Long-term effect of exposure to mustard gas on male infertility

S Shakeri^{1*}, M Yazdani², E Kheradpezhouh³

Departments of ¹Urology, ²Obstetrics and Gynecology, and ³Pharmacology, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract

Background: Sulfur mustard is a noxious chemical and a carcinogen that causes acute and chronic injuries with both local and systemic effects. This study was conducted to investigate the long-term effect of sulfur mustard (mustard gas) on male infertility in couples, in whom the husbands were highly suspected of being exposed to mustard gas.

Methods: A total of 91 couples, in whom men, highly suspicious of being exposed to mustard gas during the Iran-Iraq war, were fully examined by an urologist and a gynecologist, and urged to provide semen for three standard sperm analyses.

Results: Of 91 couples, 40 were infertile 10 years after given that the frequency is approximately 10-12% in normal population. In addition, thorough examination of the wives by a Gynecologist showed that of the foregoing 40 infertile couples, 8 (20%) of women suffered from infertility problems. The infertility of the remaining 32 (80%) was due to male factors as compared with 40-50% in the normal population. The results of the present research demonstrated that in the population under study, male factors had greater impact on infertility.

Conclusion: The exposure of males to mustard gas played a distinct role in long term infertility.

Keywords: Mustard gas; Male Infertility; Iran

Introduction

Sulfur mustard is a clear, colorless, greasy liquid with onion or garlic odor. It is a lipophilic liquid with limited solubility in water. Due to its great lipophilic property, it is rapidly absorbed by skin and cells. The skin absorbs only 20% of sulfur mustard and the remaining 80% is evaporated. Of the amount absorbed by the skin, 80%–90% enters blood

circulation and 12% binds to skin proteins. The laboratory findings showed that 50% and 90% of the absorbed gas are excreted through urine within 24 hours and 5 days respectively.¹

Sulfur mustard is a noxious chemical and a carcinogen that causes acute and chronic injuries with both local and systemic effects. The acute mustard gas injuries are mostly pulmonary, ocular and cutaneous lesions.¹ Topical exposure to this dysfunctional alkylating agent results in erythema, which appears within hours after intoxication and can subse-

^{*}Correspondence: Saeed Shakeri, MD, Department of Urology, Shiraz University of Medical Sciences, Shiraz, Iran. Tel: +8-711-233-7282, Fax: +98-711-230-7594, E-mail: sshakeri@sums.ac.ir

quently lead to edema, blisters or ulceration.² The most prominent toxic effects found in laboratory animals exposed to mustard gas, include inhibition of mitosis and cell cycle, and reduction of NAD and cellular respiration.³

The organs immediately injured after exposure to this gas, are lungs, skin and eyes. Burns resulting from mustard gas are often severe and need a long time to be repaired. In addition, many organs such as thyroid, lung, immunity system, testis, *etc.*, become prone to malfunction long time after exposure to sulfur mustard.

Azoospermia and severe oligospermia were detected in 42.5% and 57.5% of patients with a history of infertility and previous exposure to mustard gas respectively.⁴ Also, only 20% of patients with oligospermia recovered from mild to moderate form of the disease.⁵ A similar effect was observed in experimental animals exposed to other possible gonadotoxic agents such as glycerol.⁶ This

study was conducted to investigate the longterm effect of sulfur mustard (mustard gas) on male infertility in couples, in whom the husbands were highly suspected of being exposed to mustard gas.

Patients and Methods

The present study was performed on 91 couples with males aged <55 years, in order to exclude the effect of age on male infertility. The husbands were greatly suspicious of being exposed to mustard gas at least 10 years previously and selected to investigate the long-term effect of mustard gas on male infertility. The infertile couples were divided into two groups according to the history of primary or secondary infertility.

