

ORIGINAL ARTICLE

Increased Miscarriage Rate in Female Farmers Working in Saffron Fields: A Possible Effect of Saffron Toxicity

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Abstract

Background: There is much debate about effects of medicinal plants such as saffron (*Crocus sativus*) on human health. Women are highly involved in farming and processing of this plant. This study is aimed at evaluating the saffron impacts on miscarriage rate of female farmers working in saffron fields.

Methods: This was a prospective case-control study on pregnant female farmers during harvesting season of saffron in December 2005 to evaluate miscarriage rate among them. All pregnant women who were between the first and twentieth week of gestation and were participated in saffron harvesting and processing in previous years were studied. The subjects were divided into two age and gestational age-matched groups of cases and controls. The cases were prohibited from working in saffron fields and in return they were paid same as the average amount of their monthly income. They were trained not have any exposure to saffron and a team supervised them on their adherence during the study period. Nevertheless, they were free for working in other careers. On the other hand, the controls were allowed for working in the fields and processing saffron.

Results: Forty-one subjects were included in case group and 38 subjects in control group. Median age of all subjects was 25 years. The groups were not significantly different from each other according to history of miscarriage and 2nd occupation. Four subjects experienced miscarriage that all of them belonged to control group having contact to saffron. None of cases had miscarriage. Using Fisher's exact test, it was found that miscarriage rate was significantly higher (10.6% vs. 0%, $P = 0.03$) among female farmers who had saffron exposure.

Conclusion: Exposure to saffron may increase the risk of miscarriage. Hence, it is suggested that pregnant women avoid contact with considerable amounts of saffron especially for female farmers working in saffron fields.

Keywords: Abortion; *Crocus sativus*; Saffron Toxicity; Uterine Contraction

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INTRODUCTION

In recent decades, much debate has been raised about effects of medicinal plants on human health. Saffron or *Crocus sativus* is one the medicinal plants that attracted much of attention (1). It is a well-known plant in traditional Persian medicine that has been described by Avicenna as hypnotic, antidepressant, anti-inflammatory, hepatoprotective, bronchodilatory, aphrodisiac, labor inducer and emmenagogue (2). These effects have been well-documented in different studies (2-5). Moreover, anticarcinogenic properties of saffron have shown to be promising in preventing the progression of cancer (6).

In northeast of Iran, saffron farming is one the most important economic activities and its raw or processed products are exported to all over the world. Women are involved in this process from cultivation to purifying. An increase in miscarriage rate among the women exposed to

saffron during harvesting season (October to December) in the region has been stated in official reports. Saffron has been identified as a substance for inducing labor or abortion (2). In this respect, newer evidences have shown that the saffron can increase the uterine contractions (7,8). Hence, a careful evaluation of possible side-effects of this flavor and medicinal plant on women's health seems necessary. This study is aimed at evaluating the saffron impacts on miscarriage rate of female farmers working in saffron fields.

METHODS

This was a prospective case-control study on pregnant female farmers in Gonabad city, Iran during harvesting season of saffron in December 2005 to evaluate miscarriage rate among them. In this study, all pregnant women who were between the first and twentieth week of gestation and were participated in saffron harvesting and processing

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In previous years were studied. Data including age, 2nd occupation apart from farming (in non-agricultural seasons), gestational week and pregnancy history were recorded in a predesigned checklist.

The subjects were divided into two age and gestational age-matched groups of cases and controls. The cases were prohibited from working in saffron fields and in return they were paid same as the average amount of their monthly income. They were trained not have any exposure to saffron and a team supervised them on their adherence during the study period. Nevertheless, they were free for working in other careers. On the other hand, the controls were allowed for working in the fields and processing saffron. An experienced gynecologist cooperated in the study for periodic examinations of subjects. The data were analyzed with Statistical Package for the Social Sciences (SPSS Inc. Chicago, IL, USA) and P values of less than 0.05 were considered as statistically significant.

