Original article:

Is farming a occupational hazard for severe male factor infertility?

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Abstract

Objective – To study the incidence of male factor infertility and type of semen abnormality in the farmer couple attending our infertility outpatient clinic.

Method- Database of 3100 patients with male factor infertility were retrospectively reviewed. Patients were divided in two groups for analysis: group 1 - farmer, group 2 - non farmer. Records of semen analysis and serum FSH (Follicle stimulating hormone) were analyzed for two groups. Appropriate statically test was done to study the difference in two groups.

Results –Out of 3100 patients, there were 18.6% patients in farmer group 1 and -81.4% in group 2. Prevalence of semen abnormality was 33.3% of total semen abnormality which showed farmer are having higher prevalence of semen abnormality (p<0.005). Age of males presenting to infertility clinic is significantly less in farmers (p<0.005). Farmers are having higher prevalence of severe semen abnormality and also higher prevalence of non-obstructive azoospermia.

Conclusion- Farmers are increased risk of severe male factor infertility. This is likely attributed to pesticides exposure.

Keywords: farmers, pesticides, semen abnormality, FSH

Introduction

Male factor infertility contributes to 40- 50% of couple seeking treatment for conception¹. 21st century witnessed increase in male factor infertility. It is said that various environmental and life style changes brought this decline in male fertility. Stress, smoking, organic solvent, electromagnetic radiation and heat exposure are postulated as the cause of semen abnormality in various studies².In the late 1970s nematocide dibromochloropropane the affected more than 26,000 plantation workers in 12 countries; 64% had low sperm concentrations and 28% were involuntarily childless³. Pesticides include agents known as herbicides, fungicides, insecticides, fumigants and rodenticides. In India 50% of population belong to farming occupation.(the world bank)⁴. This group of people is in continuous contact with pesticides. Deliberate use of pesticides can affect non-target organism such as human. Various studies discussed role of pesticides in female and male infertility with conflicting results. Some showing pesticides having effect on semen others not showing any association. ^{5,6,7,8,9,10}. One study also found exposure to pesticides increases abortion and congenital malformation ¹⁰.

Pesticides can affect both hormonal and semen parameter abnormality. One recent study shown that pesticide can cause azoospermia. With the advent of testicular retrieval of sperm and intra cytoplasmic sperm injection pregnancy is possible in azoospermic males. Serum FSH is used to predict possibility of sperm retrieval after testicular extraction. Chen etalreported that above 19 IU/ml, there is negligible chances of sperm retrieval 12.

Very few studies carried out in Indian subcontinent ¹³, ¹⁴. We are discussing male factor infertility incidence in our farmer population. We postulated hypothesis that contact with pesticides may increase the abnormality in semen parameter. We also want to see, can pesticides cause severe sperm abnormality in comparison to non farmer population.

Material and methods

It was a case control study in the department of reproductive medicine from January 2012 to December 2014. As it was a retrospective study no ethical clearance taken. All data was collected from departmental case files. Men with age 22 years to 50 years included in study. Men with known causes of semen abnormality like, congenital testicular abnormality, erectile dysfunction, previous history of trauma or surgery, varicocele, morbidly obese males are not included in study

Total 3100 patients attended infertility clinic in which 613 had semen parameter abnormality. Total no of farmers attended in this time frame was 578. Controls were nonfarmer men with semen abnormality. We had defined farmers who were working in field and in contact of pesticides for the purpose of study. All men enrolled in study produced semen sample in

wide mouth container after 2- 7 days of abstinence. Semen analysis further divided in mild,moderate,and severe on the basis of total motile fraction- 3-5 million, 1-3 million and less than 1 million respectively¹⁵. Semen analysis judged by at least 2 semen analysis and best of two was recorded for study. Total motile fraction was calculated in post wash semen sample as concentration in million per milliliter multiplied by percentage of progressive motile sperm divided by 100. Azoospermia was defined when no sperm seen after centrifugation. Patients with Azoospermia further characterized in two groups based on cut off of 19 IU/ml of serum FSH levels. Statistical analysis was done by chi square and student t test wherever applicable.

Results:

Although farmers contributed to 18.64 % of the population attended infertility clinic yet they are responsible for one third (203/613) of total semen abnormality. Incidence of semen abnormality in farmer in our study group was 35.12% while incidence of semen abnormality in non-farmer group is 16.25%. Age group was significantly lesser in farmer group which signifies deleterious effect of pesticides on semen parameters (Table 1).

