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Anaesthetic exposure during oocyte pickup: Comparative effects of fentanyl–propofol *versus* parecoxib sodium on neonatal outcomesShiyu Yang^{1*}, Jiahe Tian^{2*}, Xiufang Gui^{1*}, Longda Wang¹, Kaiming Yuan^{2✉}, Shuhua Zhao^{1✉}¹Department of Reproductive Genetics, the First Affiliated Hospital of Kunming Medical University, Kunming 650032, China²Department of Anaesthesiology and Perioperative Medicine, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Key Laboratory of Pediatric Anaesthesiology, Ministry of Education, Wenzhou Medical University, Key Laboratory of Anaesthesiology of Zhejiang Province, Wenzhou Medical University, Wenzhou 325027, China

ABSTRACT

Objective: To evaluate the neonatal outcomes of fentanyl–propofol anaesthesia *versus* parecoxib sodium analgesia regimens used during oocyte pickup (OPU).

Methods: Couples who underwent assisted reproductive technology (ART) treatment at the Reproductive Genetics Department of the First Affiliated Hospital of Kunming Medical University from April 2016 to February 2022 were enrolled in this study. The participants were divided into two groups based on the anaesthesia protocols used during OPU: parecoxib sodium analgesia ($n=1\,124$) and fentanyl–propofol anaesthesia ($n=1\,190$). Neonatal outcomes were systematically compared between these groups, with infant birth weight as the primary outcome.

Results: A total of 2314 couples were included in the study. After adjustment for confounders, the median birth weight of infants was significantly lower in the parecoxib sodium group than in the fentanyl–propofol group [3100 g (interquartile range: 2850–3400) *vs* 3200 g (IQR: 2900–3450), adjusted $\beta = -50.9$ (95% CI: -89.4 to -12.3), $P=0.01$]. This weight difference remained particularly significant in male infants [3120 g *vs* 3200 g, $\beta = -63.4$ (95% CI: -119.2 to -7.5), $P=0.03$], whereas no significant difference was observed in female infants after adjustment [$\beta = -27.9$ (95% CI: -82.9 to 27.1), $P>0.05$].

Conclusion: Neonates born after OPU with parecoxib sodium weighed significantly less than those delivered under fentanyl–propofol, and this difference was confined to male infants.

Keywords: Anaesthesia; Assisted reproductive technology; Infertility; Pregnancy outcomes

1. Introduction

Oocyte pick-up (OPU) is a key procedure in *in vitro* fertilisation

(IVF) treatment. However, this procedure entails the penetration of the vaginal wall and ovarian sac using a puncture needle, often resulting in mild-to-moderate pain and considerable anxiety to patients[1,2]. To improve patient comfort and treatment compliance, diverse clinical anaesthetic options are used, including general anaesthesia, conscious sedation, neuraxial anaesthesia, paracervical block, and alternative therapies[3]. However, there is no consensus

Key Points

Question: What is the effect of fentanyl–propofol anaesthesia versus parecoxib sodium analgesia during oocyte pickup on infant birth weight?

Findings: In this cohort study of 2314 couples, the median birth weight was significantly lower in the parecoxib sodium group than in the fentanyl–propofol group (3100 g *vs* 3200 g), a difference that remained significant in male infants but not in females.

Meaning: Fentanyl–propofol anaesthesia may be associated with higher infant birth weight compared with parecoxib sodium analgesia.

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regarding the optimal anaesthesia for OPU[3]. When choosing an anaesthetic regimen, it is crucial to consider the potential effects and adverse reactions of the anaesthetic/analgesic agents on oocyte quality. Anaesthetic drugs may affect oocyte developmental potential through the follicular fluid pathway, in turn affecting pregnancy outcomes[4]. Although many studies have investigated the effects of different anaesthesia modalities on IVF pregnancy outcomes, their conclusions vary widely.

