Clomiphene Citrate and Oocyte Quality

Shail K Chaube1*, Meenakshi Tiwari1, Anumeegha Gupta1, Alka Sharma1, Shilpa Prasad1, Ashutosh N Pandey1, Pramod K Yadav1, Sabana Khatun1 and Tulsidas G Shrivastav2

1Department of Zoology, Institute of science Banaras Hindu University, Varanasi-221005, India
2Department of Reproductive Biomedicine, National Institute of Health and Family Welfare, New Delhi-110067, India

Introduction

Ovary is a dynamic organ and generates excess amount of reactive oxygen species (ROS) during follicular growth, development, maturation and ovulation [1]. The increased level of ROS is scavenged by antioxidant systems [2]. A moderate increase of ROS could be beneficial for oocyte meiotic maturation and reproductive outcome [3-5]. Overproduction of ROS or depletion of enzymatic antioxidant systems causes oxidative stress [2].

Anovulation is one of the major causes of reproductive failure in sub-fertile and infertile women [6,7]. In the absence of other reproductive problems, successful ovulation induction and good quality oocyte often restores normal fertility in human [8]. In a common clinical practice, gonadotropins are used to stimulate ovary in infertile or subfertile women [9,10]. However, anti-estrogens are widely used to induce ovulation in these patients. Clomiphene citrate (CC) is a non-steroidal ovulation-inducing drug that has been used in humans for more than 40 years [11,12]. Ovarian stimulation by gonadotropins is an expensive treatment. CC is an inexpensive, safe and effective alternative to gonadotropins [11].

Abstract

The clomiphene citrate (CC) is a first line of medicine used for ovulation induction in women worldwide. CC has good ovulation induction ability in anovulatory women but the pregnancy rate is very poor. This discrepancy might be due to the anti-estrogenic effect of CC at various level including ovary and oocytes. The hypoestrogenic conditions due to CC treatment inhibit follicular growth and development, induce susceptibility of oocytes towards apoptosis and deteriorate oocyte quality after ovulation. CC induces reactive oxygen species (ROS) mediated granulosa cells as well as oocyte apoptosis within the follicle of the ovary. Apoptosis deteriorates oocyte quality and thereby reproductive outcome. Supplementation of estradiol 17β or natural antioxidant such as melatonin prevents anti-estrogenic effects of CC and improves oocyte quality by scavenging CC induced generation of ROS. Thus, we propose that the supplementation of estradiol 17β and/or melatonin along with CC may be beneficial to overcome the anti-estrogenic effect of CC during infertility management in human.

Keywords: Clomiphene citrate; Ovulation induction; ROS; Apoptosis; Oocyte quality

List of Abbreviations: ROS: Reactive Oxygen Species; CC: Clomiphene Citrate; ER: Estrogen Receptors; GnRH: Gonadotropin-Releasing Hormone; M-II: Metaphase-II; H2O2: Hydrogen Peroxide; ART: Assisted Reproductive Technology
Clomiphene Citrate and Oocyte Quality

Authors: Chaube SK, Tiwari M, Gupta A, Sharma A, Prasad S, et al


Global Journal of Reproductive Medicine

Acknowledgement

Authors are thankful to Department of Science and Technology (EMR/2014/000702), New Delhi, India, for financial assistance.

Conflict of Interest

The authors declare that no conflict of interest exists.

References


