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Different methods of pain relief for IVF and ICSI oocyte retrieval – A Dutch survey

Inez Roest^{a,*}, Erato T.I.A. Buisman^{b,c}, Jan Willem van der Steeg^b, Carolien A.M. Koks^a^a Maastricht Medical Centre, Department of Obstetrics and Gynaecology, de Run 4600, 5504 DB, Veldhoven/Eindhoven, the Netherlands^b Jeroen Bosch Hospital, Department of Obstetrics and Gynaecology, Henri Dunantstraat 1, 5223 GZ, 's-Hertogenbosch, the Netherlands^c Radboudumc, Department of Obstetrics and Gynaecology, Geert Grooteplein zuid 10, 6525 GA, Nijmegen, the Netherlands

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ABSTRACT

Objective: Which analgesia methods are used during oocyte retrieval in the Netherlands?**StudyDesign:** In April 2017, an online survey containing questions on the analgesia protocol used for IVF/ICSI oocyte retrieval was sent to all clinics in the Netherlands that perform oocyte retrievals.**Results:** The response rate was 97%. We uncovered the large variety of medication protocols used for pain relief during oocyte retrieval in the Netherlands. Based on the main component of the given analgesia, we distinguished the three most frequently used analgesia protocols: intravenously (i.v.) administered opioids, intramuscularly (i.m.) administered opioids, and non-sedative oral analgesics. Aside from analgesia, 61% provided anxiolysis with a benzodiazepine. Nearly half of the clinics registered pain scores. The vital functions were monitored at all clinics administering opioids i.v., but at none of the clinics administering opioids i.m.**Conclusions:** A wide variety of analgesia protocols are used. The three most frequently used are i.v. administered opioids, i.m. administered opioids, and non-sedative oral analgesics. The variety of analgesia protocols is not desirable in the context of good clinical practice, and considering the risks of combining opioids and benzodiazepines. Monitoring of vital functions was only performed after administration of i.v. medication. A comparison of the pain scores could be a first step in finding the optimal method of analgesia, thereby forming the basis of guidelines for analgesia during oocyte retrieval.© 2019 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Historically, oocyte retrieval was performed under general anaesthesia. Now, other, lighter forms of analgesia are widely used. In a search for the optimal method of analgesia during oocyte retrieval, a number of factors are important. Because of the short duration of the procedure, the analgesia used is preferred to work fast and for a short period of time. Furthermore, the post-anaesthesia side-effects need to be minimal, and the analgesia may not have a negative effect on the oocyte quality. Many methods meet these criteria. Surveys in the United States of America [1] and the United Kingdom [2] showed that conscious sedation with a combination of opioids with benzodiazepines and/or propofol was the most frequently used method of analgesia in these countries, with rates of 95% and 84%, respectively. The depth of sedation was

not discussed in these studies. Unfortunately, no recent surveys on the analgesia methods used in other countries have been published. A Cochrane review published in 2018, concluded that no method alone is superior to another in means of analgesia. However, simultaneous use of sedation combined with analgesia such as opiates, further enhanced by paracervical block or acupuncture techniques, resulted in better pain relief than occurred with one modality alone. Furthermore, the different analgesia methods did not appear to affect the pregnancy rates [3].

Because of the variety of analgesia protocols described in the literature and the absence of recent survey-data our interest was sparked to assess which methods are used in the Netherlands. Furthermore, we wanted to assess to which extent the recommendations for monitoring the vital functions are followed.

Materials and methods

In April 2017, online questionnaires were sent to all 37 fertility clinics performing oocyte retrievals in the Netherlands. Twelve of these clinics have a laboratory where they perform in vitro

* Corresponding author.

E-mail addresses: inez.roest@mmc.nl, i.roest@student.maastrichtuniversity.nl (I. Roest).

fertilization (IVF) and intracytoplasmic sperm injection (ICSI). The other 25 clinics perform oocyte retrievals, after which the oocytes are transported to one of the 12 laboratories, where IVF and ICSI are performed. The clinics that do not have their own IVF/ICSI laboratory are called “transport clinics”.