Fentanyl is a potent synthetic opioid analgesic that acts through selective agonism of μ -type opioid receptors and is widely used for chronic pain management and perioperative analgesia because of its powerful analgesic effect[5]. The mechanism of action of propofol, as a potent intravenous anaesthetic, is closely related to γ -aminobutyric acid receptor activation[6]. In clinical surgery, propofol is often used in combination with fentanyl, which enhances anaesthesia and reduces propofol dosages[7,8]. This regimen is adopted in general anaesthesia to suppress the higher brain functions, causing a complete loss of consciousness and blockage of pain[9]. In one study, the number of embryos and pregnancy rates were higher when the fentanyl–propofol regimen was used during OPU than when midazolam and remifentanyl combined with paracervical lidocaine block were used[10]. In contrast, another study suggested that intravenous anaesthetic drugs, including fentanyl and propofol, do not affect reproductive outcomes[11].

Parecoxib sodium, a selective cyclooxygenase-2 (COX-2) inhibitor, is an effective intravenous or intramuscular analgesic that provides analgesia without sedation[12,13]. Unlike general anaesthesia, conscious sedation only slightly decreases consciousness, and the patient is able to maintain an open airway and remain responsive to verbal and somatic stimuli, enabling intraoperative patient–physician communication[14]. Studies have not demonstrated a direct effect of parecoxib sodium in expectant mothers on their pregnancy outcomes, but the use of COX inhibitors during pregnancy has been suggested to inhibit foetal prostaglandin synthesis, thereby affecting normal foetal development[15].

This retrospective study was conducted to compare the effects of anaesthetic and non-anaesthetic regimen: fentanyl–propofol and parecoxib sodium alone on pregnancy outcomes in patients treated with assisted reproductive technology (ART), aiming to provide a clinical reference point for the use of anaesthetics in ART.

2. Methods

2.1. Study population

This retrospective cohort study enrolled patients undergoing ART treatment at the Reproductive and Genetic Medicine Department of the First Affiliated Hospital of Kunming Medical University from

April 2016 to February 2022. The participants who met the eligibility criteria and underwent standardised IVF/intracytoplasmic sperm injection–embryo transfer treatment protocols following clinical standard operating procedures for therapeutic cycle management were enrolled.

2.2. Inclusion and exclusion criteria

The inclusion criteria were (1) female patients who underwent ART treatment with either fentanyl–propofol anaesthesia or complete parecoxib sodium analgesia during OPU procedures (excluding those converted to general anaesthesia during parecoxib sodium analgesia); (2) age ≥ 20 years and ≤ 43 years at treatment initiation; and (3) clinically confirmed intrauterine singleton pregnancy.

The exclusion criteria were (1) parental chromosomal abnormalities in either partner; (2) maternal preeclampsia; (3) maternal comorbidities including hypothyroidism, gestational hypertension, or diabetes mellitus; (4) uterine abnormalities (*e.g.* endometrial cancer, endometriosis); or (5) missing vital information.

2.3. Anaesthetic protocols and pharmacological administration

For OPU procedures, patients chose their preferred anaesthetic option—either fentanyl–propofol general anaesthesia or parecoxib sodium analgesia—after detailed consultation with physicians. In the fentanyl–propofol group, patients adhered to standard preoperative fasting guidelines (2 hours for clear fluids, 6 hours for light meals, and 8 hours for solids). Upon arrival, peripheral intravenous (*i.v.*) access was established with continuous multiparametric monitoring and supplemental oxygen *via* nasal cannula. Anaesthesia induction began 3 min before OPU, starting with 1 μ g/kg fentanyl *i.v.* bolus for analgesia, followed by 2 mg/kg propofol *i.v.* bolus for sedation, with an additional 1 mg/kg propofol administered if intraoperative movement occurred. Due to the risk of respiratory depression, continuous pulse oximetry was mandatory and assisted mask ventilation was provided for any hypoxemia until spontaneous breathing resumed. In the parecoxib sodium group, patients received a single 40 mg *i.v.* dose 30 min preoperatively.

2.4. Pregnancy outcomes

(1) Neonatal birth weight: The body mass of a newborn infant obtained by weighing shortly after delivery, typically within the first hour postnatally.

(2) Perinatal mortality rate: The percentage of foetal deaths (including stillbirths at or after 28 weeks of gestation and neonatal deaths within 7 days postpartum) relative to total births (stillbirths at or after 28 weeks of gestation plus live births)[16].

