2002).

In recent years, several accidental exposures to endocrine disruptors have been described as responsible for early pubertal development in children. Several environmental exposures have occurred in cities around the world, causing hormonal changes in children, for example, by eating food contaminated by estrogen (Alves et al., 2007).

Exposure to endocrine disruptors can modify hormone metabolism, synthesis and/or blocking the action of testosterone, FSH, LH, or other hormones. Most of the steroid metabolism is in the liver and this organ is also a prime target for some exogenous toxic substances (Queiroz and Waissmann, 2006).

As noted, the PM_{10} changes the amount of prolactin in such a way that could interfere with the human reproductive process. Our next challenge will be to understand the mechanisms involved in the interaction between PM_{10} and prolactin.

Interestingly, the levels of PM_{10} considered for analysis in this study remained within the range considered acceptable by CETESB. However, we found a significant relationship ($p < 0.05$, $p < 0.005$ and $p < 0.005$) when applied the logistic regression between the pollutant and the hormone prolactin.

Martins et al. (Martins et al., 2002), also found that acceptable levels of pollutants may affect human health or more specifically, may increase the prevalence of certain diseases.

When we related other hormones with prolactin we did not observe a significant relationship and also no significant differences were found between the sexes of the subjects studied. Perhaps prolactin may be a marker of infertility for both genders male and female.

As mentioned before, this was the first study linking sex hormones with pollution in the ABC region. This work may stimulate further studies that expand knowledge of the effects of pollutants as endocrine disruptors.

CONCLUSION

In conclusion, our results support the idea that air pollution may have a disruptive action in reproductive human health.

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