The questionnaire was made up of three open questions about the standard protocol of medication given before and during the procedure, possibilities for additional medication, and alternative analgesia after a first, traumatic oocyte retrieval. Furthermore, three multiple-choice questions were included about the monitoring of the vital functions, the type of observation area after the procedure, and the registration of pain scores. The clinics that did not respond on a first attempt were approached again by telephone or e-mail.

This is a descriptive study. Our aim was to identify the methods of analgesia and to categorize them into groups according to the main component. Given the descriptive nature of this study, no particular formulas were used for statistical analysis. The data obtained from the questionnaires were analysed in Microsoft Office Excel 2016.

Results

We received completed questionnaires from all 12 clinics performing IVF and ICSI in the Netherlands, and from 24 of the 25 transport clinics. This amounted to a response rate of 97% (36 out of 37 clinics). Three of the clinics that responded are private clinics, six general hospitals, eight academic centres and 19 major “top-clinical” hospitals. A major “top-clinical” hospital provides more complex care, is academically oriented and has a teaching license. The only hospital that did not respond was a public, general hospital (Table 1). In 2017, 12,036 oocyte retrieval were performed in the Netherlands.

Based on the main component of the given analgesia, we distinguished five groups of analgesia protocols (Fig. 1):

- 1 Opioids intravenously.
- 2 Opioids intramuscularly.
- 3 Non-sedative oral analgesics (Non-steroidal anti-inflammatory drugs (NSAID) and/or paracetamol).
- 4 Paracervical block.
- 5 Opioids subcutaneously.

Aside from analgesia, 22 of the 36 clinics (61%) provided anxiolytics with benzodiazepine (Fig. 2). Of these clinics, 15 (68.2%) gave this orally, six (27.3%) intravenously and one (4.5%) intramuscularly.

1. Opioids intravenously

In 15 of the 36 clinics (42%), analgesia was provided with opioids administered intravenously (Fig. 3). Five of the 15 clinics (33%) supplied no additional medication. Seven of the 15 clinics (47%) gave a benzodiazepine. One clinic combined the intravenous opioid with a paracervical block. Two clinics gave only paracetamol and/or an NSAID aside from the intravenous opioid.

Table 1

Characteristics of the different hospitals/clinics in the Netherlands that perform oocyte retrieval, and the number of respondents to the survey subdivided per category. A major “top-clinical” hospital provides more complex care than a general hospital and is academically oriented.

	Responding centers
Academic centres	8/8
Private clinics	3/3
Major “top-clinical” hospitals	19/19
General hospital	6/7

Main component of analgesia

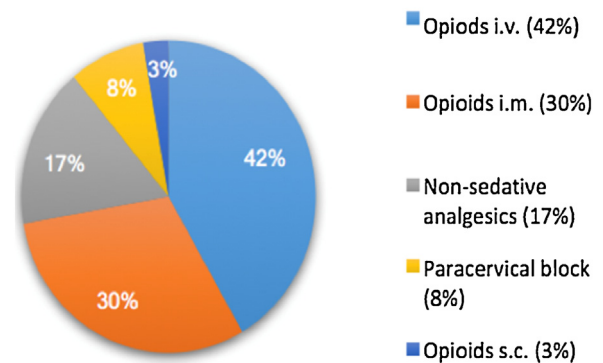


Fig. 1. This figure displays the results of the 36 clinics that responded to our questionnaire. Based on the main component of the given analgesia and the method of administration, five categories can be distinguished. i.v. = intravenously, i.m. = intramuscularly, Non-sedative analgesics = Non-Steroidal Anti-Inflammatory Drug and/or paracetamol., s.c = subcutaneously.