(3) Gestational age: Calculated as adjusted weeks, where weeks were rounded down if days were less than four (X weeks) or rounded up if days were four or more (X+1 weeks).

(4) Large for gestational age (LGA): Neonates with birth weight exceeding the 90th percentile or two standard deviations above the mean weight for their gestational age[17].

(5) Small for gestational age (SGA): Neonates with birth weight below the 10th percentile or two standard deviations (SDs) under the mean weight for their gestational age[17].

(6) Neonatal birth defect rate: The percentage of newborns presenting congenital anomalies (structural malformations, chromosomal abnormalities, genetic metabolic disorders, or functional impairments such as deafness, blindness, or intellectual disabilities) among total live births.

2.5. Data analysis

Our reproductive centre implemented strict data verification protocols to ensure accuracy. All data, including patient profiles, medical history, treatments, and outcomes, were systematically recorded through the Reproductive Genetics Department's specialised management system (v9.2.2.33). Neonatal anthropometric measurements, obstetric complications, and neonatal morbidity were prospectively documented by nurses during postpartum follow-up.

Baseline characteristics were summarised using percentages for categorical variables. Continuous variables were assessed for normality using the Anderson–Darling method, with normally distributed data expressed as mean±SD and non-normal data as median with interquartile range (IQR). Nonparametric comparisons were performed using the *Kruskal–Wallis* test, whereas *Fisher's* exact test was used to compare categorical variables with expected

frequencies less than 10. Univariate analyses (analysis of variance or χ^2 test) were used to identify risk factor–outcome associations, supplemented by stratified analyses to evaluate interactions between independent (X) and dependent (Y) variables across subgroups. Interaction tests incorporated linear regression, binary logistic regression, and multinomial logistic regression. Multivariable logistic regression models were adjusted for covariates that met the following inclusion criteria: (i) regression coefficient $P<0.10$; (ii) >10% coefficient change upon covariate inclusion; and (iii) clinical relevance as a potential confounder based on prior evidence. Variables considered as potential confounders are shown in Supplementary Table 1.

Statistical analyses were conducted using Empower Stats® (www.empowerstats.com; X&Y Solutions, Boston, MA) and R software (www.r-project.org). Two-tailed P values<0.05 were considered to indicate statistical significance.

2.6. Ethics statement

This study was performed in line with the principles of the Declaration of Helsinki. The study protocol was approved by the ethics committee of the First Affiliated Hospital of Kunming Medical University (approval no. 2025L90; approval date: March 27th, 2025).

3. Results

From April 2016 to February 2022, 3200 couples were initially enrolled using the predefined inclusion/exclusion criteria (Figure 1), of whom 2314 eligible couples were retained for analysis. Among these, 1190 (51.4%) couples received fentanyl–propofol anaesthesia during OPU, whereas 1124 (48.6%) couples received parecoxib

