IVF oocyte retrieval: prospective evaluation of the type of anesthesia on live birth rate, pain, and patient satisfaction

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Abstract

Purpose Does the type of anesthesia (paracervical block (PCB) or general anesthesia (GA)) impact live birth rate, pain, and patient satisfaction?

Methods A non-randomized prospective cohort study was conducted in women treated for IVF. Two groups of patients were prospectively included: the PCB group ($n = 234$) and the GA group ($n = 247$). The type of anesthesia was determined by the patients. The primary endpoint was cumulative live birth rate by OR. Secondary endpoints were self-assessment of the patients' peri-operative abdominal and vaginal pain vs the doctors' evaluations during PCB, post-operative abdominal and vaginal pain level, and patient satisfaction in both groups. Pain levels were assessed with a numerical rating scale (NRS).

Results The live birth rate was similar in both groups (19.8% in the GA group vs 20.9% in the PCB group, $P = 0.764$). During oocyte retrieval in the PCB group, the physicians significantly under-estimated the vaginal pain experienced by the patients (3.04 ± 0.173 for patients vs 2.59 ± 0.113 for surgeons, $P = 0.014$). Post-operative vaginal and abdominal pain were significantly greater in the PCB group compared to the GA group (2.26 ± 0.159 vs 1.66 ± 0.123, respectively, $P = 0.005$, and 3.80 ± 0.165 vs 3.00 ± 0.148, respectively, $P < 0.001$). Patients were more significantly satisfied with GA than with PBC ($P < 0.001$).

Conclusion Because the LBR was similar in both groups and patient satisfaction was high, the choice of anesthesia should be decided by the patients.

Keywords IVF · Pain relief · Paracervical block · General anesthesia · Live birth rate

Introduction

Transvaginal ultrasound-guided oocyte retrieval (OR) for assisted reproduction was first described in 1985 [1]. Pain during OR is caused by the aspirating needle puncturing the vaginal skin and ovarian capsule during its manipulation within the ovary during the procedure. OR is a relatively short outpatient procedure. The different types of anesthesia described for OR include general anesthesia (GA), neuraxial anesthesia (epidural or spinal), conscious sedation (CS), and injection of local anesthetic agents (paracervical block (PCB)), or any combination of these [2]. Many studies, with sometimes contradictory results, assessed the impact of anesthetic agents on in vitro fertilization (IVF) outcome, but two meta-analyses of analgesia during OR reported that propofol, alfentanil, or lidocaine did not affect reproductive outcome [2, 3]. In our department, except in cases of anesthetic contraindication or for organizational reasons, the type of anesthesia, GA or PCB, is chosen by the patient. The effectiveness of and

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satisfaction with PCB compared to GA has not been established in the literature. Due to the absence of recommendations, it is essential to assess pain and patient satisfaction under "real conditions" to improve anesthesia protocols. PCB is an easily handled anesthesia that is minimally invasive and does not require an anesthesiologist. Koninckx and Renaer [4] reported that the pouch of Douglas or uterosacral ligaments were more sensitive than the uterus, oviducts, or ovaries. Lignocaine, which is used in PCB, anesthetizes both the vaginal mucosa and the peritoneal membrane over the pouch of Douglas as well as the uterosacral ligaments [5].

The objective of our study was to compare the live birth rate, post-operative pain, and satisfaction associated with the anesthetic technique chosen by the patient, either PCB or GA.

Materials and methods

Population

We performed a prospective study from March 2014 to March 2015 in the Department of Gynecology, Obstetrics and Reproductive Medicine of the University Hospital La Conception (Marseille, France). Each patient gave written informed consent prior to participating in the study. Criteria for inclusion were as follows: (i) patient was admitted to the operating room for oocyte retrieval (IVF or ICSI cycle), and (ii) patient signed informed consent for the survey. Exclusion criteria were as follows: (i) patient undergoing oocyte retrieval for fertility preservation before cancer or genotoxic treatment.

