Scandinavian SSAI clinical practice guideline on the use of single shot remifentanil for rapid sequence induction of general anaesthesia for emergency caesarean section in healthy parturients

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Abstract

Background: Rapid sequence induction (RSI) is considered the gold standard in an emergency caesarean section (CS). Use of opioids has been limited to after umbilical clamping to minimize neonatal respiratory depression. Lack of opioids during induction may cause severe adverse effects to the parturient due to elevated blood pressure, especially in high-risk cases, such as pre-eclampsia and intraoperative awareness. The aim of this guideline is to determine effect of a single shot of remifentanil during induction of general anaesthesia for CS.

Methods: A PubMed search was made to identify relevant studies. The PICO method was used to formulate the clinical question and the GRADE system was employed to assess the quality of evidence and create the recommendation. Quality of evidence was rated from very low to high and recommendations were classified as weak or strong by all the members of the study group.

Results: 39 studies were identified and 5 were included in the guideline, 2 systematic reviews and 3 randomised controlled trials, all from elective CS setting. Data had to be extrapolated into emergency CS. Relative risk (RR) for neonatal ventilatory support after single shot remifentanil was 1.1592, low Apgar score (0-7) at 1 and 5 minutes were 1.8009 and 1.0192, respectively, maternal highest systolic blood pressure was lower, mean of 136.38 vs 155.65 mmHg and RR of maternal intraoperative awareness was 0,987.

Recommendations and conclusion: Overall the quality of evidence was low (neonatal ventilatory support, maternal blood pressure and intraoperative awareness) to moderate (Apgar scores at 1 and 5 minutes). We suggest a single shot remifentanil can be used in RSI of general anaesthesia to reduce maternal hypertensive response during intubation without compromising the safety of the neonate.

1. Background

General anaesthesia for caesarean section (CS) is often the first choice for emergency situations where the wellbeing of the foetus or mother is compromised. In other circumstances, general anaesthesia for CS is usually avoided because of the risks related to it during end-pregnancy. The risk of aspiration of gastric content has been a concern since the 1940's[1]. Combined with the risk of aspiration there is also a well-known risk of difficult intubation during end-pregnancy[2]. However, due to advances in obstetric anaesthesia the risks of general anaesthesia for CS have decreased significantly[3,4], but some of that change may be attributed to increase in the use of regional anaesthesia for high risk cases. It is also known that risks of general anaesthesia are greater in emergency CSs compared to elective CSs[5]. Anaesthesia-related deaths in parturients are for the majority related to general anaesthesia and most often failed intubation[6].

Because of the risk of aspiration, rapid sequence induction (RSI) has been considered the gold standard for general anaesthesia for CS for decades[7,8]. The use of opioids in RSI is a matter of some controversy. The use of opioids has historically been limited to after the clamping of the umbilical cord in order to minimize respiratory depression in the neonate. Not using opioids during induction of anaesthesia may cause elevated blood pressure due to increased secretion of catecholamines, which may lead to severe complications such as stroke in parturients, especially in high-

risk cases, such as patients with pre-eclampsia[9]. Lack of opioids during induction of anaesthesia may also increase the risk of intraoperative awareness[10].
Remifentanil is an ultra-short-acting opioid[11] that may eliminate the risk of respiratory depression in the neonate when given during RSI due to its pharmacokinetic properties. The aim of this guideline is to determine the efficacy and risks of a single shot of remifentanil during induction of general anaesthesia for CS.

2. Methods

2.1. Process

The Faculty of SSAI Obstetric Anaesthesia appointed fellows from the VI Advanced Educational Programme in Obstetric Anaesthesia 2019 – 2021 to prepare guidelines concerning general anaesthesia for emergency CS. The faculty identified four key interventions needing guidelines, including awareness, opioids in general anaesthesia, airway management and neuromuscular blocking agent.
This is the guideline on opioids in general anaesthesia for emergency CS, more specifically single shot remifentanil for RSI.

Clinical question

'Should single shot remifentanil be used for rapid sequence induction of general anaesthesia in healthy parturients for emergency caesarean section?'

Population

The population of interest was healthy parturients undergoing emergency CS in general anaesthesia.

Intervention

We assessed any dose of single shot remifentanil for RSI but excluded studies with infusion of remifentanil.