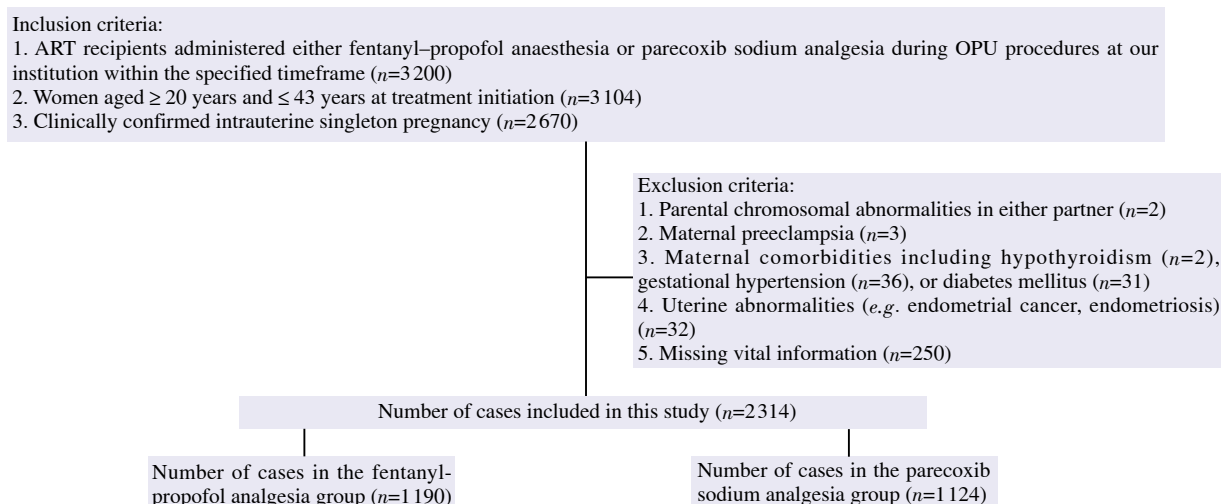


Figure 1. Flowchart of participant selection. Participants who met the eligibility criteria and underwent standardised *in-vitro* fertilisation/intracytoplasmic sperm injection–embryo transfer in accordance with standard operating procedures were enrolled into the study. ART: Assisted reproductive technology; OPU: Oocyte pick-up.

Table 1. Characteristics of the included participants.

Characteristics of included participants	Fentanyl-propofol	Parecoxib sodium	P value
<i>n</i>	1 190	1 124	174
Female age, years	30.0(27.0–33.0)	31.0(28.0–34.0)	<0.001
Female BMI, kg/m ²	22.1(20.0–24.7)	22.2(20.0–24.4)	0.33
Male age, years	32.0(29.0–35.0)	32.0(29.0–36.0)	<0.001
Male BMI, kg/m ²	24.2(21.8–26.9)	23.7(21.3–26.1)	0.001
FSH, mIU/L	6.0(4.6–7.3)	6.3(5.0–7.8)	<0.001
LH, mIU/L	5.7(3.6–9.2)	5.7(3.5–8.7)	0.34
P, ng/mL	0.2(0.1–0.5)	0.3(0.2–0.5)	0.08
PRL, ng/mL	16.7(12.3–23.0)	16.6(12.2–22.8)	0.37
T, ng/mL	0.3(0.2–0.4)	0.3(0.2–0.4)	<0.001
AMH, ng/mL	4.5(3.0–7.3)	3.7(2.1–5.9)	<0.001
Duration of infertility, years	3.0(2.0–5.0)	3.0(2.0–5.0)	0.03
Fertilization, <i>n</i> (%)			0.44
IVF	931(78.2%)	894(79.5%)	
ICSI	259(21.8%)	230(20.5%)	
Number of cycles, <i>n</i> (%)			<0.001
1	1 113(93.5%)	946(84.1%)	
2	63(5.3%)	138(12.3%)	
≥3	14(1.2%)	40(3.6%)	
Ovarian stimulation protocols, <i>n</i> (%)			<0.001
Long protocol	657(55.3%)	557(49.6%)	
Antagonist protocol	530(44.5%)	499(44.4%)	
Mild stimulation protocol	3(0.3%)	68(6.0%)	
Types of infertility, <i>n</i> (%)			<0.001
Primary	658(55.3%)	541(48.1%)	
Secondary	532(44.7%)	583(51.9%)	
Infertility diagnoses, <i>n</i> (%)			<0.001
Female factor	860(72.3%)	860(76.5%)	
Male factor	99(8.3%)	117(10.4%)	
Both	231(19.4%)	147(13.1%)	
Types of semen, <i>n</i> (%)			0.86
Husband semen	1 094(91.9%)	1 031(91.7%)	
Donor semen	96(8.1%)	93(8.3%)	
Semen source, <i>n</i> (%)			0.91
Fresh	1 092(91.8%)	1 030(91.6%)	
Frozen	98(8.2%)	94(8.4%)	
Types of embryo transfer, <i>n</i> (%)			0.03
Fresh	499(42.0%)	420(37.4%)	
Frozen	691(58.1%)	704(62.6%)	
Stages of the transferred embryos, <i>n</i> (%)			<0.001
Cleavage embryo	659(55.4%)	760(67.6%)	
Blastocyst	531(44.6%)	364(32.4%)	
Number of embryos transferred, <i>n</i> (%)			<0.001
1	379(31.9%)	272(24.2%)	
2	808(67.9%)	848(75.4%)	
3	3(0.3%)	4(0.4%)	
Gestational age, weeks, <i>n</i> (%)			0.19
34–36	88(7.4%)	102(9.1%)	
37–42	1 101(92.5%)	1 019(90.7%)	
>42	1(0.1%)	3(0.3%)	
Types of delivery, <i>n</i> (%)			0.18
Premature delivery	88(7.4%)	102(9.1%)	
Full-term delivery	1 099(92.4%)	1 016(90.4%)	
Post-term pregnancy	3(0.3%)	6(0.5%)	