Ovarian stimulation and oocyte retrieval

The gonadotropin dosage was selected individually, taking into account the patient's age, body mass index (BMI), and AMH ((μg/L), Beckman Coulter Kit, Brea, USA) levels and previous response to controlled ovarian stimulation (COS). The ovarian response was monitored via serum estradiol levels and transvaginal ultrasound. Ovulation was triggered using 10,000 IU of HCG (or Ovitrelle®, MerkSerono, Darmstadt, Germany). Transvaginal OR was performed 36 h after triggering under ultrasound guidance with a single lumen aspiration needle (17 GA, Cook, Brisbane, Australia). OR was performed by six different operators with equivalent training, and no flushing was performed in any group.

Anesthetic procedure

The anesthesia technique was decided by the patient during a consultation with the anesthetist before the start of ovarian stimulation. Patients were all counseled individually about the different techniques and possible risks of the procedure. PCB could be imposed in cases of GA contraindication or the unavailability of the anesthetist's medical staff. Patients were allowed to reconsider the choice of anesthesia at any time. On the day of OR, all patients received 25 mg of hydroxyzine at 7 am.

The PCB group also received premedication with 20 mg of nefopam (Medisol, Lyon, France) by the sublingual route 1 h before intervention. PCB with 10 mL of 2% lidocaine (200 mg lidocaine) was administered 5 min before retrieval at 2, 6, and 10 o'clock around the cervix. If necessary, patients received an additional analgesic during surgery.

In the GA group, patients received 1 g of IV paracetamol (B. Braun, Melsungen, Germany), immediately before the procedure. Induction was performed with propofol 2.5 mg/kg and alfentanil 20 μg/kg. Maintenance of anesthesia was assured by propofol boluses (1 mg/kg) and alfentanil (250 to 500 μg) if necessary, depending on the duration of the procedure. Manual ventilation was practiced with 50% O2/50% air or O2 100% and no inhalational anesthetic gas.

Patient characteristics

The clinical and biological characteristics of the patients and each IVF cycle were collected in our medical database (Medifirts, Montigni le Bretonneux, France). We assessed age, BMI, smoking, infertility duration, hormonal dosage (FSH, LH, estradiol, AMH), stimulation cycle (total dose of gonadotropin used, estradiol level day of ovulation triggering), attempt number, causes of infertility, and COS protocol.

IVF outcome

The primary outcome was cumulative live birth rate by OR, which was defined as delivery of a live fetus after 22 completed weeks. We considered cumulative live birth rates including thawing cycles. We evaluated the number of oocytes retrieved, the number of mature oocytes, 2-pronuclear zygotes (fertilized oocytes), and the number of embryos transferred. We also evaluated the clinical pregnancy rate (as defined by an ultrasound-verified pregnancy with fetal heartbeat) and first trimester miscarriage rate.

Assessment of peri-operative pain level in the PBC group

The pain level was assessed with numerical rating scale (NRS) (0 = no pain to 10 = intolerable), which is a commonly used pain assessment scale [6–8]. For the PCB group, the patient peri-operative vaginal and abdominal pain level was obtained by a nurse just after OR in the operating room. The physician's estimation of the patient's abdominal and vaginal pain during OR was blindly collected.

Assessment of post-operative pain level and satisfaction

A post-operative survey was given to all patients 4 h after oocyte recovery, and it evaluated vaginal and abdominal pain and patient satisfaction (very satisfied, satisfied, not satisfied, not satisfied at all, or no answer). For patients who had already had both types of anesthesia, we asked what type of anesthesia they would prefer for a future attempt. To investigate the relationship between pain and satisfaction, we compared the post-operative pain of "satisfied" patients (those who reported being "very satisfied" or "satisfied") with the post-operative pain of "unsatisfied" patients (those who reported "not being satisfied" or "not satisfied at all").