Comparator

The control was placebo, i.e., no opioids for induction of general anaesthesia.

Outcome(s)

The following neonatal- and maternal-important outcomes were assessed:

Critical outcomes:
1. Neonatal ventilatory support (defined as bag-mask ventilation, continuous positive airway pressure (CPAP) or intubation in the delivery/operating room, NOT tactile stimulation)
2. Neonatal 5 min Apgar score (assessed dichotomously as 0-7 or >7)

Important outcomes:
3. Neonatal 1 min Apgar score (assessed dichotomously as 0-7 or >7)
4. Maternal highest systolic blood pressure (SBP) at time of or immediately after intubation
5. Maternal awareness

We included systematic reviews of randomized clinical trials and randomized controlled trials (RCTs). A preliminary literature search found no studies on emergency CS alone, hence all categories of CS were included. We excluded trials done in parturients with co-morbidity, including pregnancy-related diseases. We excluded trials not reporting the predefined neonatal- and maternal-important outcome measures, and those not comparing single shot remifentanil with placebo, those reporting on infusion of remifentanil and those comparing other opioids.

Search strategy

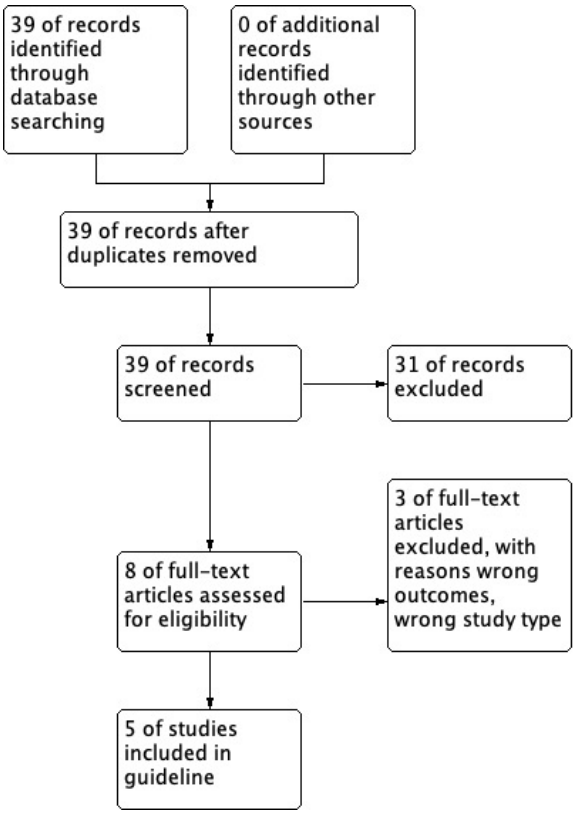
We systematically searched PubMed (January 1966 to 25 February 2020), for systematic reviews of RCTs and RCTs comparing single shot remifentanil with placebo on 25 February 2020. No language restriction was employed.

We used the following search strategies:

PubMed: ("remifentanil"[MeSH Terms] OR "remifentanil"[All Fields]) AND induction[All Fields] AND ("general anaesthesia"[All Fields] OR "anesthesia, general"[MeSH Terms] OR ("anesthesia"[All Fields] AND "general"[All Fields]) OR "general anesthesia"[All Fields] OR ("general"[All Fields] AND "anesthesia"[All Fields])) AND ("caesarean section"[All Fields] OR "cesarean section"[MeSH Terms] OR ("cesarean"[All Fields] AND "section"[All Fields]) OR "cesarean section"[All Fields]).

The Prisma flow diagram shows the process of identifying, screening and including studies.