Table 1: Semen abnormality in farmer and non-farmer groups

	Farmer	Non farmer	P value, RR(95%CI)
Study population-3100	578(18.64%)	2522 (81.36%)	
Age	33.4 ± 6.4	34.7 ± 7.4	< 0.0001
Semen abnormality	203(35.12%)	410(16.25%)	< 0.001, 2.196
			(1.898-2.542)
Mild male factor	22 (3.8%)	78 (3.1%)	0.0032
Moderate male factor	40 (6.9%)	89 (3.5%)	
Severe male factor	63 (10.9%)	119 (4.7%)	
Azoospermia – FSH- < 19	34 (5.9%)	62 (2.4%)	
Azoospermia – FSH - > 19	44 (7.6%)	62 (2.4%)	

We also observed that farmers were having more severe form of semen abnormality as compared to non-farmers (P=0.0032). It could be postulated that this is because of permanent damage to testicles. Although it can be related to time of pesticides exposure but in our retrospective study we have not asked for duration of exposure.

Discussion

Madhya Pradesh is major corn and soybean and rice producing state. Most common pesticide used is phorateand quinalphos. Farmers are in continuous contact with pesticides so most susceptible to deleterious effect on semen abnormality.¹⁶

In our study we found a higher prevalence of semen abnormality in farmers which is consistent to recent studies^{7,8,9,10,11}Cause of defective spermatogenesis proposed to be accumulation of reactive oxygen radicals and subsequent defective spermatogenesis.In one study pesticide causes increased secretion of luteinizing hormone and prolactin. ¹⁷In another study herbicide was shown to inhibit the enzymatic conversion of testosterone to 5α-dihydrotestosterone in the rat.¹⁸ Estrogenic action is also proposed for example, triazines have been shown to induce aromatase in vitro. 18 Pesticides can also affect Sertoli cell function or changes morphological appearance of these cells. Function of Leydig cells can be impaired by pesticide exposure, the result being decreased testosterone concentrations in serum and testicular tissue. 19 This occurrence, can lead to diminished Sertoli cell function and spermatogenesis²⁰.Pesticides may have both estrogenic and anti-androgenic activity. 21 Other mechanism postulated as the cause of

infertility is affection on seminal and prostatic secretions.²²Another possible mechanism is affection of sperm motility and morphology²³.Epididymal toxicity leading to efferent duct atrophy and permanent sterility is another possible mechanism proposed by one study.²⁴

In our study we found significant less age among infertile farmer group in comparison to infertile nonfarmer group which has not been studied in previous studies. Possible explanation for this is possible inhabitance near farms leading to continuous and prolonged exposure to pesticide. It was shown by Whorton et al, duration of exposure inversely affect fertility.²⁵

Total motile fraction which denotes both count and motility significantly less in farmers in comparison to non-farmers. Count and motility most consistent parameter to be found affected in previous study by Martenies et al. ²⁶We have found a significant higher azoospermia and in azoospermia follicle stimulating hormones levels more than 19 IU/ml of indicating higher non obstructive azoospermia in farmer population. Study by Aguilar-Garduñoet al ¹⁶ also shown higher FSH levels in farmers.

Conclusion

Our study found significant affection on semen parameter in farmers due to pesticide exposure. Farmers are of lesser age in infertility clinic. They have much severe semen abnormality compared to normal population. Prevalence of non obstructive azoospermiaas indicated by FSH more than 19 iu/ml is significantly higher in farmer population.

References

1- Kumar N, Singh AKAK. Trends of male factor infertility, an important cause of infertility: A review of literature. J of Human Repro Sci. 2015;8(4):191.

