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ARTICLE

Propofol versus thiopental sodium as anaesthetic agents for oocyte retrieval: a randomized controlled trial

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Abstract Clinical outcomes of IVF cycles using propofol or thiopental sodium as anaesthetic agents for oocyte retrieval were compared. The primary outcome measure was fertilization rate per patient. One hundred and eighty patients undergoing ovarian stimulation with gonadotrophins and gonadotrophin-releasing hormone antagonists for IVF were randomized to receive either propofol ($n = 90$) or thiopental sodium ($n = 90$). No significant differences in baseline characteristics were present between the two groups. Overall fertilization rates were similar between propofol and thiopental sodium groups, respectively: median (IQR): 54.8 (29.2) versus 54.6 (29.7); fertilization rates for intracytoplasmic sperm injection only: median (IQR): 70 (50) versus 75 (50), respectively. For secondary outcome measures, time under anaesthesia was significantly increased in the thiopental sodium group: median (IQR): 12(5) versus 10 (4.5) min, $P = 0.019$ compared with the propofol group. Number of cumulus oocyte complexes retrieved [median (IQR): 7.1 (6.3) versus 6.5 (5.6)] did not differ significantly between the two groups. A non-significant difference in live birth rates per randomized patient of +4.4% (95% CI: −5.7 to +14.6) in favour of propofol was observed. Use of propofol compared with thiopental sodium for general anaesthesia during oocyte retrieval results in similar fertilization rates and IVF outcomes.

KEYWORDS: fertilization rate, IVF, oocyte retrieval, propofol, thiopental sodium

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Introduction

One of the key steps during IVF is the collection of oocytes, which includes paracentesis of follicles through the vaginal wall and aspiration of follicular fluid containing the cumulus oocyte complexes (COCs) under ultrasound guidance. Pain during this stage of IVF can be significant and, for this reason, some sort of anaesthetic management is usually required to ensure that discomfort of the patient is minimized.

Several approaches are being used for the anaesthetic management of oocyte retrieval, which include local anaesthesia, regional anaesthesia, conscious sedation and general anaesthesia (Vlahos et al., 2009). General anaesthesia is more invasive and requires the presence of specialized personnel, represents an option with distinct advantages and is being used in a number of IVF clinics (Bokhari and Pollard, 1999). Several drugs have been used as anaesthetic agents for oocyte retrieval, with propofol being preferred in many cases owing to its short induction and recovery time (Boysen et al., 1989, 1990).

Nevertheless, experimental evidence has suggested that propofol may be negatively affecting the oocytes (Depypere et al., 1991). More specifically, it has been demonstrated that, in mice, exposure to propofol has a toxic effect on the ability of the oocytes to be fertilized (Depypere et al., 1991; Tatone et al., 1998). Furthermore, in humans, it has been shown that, during oocyte retrieval for IVF, propofol can be identified in the follicular fluid (Christiaens et al., 1999; Coetsier et al., 1992), although this still remains controversial (Alsalili et al., 1997; Ben-Shlomo et al., 2000). Considering the above, reasonable concerns have been expressed about the suitability of propofol as an anaesthetic agent for oocyte retrieval (Hein and Putman, 1997). As an alternative to propofol, thiopental sodium, a barbiturate, has been used for short-term general anaesthesia procedures. The use of thiopental sodium, however, is known to be associated with prolonged recovery time and other complications, such as nausea and vomiting.

Whether propofol use is associated with an inferior clinical outcome after assisted reproduction technology, compared with thiopental sodium, has so far been explored in the context of retrospective studies. In these studies, no significant differences were found in fertilization or pregnancy rates (Huang et al., 2000; Pierce et al., 1992). It is well known, however, that retrospective studies are prone to various sources of bias; therefore, evidence of higher quality is required to properly address such an important research question.

The aim of this study was to compare the clinical outcome of propofol with thiopental sodium when used as anaesthetic agents for oocyte retrieval during IVF.

Materials and methods

Patient population and randomization procedure

This randomized controlled trial (RCT) was carried out at the Unit for Human Reproduction of the 1st Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki from November 2009 to March 2013. Women undergoing oocyte retrieval for IVF under general anaesthesia, and aged 45 years or younger, were considered eligible for this trial. Women with a known hypersensitivity to the active substance of the investigating drugs or any of their excipients were excluded from this trial. Each woman was allowed to participate only once.

The study was approved by the Ethics Committee Review Board of Papageorgiou General Hospital on 23 November 2009 (approval number: A6869).

Once informed consent was obtained, women were randomized to general anaesthesia either with the use of propofol or thiopental sodium. The random allocation of women was made by the anaesthesiologist based on a table of random numbers using a 1:1 allocation ratio on the day of oocyte retrieval. The patient, the physician performing the oocyte retrieval and the embryologists were not aware of the group that each patient was allocated to.

Ovarian stimulation and oocyte retrieval

Patients were stimulated for IVF using gonadotrophins either recombinant FSH (Gonal-F, Merck Serono Europe Ltd, London, UK; Puregon, NV Organon, Oss, the Netherlands), urinary FSH (Altermon, IBSA Institut Biochimique S.A. Switzerland) or long-acting FSH (Elonva, NV Organon, Oss, the Netherlands). Prevention of premature LH surge was carried out using gonadotrophin-releasing hormone (GnRH) agonists (Arvekap, Ipsen Ltd, France) or antagonists (Orgalutran, NV Organon, Oss, the Netherlands). Recombinant (Ovitrelle, Merck Serono Europe Ltd, London, UK) or human (Pregnyl, NV Organon, Oss, the Netherlands) HCG, or a combination of both, was used to trigger final oocyte maturation. If the treating physician deemed that the patient was at a high risk for ovarian hyperstimulation syndrome, GnRH agonist (Arvekap, Ipsen Ltd, France) was used in GnRH antagonist cycles. An experienced physician retrieved oocytes 36–38 h later using a transvaginal probe with a needle guide. All follicles 11 mm in diameter or wider from each ovary were aspirated using a 17G needle.

Oocytes were handed to the embryologist and fertilization was carried out either by conventional insemination, intracytoplasmic sperm injection (ICSI), or both conventional IVF and ICSI. Sequential media was used to culture the embryo (COOK Medical, Ireland, Ltd.), up until day 5 depending on the quality and the number of the resulting embryos. Up to four embryos were transferred according to Greek laws on reproduction. Vaginal micronized progesterone (600 mg daily) was used for luteal support (Utrogestan, Basins Iscovesco, Paris, France, vaginal tablets, 200 mg three times a day).

General anaesthesia protocol

On arrival to the operating theatre patients were connected to the monitoring equipment, and a Venturi mask was placed for the delivery of oxygen. A peripheral 18-gauge catheter was placed in the cephalic or basilic vein for the administration of crystalloid fluids and anaesthetic medications.

For the induction and maintenance of general anaesthesia, patients received either propofol 2.5 mg/kg and 0.1 mg of fentanyl, with additional doses of 0.5 mg/kg of propofol if required or thiopental 5 mg/kg and 0.1 mg of fentanyl, with additional doses of 1.0 mg/kg of thiopental if required.