Prisma flow diagram



Statistics and GRADE

The clinical question was formulated using the relevant patient population and/or clinical problem (P), the intervention (I), the comparator (C), and the predefined patient-important outcomes (O) – PICO questions[12]. Review Manager (Version 5.3, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) and GRADEpro GDT (GRADE working group, https://gradepro.org) were used to prepare tables for Evidence profile and Summary of findings. 95% confidence intervals (CIs) were estimated and are reported in the Summary of finding tables. We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for assessing the quality of evidence, generating anticipated absolute effects, and for moving from evidence to recommendations[13]. We downgraded the quality of evidence (our confidence in the effect estimates) for an

intervention for identified risks of bias, inconsistency, indirectness, imprecision or publication bias[14–19]. Accordingly, the quality of evidence was rated from 'high' to 'very low'.
When moving from evidence to recommendations, we considered quality of evidence, benefits and harms. GRADE classifies recommendations as 'strong' when virtually all informed patients would choose the recommended management strategy. 'Weak' recommendations apply when fully informed patients would choose different management strategies, and reflects uncertainty regarding treatment effects, a close call between benefits and harms, questionable cost effectiveness, or variability in preferences[13,20].
The author group agreed upon all the recommendations in this guideline. Strong recommendations were given the wording 'we recommend', and weak recommendations 'we suggest'.

3. Results

3.1. Characteristics of included studies

The characteristics of the five included studies are presented below.

Behdad et al. 2013[21]

Methods	**Randomised Controlled Trial**
Participants	Women with singleton term pregnancies, and physical class status of I or II as defined by the American Society of Anesthesia (ASA), who were undergoing general anaesthesia for elective CS
Interventions	0.5 microg/kg remifentanil bolus injected over 30 seconds immediately before induction of anaesthesia
Outcomes	Maternal SBP, maternal heart rate (HR), neonatal Apgar score 1 and 5 min, neonatal ventilatory support, umbilical artery pH
Notes	

Heesen et al. 2013[22]

Methods	**Systematic Review**
Participants	5 RCTs (4 full papers, 1 abstract): 2 trials studied pre-eclamptic women, 3 reports non-pre-eclamptic parturients
Interventions	Remifentanil for induction of general anaesthesia before delivery of the baby (3 trials with 1 microg/kg bolus; 2 trials with 0.5 microg/kg bolus followed by infusion)
Outcomes	Maternal SBP, maternal HR, neonatal base excess, neonatal pH, neonatal ventilatory support, neonatal Apgar 1 and 5 min
Notes	Based upon the different population (healthy vs pre-eclamptic) and different intervention (bolus vs bolus and infusion), only 1 study (Ngan Kee et al. 2006) in this review meets our inclusion criteria about healthy parturients receiving bolus remifentanil.

Ngan Kee et al. 2006[23]

Methods	**Randomised Controlled Trial**
Participants	Women with American Society of Anesthesiologists physical status I or II and term singleton pregnancies who were scheduled to undergo elective CS for which general anaesthesia had been decided on for clinical reasons. Patients with pre-existing or pregnancy-induced hypertension, cardiovascular or cerebrovascular disease, a history of substance abuse, or known foetal abnormalities were excluded.
Interventions	1 microg/kg remifentanil bolus injected over 30 seconds immediately before induction of anaesthesia
Outcomes	Maximum maternal SBP, maternal mean arterial blood pressure (MAP), maternal HR, neonatal Apgar score 1 and 5 min, neonatal ventilatory support, plasma concentrations of remifentanil
Notes	

Noskova et al. 2015[24]

Methods	**Randomised Controlled Trial**
Participants	Parturients undergoing CS under general anaesthesia. Exclusion criteria included known allergy to remifentanil, multiple pregnancy, gestational age below the 35th week, estimated weight of foetus below 2500 grams, severe foetal hypoxia, severe maternal hypotension, and other serious foetal or maternal conditions.
Interventions	1 microg/kg remifentanil bolus injected over 30 seconds immediately before induction of anaesthesia
Outcomes	Neonatal Apgar score 1, 5 and 10 min., neonatal ventilatory support, umbilical cord blood gas analysis, maternal SBP, maternal HR, maternal bispectral index (BIS)
Notes	This study is the only included study that measures BIS - surrogate outcome for awareness

White et al. 2019[25]

Methods	**Systematic Review**
Participants	RCTs reporting on the use of induction opioids for CS. Only RCTs with a placebo control group were included. 17 studies, 10 with remifentanil (9 uncomplicated term pregnancies for elective CS, 1 pre-eclamptic women both elective and emergency CS)

