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#### **Research Article**

# Epidural Analgesia versus Remifentanil Patient Controlled Analgesia in Labor: A Survey of Practice in the Netherlands

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#### **Abstract**

**Introduction:** Epidural analgesia is widely recommended as method of choice for pain relief during labor whereas it is recommended to use remifentanil patient controlled analgesia only in the context of a randomized clinical trial.

The aim of the study was to investigate the availability and use of epidural analgesia and remifentanil patient controlled analgesia, in all Dutch hospitals.

**Material and Methods:** We extracted data on the use of epidural analgesia as pain relief for women in labor from the Netherlands Perinatal Registry. Because data on remifentanil patient controlled analgesia are not available in the registry, we also sent an anonymous online survey via email to all 90 hospitals with an obstetric ward in the Netherlands. The survey contained questions about obstetric analgesia with a focus on the availability and use of epidural analgesia and remifentanil patient controlled analgesia.

**Results:** In 2010 15% of 176,810 women giving birth in the Netherlands received epidural analgesia while 11.6 % received opioids. Response rate to the survey was 67% (60). Remifentanil patient controlled analgesia was available in 47% (28). In 67% of those hospitals remifentanil patient controlled analgesia was available for all laboring women whereas 14% only offered it to women with a contra-indication for epidural analgesia. Most hospitals use a flexible background infusion and a bolus dose of 30  $\mu$ gram. When only epidural analgesia was available 20% of women used pain relief (range 8-43%), versus 38% when epidural analgesia and remifentanil patient controlled analgesia were available (range 26-63%) (p<0.001).

**Conclusion:** Offering epidural analgesia and remifentanil patient controlled analgesia increases the use of analgesia over offering epidural analgesia alone. Despite the recommendation to use RPCA only in an experimental setting, remifentanil patient controlled analgesia is offered in almost 50% of hospitals.

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- Practice
- Survey

#### **ABBREVIATIONS**

RPCA: Remifentanil patient controlled analgesia; PCA: Patient Controlled Analgesia; EA: Epidural analgesia; NPR: Netherlands Perinatal Registry; RR: Relative Risk; CI: Confidence Interval

# **INTRODUCTION**

Analgesia during labor is an important issue for pregnant women and health care providers. The Dutch multidisciplinary

guideline "Pain relief during labor" advises that epidural analgesia (EA) is available for all parturients 24 hours a day as analgesia of first choice [1]. The guideline was written because of existing differences in availability of analgesia between hospitals, increasing demand, and concern about whether a request of women for pain relief during labor could be fulfilled 24 hours a day [1].

There is large variation in the utilization of EA between

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countries. In the United Kingdom EA is used as analgesia during labor by 28% of women, in contrast to 60% in the USA [2,3]. In the Netherlands, the use of EA during labor is 15% [4], but increasing. The Dutch obstetrical system is unique in the western world, with a large number of women under the care of community midwives antenatally (primary care). In 2010 83.9% of women started antenatal care in primary care and of those 28.8% delivered in primary care; the remaining women were referred to secondary care either during pregnancy or during labor [4]. Women who deliver under care of their community midwife either deliver at home or in a short-stay hospital setting. Medical pain relief and other medical interventions are not available in primary care. Secondary care consists of three types of hospitals: university, teaching and general. University hospitals are tertiary referral hospitals allied with one of the eight medical schools where specialized antenatal care and neonatal intensive care unit facilities are available. Teaching hospitals are general hospitals that also work with the university medical centers in training of medical interns and residents. They offer more specialized treatments. General hospitals provide standard healthcare for less specialized problems. Women of low and intermediate obstetric risk can deliver in all three hospital types. Women with a high obstetric risk deliver in teaching or university hospitals.