Categorical variables were described using percentages and continuous variables were presented as median (interquartile range). BMI: Body mass index; FSH: Follicle-stimulating hormone; LH: Luteinising hormone; P: Progesterone; PRL: Prolactin; T: Testosterone; AMH: Anti-Müllerian hormone; IVF: *In vitro* fertilisation; ICSI: Intracytoplasmic sperm injection.

sodium analgesia.

Table 1 presents the demographic and baseline characteristics of the participants. Comparative analysis of baseline clinical characteristics revealed that the couple's age and baseline follicle-stimulating hormone (FSH) levels in female patients were significantly higher ($P<0.05$), whereas the male body mass index (BMI) and female testosterone (T) and anti-Müllerian hormone (AMH) levels were significantly lower, in the parecoxib sodium group than in the fentanyl-propofol group ($P<0.05$). Significant intergroup differences were observed in treatment cycle parameters, namely the number of cycles, ovarian stimulation protocols, types of infertility, infertility diagnoses, types of embryo transfer, stages of the transferred embryos, and number of embryos transferred (all $P<0.05$). However, no significant intergroup differences were detected in female BMI, duration of infertility, fertilisation rates, types of semen, semen

source, gestational age, types of delivery, or baseline levels of luteinising hormone (LH), progesterone (P), and prolactin (all $P>0.05$).

The median birth weight of infants was significantly lower in the parecoxib sodium group than in the fentanyl-propofol group [unadjusted: 3 100 g (IQR: 2 850–3 400) *vs* 3 200 g (IQR: 2 900–3 450), $\beta = -62.3$ (95% *CI*: -103.9 to -20.8), $P=0.003$], with this difference being particularly evident in male infants [3 120 g *vs* 3 200 g, $\beta = -87.7$ (95% *CI*: -148.6 to -26.9), $P=0.005$] but not in female infants ($P>0.05$) (Table 2).

The median birth weight was also significantly lower in the parecoxib sodium group than in the fentanyl-propofol group [adjusted $\beta = -50.9$ (95% *CI*: -89.4 to -12.3), $P=0.01$]. This weight reduction was particularly prominent in male infants [adjusted $\beta = -63.4$ (95% *CI*: -119.2 to -7.5), $P=0.03$] but not in female infants

Table 2. Comparisons of outcomes between the fentanyl-propofol and parecoxib sodium groups.