Ethics statement

The French Ethical Committee of Research in Obstetrics and Gynecology (CEROG 2014-GYN-1105) approved this study. Each patient gave written informed consent prior to participating in the study.

Statistical analysis

Analysis of the data was performed with Statistical Package for Social Sciences version 17.0 (SPSS Inc., Chicago, IL, USA). Statistically significant differences between groups were determined using unpaired Student's *t* tests or chi^2 tests as appropriate. All tests were two-tailed tests, and a *P* value less than or equal to 0.05 was considered statistically significant. Values were expressed as the mean ± standard deviation unless stated otherwise. We also performed subgroup analysis of peri- and post-operative pain levels among patients undergoing their first attempt (T1) and those who had already had at least one attempt (>T1). The objective was to determine whether an OR history can affect the perception of pain experienced by patients.

Results

A total of 234 patients in the PCB group were compared to 247 patients in the GA group. The clinical and biological characteristics of the patients are shown in Table 1. We did not find significant differences between the two groups in terms of age, infertility duration, smoking, day 3 FSH, AMH level, dose of gonadotropin used, E2 level during ovulation induction, etiologies of infertility, stimulation protocol used, and number of first attempts. The BMI was higher in the PCB group (24.46 ± 5.765 vs 23.36 ± 4.828, $P = 0.026$).

The live birth rates in the GA group and PCB group were similar, 19.8 vs 20.9%, $P = 0.764$ (Table 2). In the GA group vs the PCB group, more oocytes (10.29 ± 7.163 vs 9.09 ± 5.335, $P = 0.037$) and mature oocytes (7.87 ± 5578

Table 1 Clinical and biological characteristics of patients undergoing vaginal oocyte retrieval in general anesthesia group (GA) and paracervical block group (PCB)

	GA ($n = 247$)	PCB ($n = 234$)
Patient characteristics (mean ± SD)[a]		
Age (year)	33.06 ± 5.05	33.71 ± 5.6
BMI	23.36 ± 4.83	24.46 ± 5.77*
Infertility duration (month)	53.49 ± 28.95	53.05 ± 29.65
Smoking (%)[b]	20.7	24.6
FSH	6.97 ± 2.35	7.36 ± 2.76
AMH (Beckman-Coulter Kit)	3.80 ± 2.96	3.34 ± 3.19
E2	46.57 ± 31.08	43.10 ± 25.74
Dose of gonadotrophine	2246 ± 929	2336 ± 896
E2 level day of ovulation induction	2477 ± 1253	2365 ± 1271
Number of first IVF attempt	107	109
FIV/ICSI (%)[b]	56.3/43.7	57.7/42.3
Causes (%)[b]		
Endometriosis	30	14
Unexplained	24	28
IOP	28	34
Male	89	85
Mixte	40	45
Dysovulation	8	9
Tuboperitoneal	28	21
COS protocol (%)[b]		
Antagonist	56	48
Short	52	52
Long/short agonist	32	47
Long/long agonist	107	85

COS controlled ovarian stimulation

*Statistically significant ($P < 0.05$)

[a] *t* test

[b] Chi^2

Table 2 IVF results of patients undergoing vaginal oocyte retrieval in general anesthesia group (GA) and in paracervical block group (PCB)

	GA ($n = 247$)	PCB ($n = 234$)
Oocyte retrieval results (mean ± SD)[a]		
Number of oocytes retrieved	10.29 ± 7.16	9.10 ± 5.34*
Number of mature oocytes	7.87 ± 5.88	6.68 ± 4.21*
Number 2-pronuclear zygotes	4.59 ± 4.06	4.15 ± 2.96
Number of embryos transferred	1.52 ± 0.05	1.59 ± 0.049
Pregnancy outcomes (%)[b]		
Clinical pregnancy	23.9	25.6
Miscarriage	2.42	4.27
Life birth	19.8	20.9

*Statistically significant ($P < 0.05$)

[a] *t* test

[b] Chi^2

vs 6.68 ± 4.207, $P = 0.01$) were retrieved, but there was no difference in the number of 2-pronuclear zygotes. We did not report frozen embryo numbers. However, embryo freezing was performed in 30% of AG patients ($n = 75/248$) and 25% of AL patients ($n = 59/235$). This difference was not statistically different ($P = 0.22$).