Anxiolytic

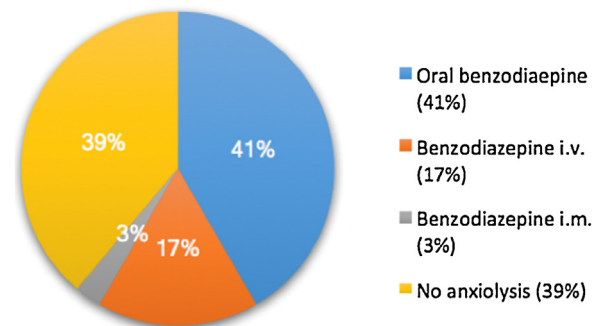


Fig. 2. At 22 of the 36 clinics (61%), anxiolytics are given additionally to analgesia. This figure displays the distribution of the use and administration methods of anxiolytics. i.v. = intravenously, i.m. = intramuscularly.

Additional medication i.v. opioids group

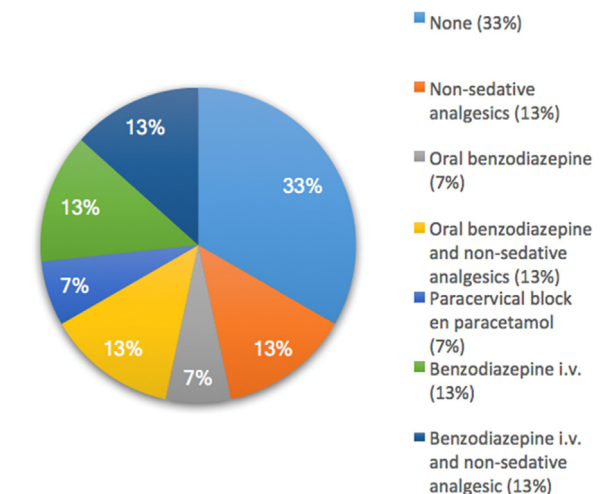


Fig. 3. At 15 of the 36 clinics (42%), an opioid is administered intravenously as main component of the analgesia protocol. This figure displays the distribution of the additional medication given at each clinic within the group of intravenous opioids. Non-sedative analgesics = Non-Steroidal Anti-Inflammatory Drug and/or paracetamol. i.v. = intravenously.

Additional medication i.m. opioids group

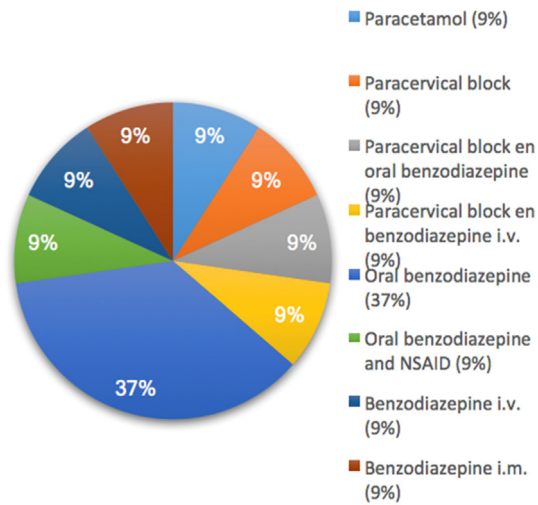


Fig. 4. At 11 of the 36 clinics (31%), an intramuscular opioid is given as the main component of analgesia. This figure displays the distribution of the additional medication given at each clinic within the group of intramuscular opioids. NSAID=Non-Steroidal Anti-Inflammatory Drug, i.v. = intravenously, i.m. = intramuscularly.

2. Opioids intramuscularly

In 11 of the 36 clinics (31%), opioids were administered intramuscularly (Fig. 4). In nine of the 11 (82%) pethidine was used. All 11 clinics provided additional medication. Three clinics (27%) administered a paracervical block. Nine of the 11 clinics (82%) supplied a benzodiazepine.