RESULTS

In this study 41 subjects were included in case group and 41 subjects in control group. Median age of all subjects was 25 years. The cases completely adhered to the study plan. Three controls were lost to follow up due to travel to other cities and cassation of working in saffron fields after few weeks of their pregnancy.

The groups were not significantly different from each other according to age, history of miscarriage and 2nd occupation (Table 1). Four subjects experienced miscarriage that all of them belonged to control group having contact to saffron. None of cases had miscarriage. Using Fisher's exact test, it was found that miscarriage rate was significantly higher (10.6% vs. 0%, $P = 0.03$) among female farmers who had saffron exposure (Table 2).

DISCUSSION

This study was the first evaluation of effect of saffron toxicity on miscarriage in human subjects. It was found that miscarriage rate was higher among women who had direct

exposure to saffron during farming and processing its products. The saffron has been previously stated as an abortogenic compound in Persian traditional medicine literature including Avicenna's Canon of Medicine (1,2). In Canon of Medicine, this substance has also been described as a menstruation and labor facilitator (2). Moreover, for some gynecologic complaints such as dysmenorrhea, it has recently been shown to have a preventive therapeutic effect (9).

In experimental studies, the saffron has been ascertained as a uterine contraction stimulant (7,8). Special features of this plant originate from its components including crocin, picrocrocin, crocetin, and safranal, though it is yet unclear which of them is responsible for induction of uterine contraction and abortion. Nevertheless, in a study by Mohamadpour et al., it was found that crocin may cause prolonged menstrual bleeding (10). Abnormal uterine bleeding was also found as a side-effect of saffron tablets on healthy volunteers (11).

In a research done by Chang et al. on guinea pigs, it was revealed that extracts of saffron has stimulatory effects on uterine due to its myogenic and neurogenic effects (12). Correspondingly, Tafazzoli et al. in an experimental case-control study ascertained that aqueous extract of saffron can significantly increase the miscarriage rate in BALB/c mice (13). Hosseini-Biouki et al. similarly showed that 0.4 g saffron can induce premature birth in Syrian mice as the result of increased motility of uterine smooth muscles especially in 3rd week of pregnancy compared to controls (14).

It is known that over 10 g saffron is effective on induction of abortion (2,3). However, in the present study, we observed that even frequent exposure to saffron particles may cause miscarriage. This necessitates raising awareness in female famers working in saffron fields through media, public health centers and providing lectures in high schools. It is also necessary to warn public about the potential risks of exposure to and using considerable amounts of saffron during pregnancy.

Table 1. Characteristics of study subjects

| Variable | Case group (n = 41) | Control Group (n = 38) | P value |
|--|------------------------|---------------------------|---------|
| Age (year), median | 25.5 | 25 | 0.94 |
| Gestational age (week), median | 12 | 10.5 | 0.36 |
| 2nd occupation, n (%) | | | |
| Housekeeper | 32 (78.1) | 31 (81.6) | |
| Government employee | 6 (14.6) | 3 (7.8) | 0.76 |
| Self-employed | 3 (7.3) | 4 (10.6) | |
| History of miscarriage (frequency of incidents), n (%) | | | |
| 1 | 9 (21.9) | 9 (23.7) | |
| 2 | 2 (4.9) | 0 (0) | 0.91 |
| 3 | 0 (0) | 1 (2.6) | |
| 0 | 30 (73.2) | 28 (73.7) | |

Table 2. Analysis of miscarriage in two groups

| Miscarriage | Case group (n = 41) | Control Group (n = 38) | P value |
|-------------|------------------------|---------------------------|---------|
| Yes, n (%) | 0 (0) | 4 (10.6) | 0.03* |
| No, n (%) | 41 (100) | 34 (89.4) | |

* Fisher's exact test was used

LIMITATIONS

Small sample size of this study can be a limitation to the findings, and thus further studies with larger sample sizes are needed to delineate the direct effect of saffron on miscarriage in human. Moreover, working hours and workload of controls that can be major factors for causing miscarriage could not be evaluated in this study.