Peri-operative vaginal pain estimated by the physicians compared to the patients' evaluations was respectively 2.59 ± 1.639 vs 3.04 ± 2.495, $P = 0.014$. The physicians' estimation of abdominal pain was not significantly different from that experienced by the patients (Table 3).

The post-operative pain level and satisfaction of various procedures as scored by the patients are summarized in Table 4. Distribution of post-operative abdominal and vaginal pain in GA and PCB group are summarized in Fig. 1. Post-operative pain was significantly higher in the PCB group than in the GA group, with NRS 2.26 ± 2.413 vs 1.66 ± 2.114, $P = 0.005$, for vaginal pain and 3.80 ± 2.499 vs 3.00 ± 2.324, $P < 0.001$, for abdominal pain. In the GA group, 98.4% of patients were very satisfied or satisfied vs 80.8% in the PCB group, and patients were more significantly satisfied in the GA group ($P < 0.001$). Patients who reported being not satisfied or not satisfied at all were almost always in the PCB group ($P < 0.001$). For patients with a history of OR with two anesthetic techniques ($n = 102$), 62.75% ($n = 64$) reported preferring GA and 37.25% preferred PCB. We reported that patients who were "not satisfied" had significantly more pain than patients who were "satisfied," with 4.47 ± 2.712 vs 1.74 ± 2.102 for post-operative vaginal pain ($P < 0.001$) and 6.25 ± 2.369 vs 3.15 ± 2.299 ($P < 0.001$) for post-operative abdominal pain, respectively.

A subgroup analysis was performed to assess whether OR history can affect the perception of pain experienced by patients, and it is summarized in Table 5. Post-operative abdominal and vaginal pain were similar in the T1 and >T1 groups. In the PCB group, peri-operative vaginal pain was higher in the T1 group than in the >T1 group (3.41 ± 2.433 vs 2.67 ± 2.502, $P = 0.029$). The peri-operative abdominal pain level was similar in both groups. On 234 patients in PCB group, 10.3% ($n = 24$) needed supplementary analgesia (five had alfentanil, seven had CS (alfentanil and propofol), four had sublingual acupan, five had inhalation of nitrous oxide, for three patients, the additional anesthesia was undefined). Two hundred thirteen patients received PCB by choice, 9 for medical reason, and 12 for the unavailability of the anesthetist's medical staff. Post-operative abdominal and vaginal pain were not statistically different between groups (Table 6).

Discussion

In this study, anesthesia protocol used had no impact on IVF LBR. Our results are similar to those reported in the literature,

Table 3 Peri-operative evaluation of vaginal and abdominal pain felt by the patient and considered by the physician in paracervical block group (numerical rating scale)

	Patient	Physician
Peri-operative pain level (mean ± SD)[a]		
Vaginal pain	3.04 ± 2.494	2.59 ± 1.639*
Abdominal pain	4.36 ± 2.628	4.00 ± 2.35

*Statistically significant ($P < 0.05$)

[a] *t* test

but these studies have a low statistical power. Bümen et al. [9] reported in 2011 the same LBR in a prospective study comparing remifentanil/propofol-based GA ($n = 32$) vs PCB (100 mg of 2% prilocaine and intramuscular (IM) meperidine) ($n = 38$). Christiaens et al. [10] reported no impact on a case-control study comparing alfentanil/propofol-based GA ($n = 101$) with PCB (400 mg mepivacaine hydrochloride with alfentanil) ($n = 101$). In our study, the number of oocytes retrieved and the number of mature oocytes was significantly higher with GA, without a clinical difference in LBR. Hammadeh et al. [11] reported in 1999 that general anesthesia improved the success rate of oocyte retrieval. They explained their results as improved comfort for both the patient and gynecologist during OR. In addition, general anesthesia enables the gynecologist to harvest even smaller follicles, increasing the retrieval of small and immature oocytes.