Interventions	Alfentanil, remifentanil or fentanyl. For remifentanil: 0.5 micro/kg as bolus, 1 microg/kg as bolus, 0.5 microg/kg as bolus followed by infusion or infusion alone
Outcomes	Apgar score 1 min and 5 min. Neonatal ventilatory support, neonatal intensive care unit admission, umbilical cord blood pH and base excess. Maternal SBP, maternal MAP, maternal HR, maternal epinephrine and norepinephrine concentrations.
Notes	4 studies in this review meets our inclusion criteria with healthy parturients and bolus remifentanil (Behdad et al. 2013, Bouattour et al., Ngan Kee et al. 2006 and Noskova et al. 2015)

Since we included two systematic reviews[22,25], Heesen et al. and White et al., we have gone through the RCTs in these reviews to find those RCTs which meet our inclusion criteria. In Heesen et al. only the RCT by Ngan Kee et al.[23] meets our inclusion criteria. In White et al. Behdad et al.[21], Bouattour et al.[26], Ngan Kee et al.[23] and Noskova et al.[24] meet our inclusion criteria. Therefore, our five included studies result in data from four RCTs.

3.2. Recommendations

The results and recommendations based on the PICOs are presented below, in the Evidence profile and in the Summary of findings tables.

A. Neonatal effects of single shot remifentanil for RSI of general anaesthesia in emergency CS

> We suggest that single shot remifentanil can be used for RSI of general anaesthesia in emergency CS without compromising the safety of the neonate

In a newly published meta-analysis, where four RCTs met our inclusion criteria, we found no statistically significant differences in our critical neonatal outcomes; that is neonatal ventilatory support and neonatal 5 min Apgar score ≤ 7. Neonatal 1 min Apgar score was statistically significant lower in the remifentanil group compared to no opioids, but since no more neonates required ventilatory support or had a lower 5 min Apgar score, it is plausible to say that the neonates with low 1 min Apgar scores recovered quickly with the aid of tactile stimulation.

B. Maternal effect of single shot remifentanil for RSI of general anaesthesia in emergency CS

> We suggest that single shot remifentanil should be used for RSI of general anaesthesia in emergency CS to reduce the maternal hypertensive response during intubation

In a newly published meta-analysis, where four RCTs met our inclusion criteria, we found a statistically significant lower maternal systolic blood pressure at/after intubation in the remifentanil group compared to no opioids.
We found no studies assessing maternal awareness, but one study reported on BIS as a pseudo-outcome for awareness and found no statistically difference between the remifentanil group and no opioids.

Evidence profile

Single shot remifentanil compared to no opioids for rapid sequence induction in healthy parturients undergoing caesarean section in general anaesthesia

Patient or population: **rapid sequence induction in healthy parturients undergoing caesarean section in general anaesthesia**
Intervention: **Single shot remifentanil**
Comparison: **no opioids**

Outcomes	№ of participants (studies and design)	Study limitations (risk of bias)	Inconsis-tency	Indirect-ness	Impre-cision	Publica-tion bias	Overall quality	Event rate or mean score/value*		Relative risk or mean difference (95% CI)	Importance
								With no opioids	With Single shot remifentanil		
Neonatal ventilatory support	311 (4 RCTs)	No serious limitations	No serious limitations	No serious limitations	Very serious limitations	No serious limitations	⨁⨁◯◯ LOW	8 per 100	9 per 100 (4 to 19)	1.1592 (0.5540 to 2.4255)	Critical
Neonatal 1 min Apgar score 0-7	311 (4 RCTs)	No serious limitations	No serious limitations	No serious limitations	Serious limitations	No serious limitations	⨁⨁⨁◯ MODERATE	10 per 100	19 per 100 (11 to 33)	1.8009 (1.02 to 3.1796)	Important, but not critical
Neonatal 5 min Apgar score 0-7	311 (4 RCTs)	No serious limitations	No serious limitations	No serious limitations	Serious limitations	No serious limitations	⨁⨁⨁◯ MODERATE	1 per 100	1 per 100 (1 to 19)	1.0192 (0.6188 to 14.7305)	Critical
Maternal highest SBP at/after intubation	311 (4 RCTs)	No serious limitations	No serious limitations	No serious limitations	Very serious limitations	No serious limitations	⨁⨁◯◯ LOW	Mean 155.65 mmHg	Mean 136.38 mmHg (115.96 to 156.8)	19.27 mmHg (-1.15 to 39.69)	Important, but not critical
Maternal awareness (assessed as BIS > 60% at intubation)	151 (1 RCT)	No serious limitations	No serious limitations	No serious limitations	Very serious limitations	No serious limitations	⨁⨁◯◯ LOW	0 per 100	0 per 100 (0 to 0)	0.9870 (0.0198 to 49.1116)	Important, but not critical