CONCLUSION

Exposure to saffron may increase the risk of miscarriage. Hence, it is suggested that pregnant women avoid contact with considerable amounts of saffron especially for female farmers working in saffron fields.

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REFERENCES

- Schmidt M, Betti G, Hensel A. Saffron in phytotherapy: pharmacology and clinical uses. *Wien Med Wochenschr* 2007;157:315-9.
- Hosseinzadeh H, Nassiri-Asl M. Avicenna's (Ibn Sina) the Canon of Medicine and saffron (*Crocus sativus*): a review. *Phytother Res* 2013;27:475-83.
- Ghasemi T, Abnous K, Vahdati F, Mehri S, Razavi BM, Hosseinzadeh H. Antidepressant Effect of *Crocus sativus* Aqueous Extract and its Effect on CREB, BDNF, and VGF Transcript and Protein Levels in Rat Hippocampus. *Drug Res (Stuttg)* Forthcoming 2014.
- Moshiri E, Basti AA, Noorbala AA, Jamshidi AH, Hesameddin Abbasi S, Akhondzadeh S. *Crocus sativus* L. (petal) in the treatment of mild-to-moderate depression: a double-blind, randomized and placebo-controlled trial. *Phytomedicine* 2006;13:607-11.
- Poma A, Fontecchio G, Carlucci G, Chichiricò G. Anti-inflammatory properties of drugs from saffron crocus. *Antiinflamm Antiallergy Agents Med Chem* 2012;11:37-51.
- Samarghandian S, Borji A. Anticarcinogenic effect of saffron (*Crocus sativus* L.) and its ingredients. *Pharmacognosy Res* 2014;6:99-107.
- Sadraei H, Ghannadi A, Takei-bavani M. Effects of *Zataria multiflora* and *Carum carvi* essential oils and hydroalcoholic extracts of *Passiflora incarnata*, *Berberis integerrima* and *Crocus sativus* on rat isolated uterus contractions. *Int J Aromatherapy* 2003;13:121-7.
- Inoue E, Shimizu Y, Shoji M, Tsuchida H, Sano Y, Ito C. Pharmacological properties of N-095, a drug containing red ginseng, polygala root, saffron, antelope horn and aloe wood. *Am J Chin Med* 2005;33:49-60.
- Nahid K, Fariborz M, Ataolah G, Solokian S. The effect of an Iranian herbal drug on primary dysmenorrhea: a clinical controlled trial. *J Midwifery Womens Health* 2009;54:401-4.
- Mohamadpour AH, Ayati Z, Parizadeh MR, Rajbai O, Hosseinzadeh H. Safety Evaluation of Crocin (a constituent of saffron) Tablets in Healthy Volunteers. *Iran J Basic Med Sci* 2013;16:39-46.
- Modagheh MH, Shahabian M, Esmaeili HA, Rajbai O, Hosseinzadeh H. Safety evaluation of saffron (*Crocus sativus*) tablets in healthy volunteers. *Phytomedicine* 2008;15:1032-7.
- Chang PY, Wang CK, Liang JD, Kuo W. Studies on the Pharmacological Action of Zang Hong Hua (*Crocus sativus* L.). I. Effects on Uterus and Estrus Cycle. *Yao Xue Xue Bao* 1964;11:94-100. (In Chinese)
- Tafazoli M, Kermani T, Saadatjoo A. Effects of saffron on abortion and its side effect on mice balb/c. *Horizon Med Sci* . 2004;10:53-5. (In Persian)
- Hosseini-Biouki, Anvari M, Dashti MH, Zeinali F. Teratogenic and Abortogenic Effects of Different Doses of Brewed Saffron Plant (*Crocus sativus*) in Syrian Mice. In: *Proceedings of International Congress of Saffron: a Herbal Medicine of 3rd Millennium*; 2009 May 12-13, Mashhad, Iran. Mashhad: Publications of Mashhad University of Medical Sciences; 2009. p.53.