3. Non-sedative oral analgesics (NSAID and/or paracetamol)

Six of the 36 clinics (17%) gave only non-sedative oral analgesics as analgesia. Four of these (67%) provided an additional benzodiazepine orally, while two (33%) administered a benzodiazepine intravenously.

4. Paracervical block

In three of the 36 clinics (8.3%), a paracervical block was administered, without additional opioids, but with an NSAID. Two clinics also provided paracetamol. None of these clinics gave an anxiolytic.

5. Opioids subcutaneously

One clinic (2.8%) provided analgesia with a subcutaneous opioid. Additionally, an oral benzodiazepine and paracetamol were given.

Dosages

Table 2 displays the range of dosage of the administered drugs. Not all clinics provided the dosage in their response. Most clinics declared to increase the dosage upon patient's request during the procedure, or, in case of a very painful previous procedure, at the start of the procedure.

Vital functions

The vital functions were monitored in all clinics administering opioids intravenously or subcutaneously, and in none of the clinics administering an opioid intramuscularly. The clinics that provided non-sedative oral analgesics or that administered a paracervical block did not monitor vital functions, except for one of the two clinics that additionally administered a benzodiazepine intravenously.

Table 2

Minimal and maximal dosages per drug are displayed.

Drug	Dosage
Opioids	
Alfentanil i.v.	0.25–1 mg
Alfentanil i.m.	1 mg
Fentanyl i.v.	50–150µg
Pethidine i.m.	50–100mg
Methadone i.m.	5–7.5mg
Morfine s.c.	0.1 mg/kg, max10 mg
NSAIDs	
Naproxen supp.	500 mg
Naproxen not spec.*	50, 100, 250, 500 mg
Diclofenac supp	50, 100mg
Diclofenac not spec.*	50mg
Indometacine	100mg
Benzodiazepines	
Oxazepam	10–20mg
Diazepam	10–20mg
Temazepam	10mg
Lorazepam	1 mg
Midazolam oral	7.5mg
Midazolam i.v.	2–5mg
Midazolam i.m.	5mg

* Method of administration is not specified. i.v. = intravenously, i.m. = intramuscularly, s.c. = subcutaneously.

Recovery

In 31 of the 36 clinics (86%), patients were monitored after the procedure in a room near the procedure room. In three of the 36 clinics (8.3%), patients were admitted to a formal recovery room similar to those used after surgery. Two of these clinics gave intravenous opioids without anxiolytics and one clinic gave intramuscular opioids with a paracervical block and an intravenous benzodiazepine. Patients were not monitored at all after oocyte retrieval in one clinic. This was a clinic where an NSAID and an oral benzodiazepine were given. Another clinic used a recovery room as well as a non-equipped room, but they did not specify which criteria they based the selection of one of these two rooms on.

Pain scores

Seventeen of the 36 clinics (47%) registered pain scores during or directly after the procedure.

Discussion

This survey displays the large variety of protocols used for pain relief during oocyte retrieval in the Netherlands. The strength of this survey is the response rate of 97%. We can therefore state that our findings give an accurate view of the pain protocols used in the Netherlands. The protocols can be divided into five groups: intravenous opioids, intramuscular opioids, non-sedative oral analgesics, paracervical block and subcutaneous opioids. Within these groups, a variety of additional medication was given, resulting in many different combinations of drugs.

A number of studies have been performed comparing various conscious sedation and analgesia protocols during oocyte retrieval. In a Cochrane review published in 2018, the studies comparing conscious sedation and analgesia to other interventions were selected [3]. The other interventions were placebo or no medication, general anaesthesia, spinal anaesthesia, a paracervical block, acupuncture, patient-administered sedation, and physician-administered sedation. None of these methods proved to be superior to another in means of analgesia. However, two methods combined did result in lower pain scores than any single method by itself. The evidence was generally of low to very low quality. The

depth of sedation and analgesia was not discussed. Due to heterogeneity in methods and moments of measurement of pain, the studies published thus far are difficult to compare.