Outcomes	Fentanyl-propofol group	Parecoxib sodium group	β /OR (95% <i>CI</i>)	<i>P</i>	Adjusted β /OR (95% <i>CI</i>)	Adjusted <i>P</i>
<i>n</i>	1 190 (51.4%)	1 124 (48.6%)				
Neonatal weight (g)	3 200(2900–3450)	3 100(2850–3400)	-62.3(-103.9, -20.8)	0.003	-50.9(-89.4, -12.3)	0.01
Weight of boy (g)	3 200(2985–3500)	3 120(2820–3455)	-87.7(-148.6, -26.9)	0.005	-63.4(-119.2, -7.5)	0.03
Weight of girl (g)	3 115(2870–3400)	3 100(2850–3320)	-37.3(-93.3, 18.8)	0.19	-27.9(-82.9, 27.1)	0.32
Neonatal length (cm)	50.0(49.0–50.0)	50.0(49.0–51.0)	-0.1(-0.3, 0.1)	0.50	-0.1(-0.3, 0.1)	0.21
Gestational age (weeks)	39.0(38.0–40.0)	39.0(38.0–40.0)	-0.1(-0.3, 0)	0.09	0.0(-0.2, 0.1)	0.44
SGAs, <i>n</i> (%)	149(12.6%)	151(13.5%)	1.1(0.9, 1.4)	0.51	1.1(0.8, 1.5)	0.45
LGAs, <i>n</i> (%)	118(9.9%)	112(10.0%)	1.0(0.8, 1.3)	0.96	1.0(0.7, 1.4)	0.94
Preterm infants, <i>n</i> (%)	88(7.4%)	102(9.1%)	1.2(0.9, 1.7)	0.14	1.0(0.0, Inf)	>0.999
Low birth weight infants, <i>n</i> (%)	90(7.6%)	94(8.4%)	1.1(0.8, 1.5)	0.48	1.1(0.7, 1.6)	0.64
Macrosomia, <i>n</i> (%)	31(2.6%)	24(2.1%)	0.8(0.5, 1.4)	0.46	0.8(0.4, 1.4)	0.41
Neonatal deaths, <i>n</i> (%)	2(0.2%)	4(0.4%)	2.1(0.4, 11.6)	0.39	1.3(0.1, 13.6)	0.81
Perinatal mortality, <i>n</i> (%)	3(0.3%)	2(0.2%)	0.7(0.1, 4.2)	0.70	0.5(0.1, 4.0)	0.48
Neonatal defects, <i>n</i> (%)	12(1.0%)	17(1.5%)	1.5(0.7, 3.2)	0.28	1.4(0.6, 2.9)	0.41
Composite neonatal deaths/ birth defects, <i>n</i> (%)	13(1.1%)	21(1.9%)	1.7(0.9, 3.5)	0.13	1.5(0.7, 3.2)	0.33

Categorical variables were described using percentages and continuous variables were presented as median (interquartile range). LGA: Large for gestational age; SGA: Small for gestational age.

Table 3. Subgroup analysis between foetal weight and anaesthesia protocol.

Characteristics	<i>n</i>	Weights of male and female foetuses		Weights of male foetuses		Weights of female foetuses	
		β (95% <i>CI</i>)	Interaction <i>P</i> value	β (95% <i>CI</i>)	Interaction <i>P</i> value	β (95% <i>CI</i>)	Interaction <i>P</i> value
Female age, years							
<30	1 013	-58.6(-119.9, 2.8)	0.87	-66.5(-153.0, 20.0)	0.75	-51.1(-143.5, 41.4)	0.85
<35	895	-26.0(-85.7, 33.6)		-57.1(-144.7, 30.5)		5.4(-76.4, 87.3)	
≥35	406	-56.9(-149.5, 35.6)		-70.9(-216.5, 74.7)		-57.2(-187.8, 73.5)	
Types of semen							
Husband semen	2 125	-50.0(-90.2, -9.7)	0.73	-51.6(-109.9, 6.7)	0.16	-37.8(-95.5, 19.8)	0.33
Donor semen	189	-61.3(-195.9, 73.2)		-182.9 (-381.2, 15.4)		110.2(-93.8, 314.1)	
Fertilisation							
IVF	1 825	-46.9(-90.5, -3.3)	0.56	-73.9(-137.2, -10.7)	0.55	-16.7(-78.7, 45.2)	0.18
ICSI	489	-72.8(-155.9, 10.4)		-61.5(-179.8, 56.8)		-76.0(-198.0, 46.0)	
Types of embryo transfer							
Fresh	919	-80.1(-140.7, -19.6)	0.31	-76.0(-165.9, 13.8)	0.82	-87.9(-173.8, -2.0)	0.20
Frozen	1 395	-25.0(-75.1, 25.0)		-35.2(-106.4, 36.0)		-4.6(-76.3, 67.2)	
Stages of transferred embryos							
Cleavage embryo	1 419	-68.8(-117.2, -20.5)	0.55	-105.3(-176.8, -33.7)	0.31	-23.1(-90.5, 44.3)	0.66
Blastocyst	895	-15.7(-80.5, 49.0)		16.0(-74.8, 106.9)		-37.0(-130.7, 56.6)	

IVF: *In vitro* fertilisation; ICSI: Intracytoplasmic sperm injection.