In the present study, we observed significantly higher post-operative vaginal and abdominal pain with PCB than GA. To our knowledge, there are no clinical trials comparing post-operative pain associated with these two types of anesthesia. We consider that the significant difference in the post-operative pain level for both types of anesthesia is clinically

Table 4 Four hour post-operative vaginal and abdominal pain (numerical rating scale) and satisfaction after oocyte retrieval between general anesthesia (GA) and paracervical block (PCB)

	GA $n = 247$	PCB $n = 234$
All patients post-operative (mean ± SD)[a]		
Vaginal pain	1.66 ± 2.114	2.26 ± 2.413*
Abdominal pain	3.00 ± 2.324	3.80 ± 2.499*
Satisfaction (%)[b]		
Very satisfied	66.0	51.7*
Satisfied	32.4	29.1*
Not satisfied	0.0	11.3*
Not satisfied at all	0.4	2.2*
No response	1.2	5.7*

NS non-significant difference

*Statistically significant ($P < 0.05$)

[a] *t* test

[b] Chi^2

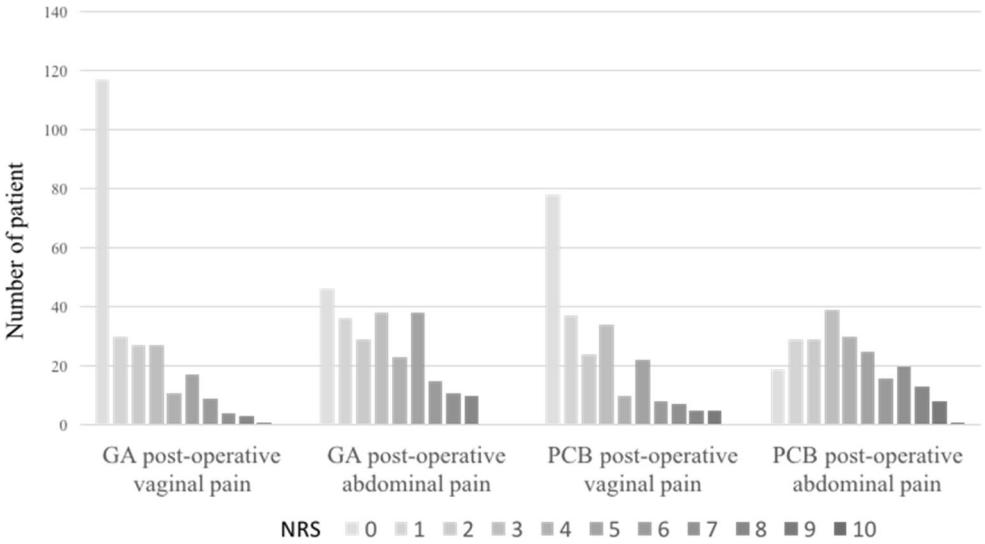

Fig. 1 Distribution of post-operative abdominal and vaginal pain in general anesthesia group (GA) and paracervical block (PCB) group. *NRS* numerical rating scale

acceptable. Indeed, post-operative vaginal pain was <3 in both groups, and the difference in post-operative abdominal pain scores, 3 for GA and 3.8 for PCB, was not clinically significant.

