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Occupational exposure to pesticides, reproductive hormone levels and sperm quality in young Brazilian men

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ABSTRACT

The association of occupational exposure to current-use pesticides with reproductive hormones, semen quality, and genital measures was investigated among young men in the South of Brazil. A cross-sectional study was conducted in 99 rural and 36 urban men aged 18–23 years. Information on pesticide use was obtained through questionnaire. Serum and semen samples were analyzed for sex hormones and sperm parameters, respectively, and measurement of anogenital distance (AGD) and testis volume (TV) were performed. Associations were explored using multivariate linear regression. Rural men had poorer sperm morphology, higher sperm count, and lower LH levels relative to urban subjects. Lifetime use of pesticides, especially herbicides and fungicides, was associated with poorer morphology and reduced LH and prolactin, with evidence of a linear pattern. Maternal farming during pregnancy was associated with larger AGD and TV. Chronic occupational exposure to modern pesticides may affect reproductive outcomes in young men.

1. Introduction

Endocrine disrupting chemicals (EDCs) are compounds that alter the normal functioning of the endocrine system of both wildlife and humans [1]. Increasing human exposure to EDCs has been hypothesized to play a causative role in some of the observed adverse trends in male reproductive health, such as undescended testes, hypospadias, decreased sperm quality, and testicular cancer [2].

Many modern pesticides possess hormonal activity and have thus been classified as EDCs. *In vitro* studies of a variety of non-persistent pesticides suggest that they may exert estrogenic and anti-androgenic activity and disturb sex steroid-synthesizing enzymes [3,4]. Given their endocrine-disrupting potential, several epidemiological studies have explored the association between exposure to currently-used pesticides and altered sperm quality [5–8]. Most data are from occupational studies linking exposure to moderate-high levels of multiple pesticides and poor semen quality, based on decreased concentration and motility, low percentage of morphologically normal spermatozoa, and changes in sperm DNA [6,9]. Because pesticides are a heterogeneous group of substances with diverse chemical structures and mechanisms of action, some pesticides may directly affect spermatogenesis by damaging or destroying Sertoli cells and other spermatogenesis support cells, whereas others may act indirectly by altering hormonal signaling [10]. Accordingly, a growing number of human studies have demonstrated an association between exposure to certain non-persistent pesticides and changes in circulating lev-

Abbreviations: AChE, acetylcholinesterase; AGD, anogenital distance; BChE, butyrylcholinesterase; EDCs, endocrine disrupting chemicals; FAI, free androgen index; FSH, follicle-stimulating hormone; LH, luteinizing hormone; OP, organophosphate; SHBG, sex hormone-binding globulin; TDS, testicular dysgenesis syndrome; TV, testicular volume.

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Table 1
Sociodemographic and occupational characteristics, lifestyle, gestational and birth factors of study population.

N (%)	Total N = 135	Rural N = 99	Urban N = 36	p-value[a]
Sociodemographic and occupation				
Age (years)				
18–20	77 (57.0)	63 (63.6)	14 (38.9)	0.01
21–23	58 (43.0)	36 (36.4)	22 (61.1)	
Years of education				
≤8	12 (8.9)	12 (12.1)	0	<0.01
9–11	81 (60.0)	64 (64.6)	17 (47.2)	
≥12	42 (31.1)	23 (23.2)	19 (52.8)	
Occupation				
Non farmer	65 (48.1)	29 (29.3)	30 (100)	<0.01
Farmer	70 (51.9)	70 (70.7)	0	
Employed in the last 3 months				
No	9 (6.7)	3 (3.0)	6 (16.7)	0.01
Yes	126 (93.3)	96 (97.0)	30 (83.3)	
Lifestyle				
Current smoking status				
Non-smokers	127 (94.1)	91 (91.9)	36 (100)	0.11
Smokers	8 (5.9)	8 (8.1)	0 (0)	
Regular alcohol intake in the last 30 days				
No	54 (40.0)	32 (32.2)	22 (61.1)	<0.01
Yes	81 (60.0)	67 (67.7)	14 (38.9)	
Regular physical activity in the last 3 months				
No	53 (39.3)	34 (34.3)	19 (52.8)	0.05
Yes	82 (60.7)	65 (65.7)	17 (47.2)	
Stress in the last 3 months				
No	100 (74.1)	69 (69.7)	31 (86.1)	0.05
Yes	35 (25.9)	30 (30.3)	5 (13.9)	
Body mass index (BMI)				
Eutrophic (<25 kg/m^2)	91 (67.4)	68 (68.7)	23 (63.9)	0.60
Overweight or obese (≥25 kg/m^2)	44 (32.6)	31 (31.3)	13 (36.1)	
Gestation and birth				
Maternal occupation during pregnancy				
Non farmer	66 (48.9)	33 (33.3)	33 (91.7)	<0.01
Farmer	69 (51.1)	66 (66.7)	3 (8.3)	
Maternal smoking during pregnancy				
No	120 (88.9)	87 (87.9)	33 (91.7)	0.76
Yes	15 (11.1)	12 (12.1)	3 (8.3)	
Premature birth				
No	106 (78.5)	82 (82.8)	26 (72.2)	0.17
Yes	27 (21.5)	17 (17.2)	10 (27.8)	
Birth weight (g)				
<2500	11 (8.1)	8 (8.1)	3 (8.3)	1.00
≥2500	124 (91.9)	91 (91.9)	33 (91.7)	
Birth length (cm)				
<50	55 (40.7)	40 (40.4)	15 (41.7)	1.00
≥50	80 (59.3)	59 (59.6)	21 (58.3)	

SD: standard deviation.
[a] Chi-square or Fisher test.

els of reproductive hormones, particularly among occupationally exposed males [11–16]. Despite this, epidemiological evidence on the effects of pesticides in current use on male reproductive system remains inconclusive.

Male anogenital distance (AGD), which is the distance from anus to scrotum, has been used as a measure of androgen status in experimental animals [10]. In human males, testicular volume (TV) and penile length have traditionally been used as indicators of androgenicity [17], and use of AGD has been rare [18]. However, recent epidemiological studies suggest that *in utero* exposure to anti-androgenic compounds may be associated with shortened AGD [18,19], whilst shorter AGD may predict poorer testicular function in adult men [20,21].

The effects of environmental and occupational exposure to pesticides on male reproductive system are of continuing concern. Developing countries account for one third of global pesticide consumption. In 2008, Brazil became the world's largest consumer [22], with continued use of active ingredients already banned in other countries. Serra Gaúcha is a mountainous region in the South of Brazil settled by German and Italian immigrants characterized by family farms producing fruit, mostly grapes for wine production. The present study aimed to: 1) investigate the association of occupational exposure to modern pesticides with reproductive hormone levels, sperm quality, and TV among rural and urban young men residents from this region, and 2) examine reproductive hormone levels, sperm quality, and AGD and TV measurements in relation to potential gestational exposures, including maternal farming and smoking during pregnancy.

2. Materials and methods

2.1. Study design and population

A cross-sectional study was conducted between 2012 and 2013 with a random sample of men aged 18–23 years from the agricultural population of the municipality of Farroupilha, in Rio Grande do Sul, the southernmost state of Brazil. A control group of the same age was selected from the urban area of the town. Considering a population of about 800 men in the age group of 18–23 years residing in the rural area of Farroupilha, a prevalence of acute pesticide