Remifentanil patient controlled analgesia (RPCA) was first introduced as an alternative for women who had a contraindication to receive EA [5,6]. Remifentanil is a synthetic opioid with direct action on μ-opioid receptors. It has a short half-life and latency to peak effect which make it very suitable for administration through patient controlled analgesia (PCA) [7]. The rapid onset of analgesia (30-60 s), which peaks at 2.5 minutes [8] make remifentanil very suitable for PCA. In PCA an intravenous cannula is placed and medication is selfadministered through a PCA pump by pressing a button. The PCA device is programmed to deliver a bolus with a standard lockout time. The only opioid that is used in patient controlled analgesia in the Netherlands is remifentanil. Other opioids that are used for analgesia during labor include intramuscular meperidine and subcutaneous morphine. Efficacy of EA is superior to RPCA but studies showed comparable pain appreciation (satisfaction with analgesia) [9,10]. In the Netherlands, RPCA is used frequently by women without a contra-indication for EA. An explanation might be non-availability of EA in the evening/night. This is in contrast with the recommendation of the Dutch guideline, which advises to use RPCA only in controlled (research) setting and recommends a large trial because of insufficient evidence of its efficacy and side effects and the potential risk for serious maternal complications [1]. As with EA there is large variation in the use of opioids during labor worldwide; reported numbers range from 5-66% [11]. For example, patient controlled analgesia with an opioid is available for analgesia during labor in approximately 50% of all hospitals in the UK [12]. One of the main concerns with potent opioids like remifentanil is the risk of respiratory complications (desaturation, respiratory depression). Maternal parameters should be monitored continuously in women using remifentanil and as desaturation can be a late sign of respiratory depression one to one nursing by a professional trained in basic life support is advised [1,9].

In preparation of a randomized controlled trial comparing RPCA versus EA in labor (the RAVEL trial, NTR 2551 [13]), we surveyed current practice regarding pain relief during labor. This trial has been published showing that RPCA is not equivalent to EA with respect to satisfaction with pain relief [14].

# **MATERIAL AND METHODS**

# **Netherlands Perinatal Registry (NPR)**

Data on pregnancy, delivery and neonatal care are available in a national database; the Netherlands Perinatal Registry (NPR) [4]. The NPR contains data on 97% of all births in 2010 in the Netherlands. The NPR database relies on reports of community midwives, general practitioners and obstetricians for information on all births attended. For our survey we evaluated the deliveries in the year 2010 and extracted data on the use of EA during labor. Information obtained from the NPR database were; number of women that used EA as analgesia during labor, parity, start of labor (spontaneous versus induction) and if a woman was in primary or secondary care at the start of labor. The NPR does not discriminate between different types of epidural analgesia (continuous infusion, patient controlled epidural analgesia and combined-spinal epidural analgesia). Also, only opioids as a group are registered in the database, these could be any type of opioid. Data on the use of RPCA are not available in the NPR.

# Survey

A link to an anonymous online survey was sent by email to all obstetrical units of the 90 hospitals in the Netherlands with an obstetric practice. To maximize response rates the link to the survey was sent four times from August 2011 to January 2012. The survey requested data of the year 2010 on the number of deliveries and clinical management for labor analgesia. It focused on EA and RPCA for pain relief during labor. A translated version of the questionnaire can be found in appendix A. It consisted of 12 multiple choice questions with the possibility to provide additional comments. The survey addressed aspects of demography, the type of hospital (university, teaching, and general), the number of births in 2010, and percentage of births in which EA or RPCA was used. Respondents were asked about availability of EA, 24 hours a day for all women or just for a specific group, and their protocol for administration of EA (continuous infusion, patient controlled epidural analgesia, combined spinal epidural analgesia). The next part focused on the availability of RPCA, if it was available for all parturients or for a specific group of women, and on the dosage used in administration of RPCA. If RPCA was not available for all women, we asked for reasons for not offering RPCA to all women. We did not enquire about adverse events in women using RPCA. Respondents were asked to report on actual numbers. It was decided to analyze teaching and university hospitals as one group, as university hospitals are teaching hospitals as well, and general hospitals as a separate group. Use of EA and RPCA are also reported, however, according to hospital type.

Response rate and the availability of RPCA were tested using the chi square test. The mean use of analgesia was analyzed using the Student's t-test. All analyses were performed using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA).

Since this study does not involve human subject's ethics approval was not obtained.

#### **RESULTS**

#### **NPR**

The total number of registered deliveries in the Netherlands in 2010 was 176,810; 26.6% of these women received analgesia (15% EA, 11.6% opioids) during labor. The other women did not receive medical pain relief during labor. Use of EA during labor was higher in nulliparous women than multiparous women (22.6% versus 7.9% (RR 2.8 95% [CI 2.8-2.9]), in women who were induced compared to spontaneous start of labor (29.1% versus 12.3% (RR 2.3 [95% CI 2.3-2.4]) and in women who started labor under supervision of an obstetrician versus women who started of labor under care of a community midwife (20.4% versus 9.6% (RR 2.1 [95% CI 2.1-2.2]).