One of the main limitations of this study is the lack of randomization. The aim of our study was not to assess the superiority of one method over the other. Our goal was to assess pain and patient satisfaction "in real life," when the type of anesthesia is decided by the patient. Only BMI differed slightly in the patient characteristics between the two groups. The BMI was higher in the PCB group than in the GA group. Other authors observed in a randomized study comparing PCB with vaginal gel that BMI is positively correlated with total pain [12, 13], which could partly explain the difference in pain scores between our two groups. We consider two other weaknesses of our study. First, because we did not randomize, anesthesia protocols and the management of post-operative pain were not standardized. We did not quantify the amount of analgesic used to relieve patient post-operative pain. Second, patient's anxiety before OR was not assessed in our study. Indeed, higher levels of anxiety during oocyte retrieval seem positively associated with pain intensity and anxiety [14–16].

Table 5 Subgroup analysis of OR pain level among patients undergoing their first IVF attempt (T1) and those who already had at least one IVF attempt (>T1)

	T1	>T1
PCB peri-operative pain level (mean ± SD)[a]		
Vaginal pain	3.41 ± 2.433	2.67 ± 2.502*
Abdominal pain	4.25 ± 2.74	4.39 ± 2.547
PCB post-operative pain level (mean ± SD)[a]		
Vaginal pain	2.50 ± 2.534	2.04 ± 2.290
Abdominal pain	3.88 ± 2.701	3.74 ± 2.317
GA post-operative pain level (mean ± SD)[a]		
Vaginal pain	1.6 ± 2.060	1.71 ± 2.161
Abdominal pain	2.88 ± 2.350	3.09 ± 2.308

*Statistically significant ($P < 0.05$)

[a] *t* test

We report a high degree of satisfaction in both groups, but patients who reported being not satisfied or not at all satisfied were almost always in the PCB group. In a prospective randomized study between PCB and PCB+CS, 80% of patients with PCB alone were very satisfied or satisfied [17]. In the literature, there is satisfaction with GA of between 88 and 100% [18–20]. The lowest degree of satisfaction in our PCB group may be related to the higher peri- and post-operative pain for these patients. Notably, despite the high peri-operative pain in the PCB group, only 10.3% of patient needed additional analgesia during the retrieval (89.7% of retrievals were performed with PCB only). For [17], oocyte retrieval was successfully performed without any additional sedation in 89.3% of patients in the PCB group. This paradox may indicate that infertile patients undergoing oocyte retrieval are highly motivated and may be reluctant to demonstrate pain for fear of distracting the surgeon and interfering with the success of the procedure [21]. This is supported by the observation that despite the high satisfaction rate in both groups, most patients who already had two types of anesthesia would choose GA for a future IVF attempt.

Some studies reported that pain scores during OR may be influenced by previous experience. Gohar et al. [22] reported that the second cycle was less painful than the first cycle. In our study, post-operative pain was not related to the number of attempts.

In conclusion, the type of anesthesia chosen by our patients had no impact on LBR. GA seems to be the least painful and most satisfactory technique for our patients. Nevertheless, PCB seems a reasonable alternative, and the choice of anesthesia

Table 6 Paracervical block group: Comparison of pain level between patients who had a PCB by choice or by obligation (general anesthesia (GA) contraindication, unavailability of the anesthetists' medical staff) (numerical rating scale)

	Post-operative vaginal pain level (mean ± SD)[a]	Post-operative abdominal pain level (mean ± SD)[a]
Choice	2.12 ± 2.305	3.70 ± 2.401
$n = 213$		
GA contraindication	3.00 ± 3.055	4.78 ± 2.700
$n = 9$		
Unavailability of the medical staff	3.46 ± 2.700	4.07 ± 3.050
$n = 12$		

*Statistically significant ($P < 0.05$)

[a] *t* test

(excluding medical contraindication) may be given to patients but patients should be advised that PCB IVF may be more painful. In our center, many parameters, such as peri- and post-operative pain management and psychological factors, must be evaluated and improved to make this procedure more endurable.

Compliance with ethical standards The French Ethical Committee of Research in Obstetrics and Gynecology (CEROG 2014-GYN-1105) approved this study. Each patient gave written informed consent prior to participating in the study.

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Conflicts of interest The authors declare that they have no competing interests.

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