At all clinics that responded to our survey, the aim of their protocol was to provide analgesia with minimal sedation, during which patients were completely conscious and verbal communication remained possible. At 17% of the Dutch clinics, oral, non-sedative analgesia was given, sometimes combined with an anxiolytic. Thus far, this method of analgesia has not been compared to the more commonly used analgesics, such as opioids, with or without an anxiolytic.

Aside from the administered analgesia, pain scores are also affected by psychosocial factors. A study by Frederiksen et al. showed that women who had a high level of anxiety, a low level of perceived control, or negative gynaecological experiences in the past, reported higher pain scores [4]. These findings support the administration of an anxiolytic in order to reduce pain during oocyte retrieval. An anxiolytic was given before or during the procedure in 22 of the 36 responding clinics (61%). However, the combination of opioids and anxiolytics such as benzodiazepines is not without risks. Therefore, the anaesthesiology guidelines recommend caution with the combination of opioids and sedatives. The physician needs to be aware of the risk of depression of the breathing centre, which could, particularly after the painful stimulus has been terminated, lead to respiratory depression or arrest, or in extreme cases, to a circulatory arrest. Personal and instrumental monitoring of vital functions is advised after procedural sedation and/or analgesia [5–7]. Escape medication, such as atropine and naloxone, should be available in case of disturbance of the vital functions. A short-acting opioid is recommended for short procedures such as oocyte retrieval.

Our results display a variety in the extent of monitoring of the vital functions. All clinics which administered opioids intravenously, but none of the clinics which administered opioids intramuscularly monitored the vital functions. Monitoring varies in the group providing pain relief with a non-sedative analgesic, depending on whether an anxiolytic was given and, if so, whether this was given orally or intravenously. When opioids and benzodiazepines are combined, there is a risk of respiratory depression and arrest [6,7]. This risk is higher when opioids are administered intramuscularly and combined with an anxiolytic, due to the unpredictable sedation level and the unpredictable duration of the effect [5]. It is therefore, striking that women were admitted to a formal recovery room in only three clinics. However, many clinics reported that patients were monitored after the procedure in a resting room near the procedure room. A shortcoming of our survey was that we did not retrieve whether these rooms contain the recommended facilities for monitoring of recovery, facilities for basic life support, nor did we ask whether escape medication such as atropine was present.

In conclusion, we uncovered the large variety of medication protocols used for pain relief during oocyte retrieval in the Netherlands. Based on the main component of the given analgesia, the three most frequently used analgesia protocols are intravenously administered opioids, intramuscularly administered opioids, and non-sedative oral analgesics. Aside from analgesia, 61% of the respondents provided anxiolysis with a benzodiazepine. A uniform guideline ensures that all patients, regardless of the

clinic that they visit, receive correct analgesia under safe circumstances during their oocyte retrieval. Only half of the clinics that responded to our questionnaire registered pain scores. First, it is important that all clinics report their pain scores. Subsequently, a comparison of these scores could be the first step in finding the optimal method of analgesia and/or anxiolysis, and could thereby form the basis of an international guideline for analgesia during oocyte retrieval. Further analysis of these pain scores could also uncover factors to base individualized analgesia protocols on as a next step. Furthermore, it would be interesting to perform similar surveys in other countries, to gain information on the current methods of pain relief during oocyte retrieval used worldwide.

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Author's roles

IR: study conception and design, acquisition of data, analysis and interpretation of data, drafting of manuscript, final approval. EB: acquisition of data, analysis and interpretation of data, drafting of manuscript, final approval. JS: interpretation of data, critical revision, final approval. CK: study conception and design, interpretation of data, critical revision, final approval.

Key message

In the Netherlands, a wide variety of analgesia protocols are used during oocyte retrieval. This is not desirable in the context of good clinical practice. Comparing pain scores could be a first step in finding the optimal method of analgesia, and forming guidelines for analgesia during oocyte retrieval.

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