# **SURVEY**

## **Baseline characteristics**

The response rate to the survey was 67% (60). The response rate was higher for teaching and university hospitals than for general hospitals: 85% (39) versus 47% (21) (p<0.001) (Table 1). Not all respondents answered all non-mandatory questions in the survey. For the units responding to the survey, the mean number of deliveries in 2010 was 1718 (range 624-3050). The mean number of deliveries for teaching hospitals, including university hospitals, was 2084, for general hospitals 1039. The total of deliveries in responding hospitals was 103,097. 71% of 176,810 women delivered in secondary care in 2010. The results of our survey cover 82% of all registered births in the Netherlands.

# Availability of pain relief

In all responding hospitals, EA was available for pain relief during labor. 95% (57) of respondents stated that EA was available 24/7 in their hospital. RPCA was available in 47% of responding hospitals, in 44% (17 of teaching hospitals and 48 (11) of general hospitals (p= 0.59). Of the 21 respondents that use RPCA in their hospital 67% (14) answered that RPCA was available for all parturients while 14% (3) used RPCA only if EA was contra-indicated. 43% (9) offered RPCA only in the last phase of the first stage, more answers were possible. Reasons for not offering RPCA to all women are listed in Table 2.

#### Use of pain relief

The use of EA during labor varied between responding hospitals from 3% to 43% (mean 20%). Mean use of RPCA in hospitals that offered RPCA was 20% (Table 3). Comparing results of hospitals only offering EA to hospitals offering both EA and RPCA shows that in hospitals where only EA was available the use of analgesia was 20% (8-43%) while in hospitals where both were available the use of analgesia was 38% (26-63%) mean difference -17; 95% CI -22 to -12 (p<0.001).

Fourteen respondents answered the questions about their protocol for RPCA. Most hospitals (86%) used a flexible background infusion of 80-100-120  $\mu$ gram and 11/14 used

Table 1: Overview of survey respondents according to type of hospital.

Type of hospital

University hospital N=8

Teaching hospital N=38

General hospital N=44

Returned surveys
% (n)

75 (6)

87 (33)

47 (21)

**Table 2:** Reasons for not using RPCA for labor analgesia or not offering RPCA to all women. More than one answer was possible.

	Obstetrician % (n) N=32	
Analgesia of RPCA is insufficient, EA is the gold standard.	16 (5)	
Not enough evidence for effect and side effects	38 (12)	
Risk of serious side-effects like respiratory depression	44 (14)	
Surveillance on labor ward is insufficient	31 (10)	
Potential risks for neonate	6 (2)	
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**Abbreviations:** RPCA: Remifentanil Patient Controlled Analgesia; EA: Epidural Analgesia

**Table 3:** Percentage of deliveries in which EA or RPCA is used as analgesia.

	EA	RPCA
University hospital (mean [range])	26% [20-30]	Sporadic
Teaching hospital (mean [range])	21% [3-36]	24% [3-50%]
General hospital (mean [range])	18% [5-43]	19% [13-28%]

**Abbreviations:** RPCA: Remifentanil Patient Controlled Analgesia; EA: Epidural Analgesia

an initial bolus dose of 30  $\mu gram.$  No data were available on maximum bolus dose or lockout time.

With respect to the mode of EA most hospitals use EA with a continuous infusion (86%). But patient controlled EA and combined spinal epidural analgesia are also used in 17% and 14% respectively.

#### **DISCUSSION**

This study was performed to evaluate the use of medical pain relief during labor in the Netherlands, with a special focus on RPCA. The results show that EA was used in 15% of all births in the Netherlands (primary and secondary care) but in 20% of births in our responding secondary care hospitals. There seems to be a large variation in the availability and use of EA and RPCA during labor between hospitals.

The difference between the uptake of EA of 15% in the NPR and the self-reported uptake of 20% in the survey is explained by the difference in denominators. The NPR reports on all births in the Netherlands, primary and secondary care combined. 28.8% of women delivered in primary care in 2010 and medical pain relief is not available in primary care. 15% of all deliveries (176.810) are 26.521 women receiving EA. 20% of all deliveries in secondary care (125.889) are 25.177 women receiving EA.



Birth is traditionally viewed by midwives and doctors in the Netherlands as a natural process where interventions are not routinely necessary and medical pain relief and interventions are seen traditionally as a last resort in difficult labor. Over the past decades we have seen increasing medicalization of pregnancy and birth, also in the Netherlands, and as a result increasing numbers of women asking for medical pain relief. Traditionally labor pain was viewed conservatively as a normal physiological phenomenon that serves a purpose (increasing bond between mother and child). Nowadays, more and more women view labor pain as unnecessary, and because of this are more likely to request medical pain relief during labor. In this article we discuss the use of analgesia in the year 2010. The number of women using EA has been increasing with 1-2% per year in the past years and was 20% in 2014.