($P>0.05$). Other pregnancy outcomes showed no significant between-group differences (all $P>0.05$, both before and after adjustment) (Table 2).

During OPU procedures, compared with the fentanyl–propofol group, patients in the parecoxib sodium group demonstrated a consistent trend towards lower total infant birth weights across all subgroups ($\beta<0$). Male infant birth weights in the parecoxib sodium group also showed a decreasing trend ($\beta<0$) in most subgroups, with the exception of an increasing trend ($\beta>0$) observed in the subgroup of blastocyst-stage embryo transfer. Female infant birth weights exhibited an increasing trend ($\beta>0$) in both the 30–35-year-old female cohort and the group receiving sperm donation. To further assess the stability of the relationship between anaesthesia regimens and infant birth weight across strata, interaction tests were performed, which revealed no significant differences in this relationship between different stratification levels ($P>0.05$), indicating consistent associations between anaesthesia regimens and infant birth weight across all subgroups (Table 3).

4. Discussion

The potential effects of anaesthetic agents administered during OPU on subsequent pregnancy outcomes remain a subject of ongoing scientific debate[18,19]. Our study showed that although parecoxib sodium analgesia moderately reduced neonatal birth weight, particularly in male newborns, it did not increase the risk of abnormal birth weight categories or other adverse perinatal outcomes. This suggests the anaesthetic and non-anaesthetic regimens have varying degrees of effect on foetal development, but they are generally safe in normal pregnancy populations. This finding aligns with previous studies demonstrating that propofol exposure does not clinically affect pregnancy outcomes, although it should be noted that those studies primarily focused on oocyte maturation and embryogenesis rather than neonatal outcomes[20–23].

Although direct evidence on parecoxib sodium's reproductive effects remains limited, its pharmacokinetic profile suggests potential mechanisms: rapid hepatic conversion to valdecoxib (peak plasma concentration in 15 min, $t_{1/2}=5.4\text{--}9.9$ h) may allow follicular fluid penetration due to moderate lipophilicity[24,25]. As a potent COX-2 inhibitor, it significantly suppresses prostaglandin (PG) synthesis[26,27]. Granulosa cells in stimulated follicles normally exhibit elevated PG production during controlled ovarian hyperstimulation[28,29]. Thus, even brief exposure during the critical 30 min window may alter the oocyte microenvironment through PG modulation, potentially affecting subsequent developmental competence.

Preconception health posits that the foetus is shaped not only by the nine months of gestational exposure but also by the mother's pre-

pregnancy condition[30]. Excess glucocorticoids during pregnancy reprogramme development and heighten the risks of intrauterine growth restriction and preterm birth[31–33]. When only parecoxib sodium is used for intra-operative analgesia, patients remain fully conscious; recent data show that the pain of needle puncture and even routine surgical words (“scalpel”, “incision”) act as potent psychological stressors, especially in women[34]. This stress is amplified by the hypothalamic-pituitary-adrenal (HPA) axis, elevating maternal cortisol and potentially exposing the oocyte to supraphysiological glucocorticoids[35]. The resulting disruption of glucocorticoid signalling within the oocyte perturbs early embryonic metabolic and epigenetic programming, ultimately lowering birth weight and increasing later metabolic risk[36,37]. Investigating how different OPU anaesthetic regimens modulate this stress response may therefore clarify neonatal weight differences and improve ART outcomes.

Male infants showed greater weight-shift risk, echoing prior evidence that maternal stress operates in a sex-dimorphic manner: anxious mothers delivered sons with accelerated growth and daughters with suppressed weight[38]. Mechanistically, prenatal glucocorticoids down-regulated key genes in female placentas while leaving the same loci stable or up-regulated in males[39–41]. One explanation holds that male foetuses adopt a “minimal-placental-adjustment” strategy to sustain growth, rendering them more vulnerable, whereas females enhance resilience through multi-layer placental reprogramming[42]. Furthermore, female placentae dynamically modulate receptor sensitivity to glucocorticoid fluctuations, whereas male placentae display metabolic resistance[43,44]. These findings collectively suggest that elevated maternal prenatal cortisol levels differentially stimulate foetal growth *via* sex-dimorphic regulatory pathways mediated by placental adaptation mechanisms.