- 2- Ould HS, Perrin J, Achard V, Courbière B, Grillo JM, Sari-Minodier I. [Association between sperm abnormalities and occupational environment among male consulting for couple infertility]. Journal de gynecologie, obstetriqueetbiologie de la reproduction. 2016;45(1):1-0.
- 3- Slutsky M, Levin JL, Levy BS. Azoospermia and oligospermia among a large cohort of DBCP applicators in 12 countries. International J occup and environ health. 1999;5(2):116-22.
- 4- The worldBank. Employment in agriculture (%of total employment) available at http://data.worldbank.org/indicator/SL.AGR.EMPL.ZS assessed on 02.05.2016
- 5- Chia SE, Tay SK. Occupational risk for male infertility: a case-control study of 218 infertile and 227 fertile men. J occup and environ Med. 2001;43(11):946-51.
- 6- Swan SH, Kruse RL, Liu F, Barr DB, Drobnis EZ, Redmon JB et al. Study for Future Families Research Group. Semen quality in relation to biomarkers of pesticide exposure. Environmental health perspectives. 2003;111(12):1478.
- 7- Swan SH. Semen quality in fertile US men in relation to geographical area and pesticide exposure. International J Andrology. 2006;29(1):62-8.
- 8- Bretveld R, Brouwers M, Ebisch I, Roeleveld N. Influence of pesticides on male fertility. Scand J Work Environ Health. 2007;1:13-28.
- 9- Neghab M, Momenbella-Fard M, Naziaghdam R, Salahshour N, Kazemi M, Alipour H. The effects of exposure to pesticides on the fecundity status of farm workers resident in a rural region of Fars province, southern Iran. Asian Pac J trop Biomed. 2014;4(4):324-8
- 10- Melgarejo M, Mendiola J, Koch HM, Moñino-García M, Noguera-Velasco JA, Torres-Cantero AM. Associations between urinary organophosphate pesticide metabolite levels and reproductive parameters in men from an infertility clinic. Environ Res . 2015;137:292-8.
- 11- Chen SC, Hsieh JT, Yu HJ, Chang HC. Appropriate cut-off value for follicle-stimulating hormone in azoospermia to predict spermatogenesis. Reprod Biol Endocrinol. 2010;8:108.
- 12- Rozati R, Reddy PP, Reddanna PA, Mujtaba R. Role of environmental estrogens in the deterioration of male factor fertility. Fertility and sterility. 2002;78(6):1187-94.
- 13- Centre for science and environment 2013- state of pesticide regulation in India. Available at http://www.cseindia.org/userfiles/paper_pesticide.pdf. assessed on 02.05.2016
- 14- Tennant MK, Hill DS, Eldridge JC, Wetzel LT, Breckenridge CB, Stevens JT. Chloro-s-triazine antagonism of estrogen action: Limited interaction with estrogen receptor binding. Journal of Toxicology and Environmental Health, Part A Current Issues. 1994;43(2):197-211.
- 15- Merviel P, Heraud MH, Grenier N, Lourdel E, Sanguinet P, Copin H. Predictive factors for pregnancy after intrauterine insemination (IUI): an analysis of 1038 cycles and a review of the literature. Fertility and sterility. 2010 Jan 1;93(1):79-88.
- 16- Aguilar-Garduño C, Lacasaña M, Blanco-Muñoz J, Rodríguez-Barranco M, Hernández AF, BassolS, et al. Changes in male hormone profile after occupational organophosphate exposure. A longitudinal study. Toxicology. 2013;307:55-65.

- 17- Kniewald J, Osredečki V, Gojmerac T, Zechner V, Kniewald Z. Effect of s-triazine compounds on testosterone metabolism in the rat prostate. J Appl Toxicol. 1995;15(3):215-8.
- 18- Sanderson JT, Letcher RJ, Heneweer M, Giesy JP, van den Berg M. Effects of chloro-s-triazine herbicides and metabolites on aromatase activity in various human cell lines and on vitellogenin production in male carp hepatocytes. Environmental Health Perspectives. 2001;109(10):1027.
- 19- Bretveld R, Brouwers M, Ebisch I, RoeleveldN.Influence of pesticides on male fertility. Scand J Work Environ Health 2007;33(1):13-28
- 20- Takahashi KL, Aoyama H, Kawashima K, Teramoto S. Effects of dinoseb, 4, 6-dinitro-o-cresol, and 2, 4-dinitrophenol on rat Sertoli-germ cell co-cultures. Reprod Toxicol. 2003;17(2):247-52.
- 21- Friedmann AS. Atrazine inhibition of testosterone production in rat males following peripubertal exposure. Reproductive Toxicology. 2002;16(3):275-9.
- 22- Pant N, Mathur N, Banerjee AK, Srivastava SP, SaxenaDK.Correlation of chlorinated pesticides concentration in semen with seminal vesicle and prostatic markers. Reprod Toxicol. 2004;19(2):209-14.
- 23- Pant N, Pant AB, Chaturvedi PK, Shukla M, Mathur N, Gupta YK, Saxena DK. Semen quality of environmentally exposed human population: the toxicological consequence. Environmental Science and Pollution Research. 2013 Nov 1;20(11):8274-81.
- 24- Hess RA. Effects of environmental toxicants on the efferent ducts, epididymis and fertility. J ReprodFertil Suppl. 1998;53:247-59.
- 25- Whorton D, Krauss R, Marshall S, Milby T. Infertility in male pesticide workers. The Lancet. 1977;310(8051):1259-61
- 26- Martenies SE, Perry MJ. Environmental and occupational pesticide exposure and human sperm parameters: a systematic review. Toxicology. 2013;307:66-73