Despite recommendations of the guideline to use RPCA only in a controlled (research) setting, RPCA is used in almost 50% of responding hospitals and in only 14% reserved for women with a contra-indication for EA. We found that the use of analgesia during labor seems significantly higher in hospitals that offer both EA and RPCA than use of analgesia in hospitals that offer only EA. In hospitals that use RPCA as well as EA for pain relief during labor, EA is used in approximately 20% of all deliveries (range 3-43%), equal to hospitals that do not offer RPCA, and RPCA is used in a little over 20% additional deliveries in these hospitals (range 3-50%). The higher uptake of analgesia in hospitals that use RPCA could suggest that in these hospitals RPCA is not used as an alternative to EA but may be used in addition to other methods of pain relief that are available (Figure 1).

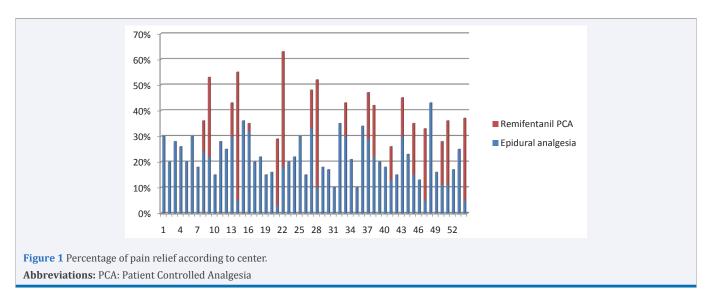
There could be several reasons for a higher use of pain relief in hospitals that offer both EA and RPCA. The first is the perception of women and/or caretakers (community midwives/obstetricians) that RPCA is a less invasive method of pain relief than EA, because only intravenous access is required. Hence, women who are reluctant to ask for EA could be more likely to request RPCA. A second reason could be that women who are expected to give birth within a relatively short period of time are given RPCA when they request pain relief at this stage of

labor. These are women who are expected to deliver soon and who might be too late to receive EA. This theory is supported by the findings of Logtenberg et al., who found a significant larger number of multiparous women receiving analgesia when randomized to RPCA (unpublished data). Another explanation could be that RPCA is more easily available than EA for women asking for pain relief because the presence of an anesthesiologist is not required. The decision to start RPCA is made by the obstetrician or clinical midwife in most Dutch hospitals and not all hospitals require presence of an anesthesiologist at the start of RPCA. It is not likely that the higher use of pain relief in hospitals that offer both EA and RPCA is explained by a different population of parturients, e.g. higher risk deliveries, since RPCA is used most in teaching and general hospitals but not in university hospitals (which have the highest risk population). The last explanation for this difference is response bias, because not all units responded to our questionnaire it is possible we got response from the units with a higher uptake of analgesia.

Little is known about the percentages of births in which RPCA is used worldwide. To our knowledge three surveys addressed this [12,15,16]. So it is difficult to know whether our findings are generalizable to the situation in other countries. In the UK PCA with an opioid was used in almost 50% of responding units in 2004-2005, in 35% of those remifentanil was used. In Germany PCA with an opioid was used in 8% of responding units with the use of remifentanil in 68%. In the French part of Belgium 36% of respondents use PCA in their unit and 77% of those use remifentanil as the opioid of choice. Comparing our findings and previous reports, the use of EA and the use of patient controlled analgesia seem comparable in the Netherlands, the UK and Belgium [11,12]. Our survey only asked about remifentanil PCA. To our knowledge no other opioids are used for PCA in the Netherlands and following the results of Douma et al., remifentanil provides better analgesia than fentanyl or meperidine through PCA [17].

#### Strengths and limitations

The main strength of this study is that it is one of only a few studies reporting on the use of RPCA as analgesia during labor.



# **SciMed**Central

A weakness is the response rate. Our overall response rate was acceptable with a response of 67%: high for teaching hospitals (87%) but low for general hospitals (47%). Since the response rate of teaching hospitals, which are the bigger centers, was 87%, we believe the results give a representative view of practice and beliefs regarding pain relief during labor in the Netherlands.

## **CONCLUSION**

In the Netherlands, there is large variation in the availability and use of EA and RPCA during labor. Despite recommendations of the guideline to use EA as analgesia of first choice and RPCA only in a controlled (research) setting, RPCA is used in almost 50% of hospitals and offered to all women in 67% of those.

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