Although this study provides new insights into the effects of anaesthetic and non-anaesthetic regimens on pregnancy outcomes, it has some limitations. First, given the lack of standardised obstetric evaluation criteria in ART, we referred to the obstetric indicators of the normal pregnancy population for assessment. However, the ART-treated population and the natural pregnancy population show significant differences in their whole pregnancy process as well as the long-term development of their offspring[45–47]. Moreover, owing to ethical concerns regarding non-analgesic protocols, our institution lacks a blank control group without pharmacological intervention. Nevertheless, our findings demonstrate that anaesthetic analgesics/sedatives do not pose additional risks compared to non-anaesthetic analgesics, thereby providing evidence supporting the safety of anaesthetised oocyte retrieval. Second, patients undergoing ART treatment often receive subsequent prenatal care at different hospitals, where varying gestational management protocols may lead to disparities in neonatal birth weights.

In summary, this study presents novel evidence suggesting that the parecoxib sodium-based analgesic regimen during oocyte retrieval procedures is associated with reduced neonatal birth weight, with observed gender-specific effects. These findings have important clinical implications for optimising anaesthesia protocols to enhance ART success rates. However, further rigorous investigations are warranted to both validate these preliminary observations and elucidate the precise mechanistic pathways through which anaesthetic agents may influence pregnancy outcomes.

Conflict of interest statement

The authors declare that there are no conflict of interest.

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Data availability statement

The datasets generated and/or analysed during the current study are not publicly available to protect patient privacy and maintain research integrity but are available from the corresponding author on reasonable request.

Authors' contributions

Shiyu Yang conducted the statistical analysis and wrote the main manuscript text. Jiahe Tian and Xiufang Gui assisted with the analysis and edited the draft manuscript. Longda Wang provided input on the design and revision. Kaiming Yuan and Shuhua Zhao designed and directed the entire study and extracted all data from medical records. All authors have read and approved the final version.

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Anaesthetic exposure during oocyte pickup: Comparative effects of fentanyl–propofol versus parecoxib sodium on neonatal outcomes

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Supplementary Materials

Supplementary Table 1. Selection of confounders.

Items	Female age	Female BMI	Male age	Male BMI	Fertilization	Number of cycles	Year of infertility	Types of infertility	Infertility diagnosis	Types of semen	Types of embryo transfer	Day of embryo transfer	Number of embryos transferred	Date of delivery	Foetal sexes	Type of delivery
Neonatal weight	-	×	-	-	-	-	-	-	-	-	-	-	-	×	×	×
Weight of boy	-	-	-	-	-	-	-	-	-	-	-	-	×	×	×	×
Weight of girl	×	×	-	-	-	×	-	-	-	-	×	×	×	×	×	×
Neonatal length	×	×	-	×	-	×	-	-	-	-	-	-	×	×	×	×
Gestational age	-	×	-	-	-	-	-	×	-	×	×	×	×	×	×	×
SGAs	-	×	-	-	×	×	-	×	×	-	-	×	×	×	-	-
LGAs	×	×	×	×	×	×	×	×	×	×	×	×	×	×	×	×
Preterm birth	-	×	-	-	-	×	×	×	×	-	×	-	-	×	×	×
Low birth weight infants	×	-	×	×	×	×	×	×	-	-	-	×	-	×	×	×
Macrosomia	-	×	×	×	-	-	-	-	×	-	×	×	×	×	×	×
Neonatal deaths	×	×	×	-	×	×	×	×	×	×	×	×	×	×	×	×
Neonatal birth defects	-	-	-	-	-	-	-	-	-	-	×	×	-	-	-	-
Composite neonatal mortality/birth defects	-	-	-	-	-	-	-	-	-	-	×	×	-	×	-	×

×: included variables, -: excluded variables.