The wives were then fully examined by a gynecologist for any infertility problem. The results were analyzed using Chi-square test and SPSS 11.5, and compared with those of normal population. Finally, three semen

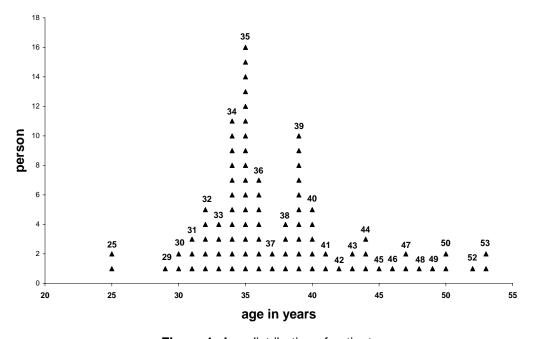


Figure 1: Age distribution of patients

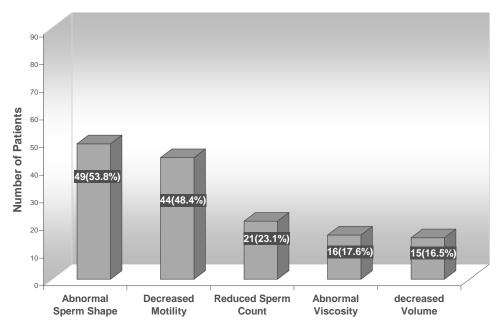


Figure 2: The abnormality criteria of semen analysis

specimens provided by each husband, from 2 to 7 days after any intercourse, were examined to detect any abnormalities of reproductive function.

All finding were analyzed by SPSS 11.5 and compared with statistical results in normal population from other researches.

Results

A total of 91 couples, in which the men were highly suspected of being exposed to mustard gas during Iran-Iraq war, were fully examined for any infertility due to male factors. The exposure of men to mustard gas was demonstrated by taking a thorough medical history, investigating their military profiles and matching the time and the place of injuries. The mean±SD of men was 37.5±6 (range: 25–53) years (Figure 1). The infertility rate in our study was 44% compared to 10%–12% of normal population⁷ (P<0.025).

Thorough examination of the foregoing subjects showed infertilities in 40 couples (≈44%). Among these, 28 couples had primary and the remaining 12 had secondary infertilities. In addition, the examination of all wives by a gynecologist showed that in 8 cases the infertilities were due to female factors and in the remaining 32 couples, the infertilities were due to male factors. The ratio of male and female factors in relation to infertility was 8 (20%) and 32 (80%), respectively. The results of semen analysis of 56 patients were 56 (62%) and 35 (38%) in normal and abnormal persons respectively. Figure 2 demonstrates that the most prevalent abnormality of semen was due to abnormal sperm morphology in 49 patients (53.8%), followed by decreased motility mo in 44 (48.4%), reduced sperm count in 21 (23.1%), abnormal viscosity in 16 (17.6%) and decreased volume in 15 patients (16.5%).

Discussion

The male factors, in infertile couples of normal population, were responsible for 40%–50% of infertility in infertile couples. However, according to our results; the male factors were responsible for 80% of infertility. Thereafter comparing our rates with the rates in normal population by using χ^2 test, we found that, the infertility rate due to male factors in our group of study was much higher than in normal population. The exposure of males to sulfur mustard gas plays a distinct role in

long-term infertility. As the present investigation was based on taking history and military profiles, further studies are needed to substantiate the contact with mustard gas by demonstrating structural changes in DNA, a specific target for sulfur mustard.

Acknowledgment

We would like to thank Dr. D. Mehrabani of Center for Development of Clinical Studies at Nemazee Hospital for editorial assistance.

References

- 1 Somani SM, and Babu SR. Therapeutic Review: Toxicodynamic of sulfur mustard. *Int J Clin Pharmacol Ther Toxicol* 1989;27:419-35.
- 2 Wormser, U. Toxicology of mustard gas. *Trends Pharmacol Sci 1991;***12:** 164-7.
- 3 Lin PP; Bernstein-Isadore A, Vaughan-Frizell L. Bis (2-chloroethyl) sulfide (BCES) disturbs the progression of rat
- keratinocytes through the cell cycle. *Toxicology Letters 1996;***84:**23-32. Safarinejad MR. Testicular effect of
- mustard gas. *Urology 2001;***58:**90-4. **5** Azizi F, Keshvarz A, Roshanzamir F.
 Reproductive function in men following exposure to chemical warfare with sul-
- fur mustard. *Med War 1995;***11:**34-44.Wiebe JP, Barr KJ, Buckingham KD.Sustained azoospermia in squirrel
- monkey, Saimiri sciureus, resulting from a single intertesticular glycerol injection. *Contraception 1989;***39**:447-57
- 7 Jarow JP, Sigmoan M. Office evaluation of the infertile male. AUA Update Series 1999;18:177-84.