***The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).**
CI: **Confidence interval**

GRADE assessment of the five factors that can reduce the quality of evidence (study limitations, inconsistency, indirectness, imprecision and publication bias):
No serious limitations: **Most evidence is from studies with low risk of the factor**
Serious limitations: **Most evidence is from studies with moderate risk of the factor**
Very serious limitations: **Most evidence is from studies with high risk of the factor**

GRADE overall quality of evidence:
High: **Further research is very unlikely to change our confidence in the estimate of effect**
Moderate: **Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate**
Low: **Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate**
Very low: **Any estimate of effect is very uncertain**

GRADE importance of outcome:
Critical
Important but not critical
Not important

Summary of findings

Single shot remifentanil compared to no opioids for rapid sequence induction in healthy parturients undergoing caesarean section in general anaesthesia

Patient or population: **Rapid sequence induction in healthy parturients undergoing caesarean section in general anaesthesia**
Intervention: **Single shot remifentanil**
Comparison: N**o opioids**

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with no opioids	Risk with Single shot remifentanil			
Neonatal ventilatory support	8 per 100	9 per 100 (4 to 19)	RR 1.1592 (0.5540 to 2.4255)	311 (4 RCTs)	⨁⨁⨀⨀ LOW [1,2]
Neonatal 1 min Apgar score 0-7	10 per 100	19 per 100 (11 to 33)	RR 1.8009 (1.02 to 3.1796)	311 (4 RCTs)	⨁⨁⨁⨀ MODERATE [3]
Neonatal 5 min Apgar score 0-7	1 per 100	1 per 100 (1 to 19)	RR 1.0192 (0.6188 to 14.7305)	311 (4 RCTs)	⨁⨁⨁⨀ MODERATE [3]
Maternal highest SBP at/after intubation	Mean 155.65 mmHg	mean 136.38 mmHg (115.96 to 156.8)	-	311 (4 RCTs)	⨁⨁⨀⨀ LOW [1,2]
Maternal awareness (assessed as BIS > 60% at intubation)	0 per 100	0 per 100 (0 to 0)	RR 0.9870 (0.0198 to 49.1116)	151 (1 RCT)	⨁⨁⨀⨀ LOW [1,2,4]

***The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).**
CI: **Confidence interval; RR: Risk ratio**

GRADE Working Group grades of evidence:
High certainty: **We are very confident that the true effect lies close to that of the estimate of the effect**
Moderate certainty: **We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different**
Low certainty: **Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect**
Very low certainty: **We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect**

Footnotes
[1] OIS are not met
[2] 95% CI is on the same side as the clinical decision threshold
[3] Power calculations show, that 43 patients are needed in each group to detect a difference in Apgar score, but sample size are still small
[4] Very wide 95% CI

4. Discussion

The literature search for this guideline yielded evidence to support our recommendations, but the overall level of evidence was quite low.

We included five studies, two of them systematic reviews, identifying four different RCTs that were eligible according to our criteria[21,23,24,26]. Using the GRADE system, we have collected and analyzed data to present a clinical guideline covering the role of remifentanil in CS.

We could not find any relevant trials studying the use of remifentanil for CS in the emergency setting, given the more difficult and stressful conditions when emergency CSs take place. We have therefore chosen to extrapolate our findings from elective CSs, regarding both the mother and the newborn, to the emergency ones. Naturally, this must be considered as a limitation to our guideline, as both mother and neonate can be in a state of more physical stress, and with less reserves in such a situation. Some examples can be an exhausted mother after prolonged labour, or a foetus in distress due to asphyxia. We still reckon that the effects of remifentanil seen in the mother and the neonate after using this drug for RSI, to an acceptable extent, can be extrapolated to the emergent CS.

Our main results for maternal outcomes are a confirmation of more stable haemodynamics between RSI and surgical delivery after remifentanil. Maternal awareness during intubation and surgery was not examined directly in any of the studies.

The ability of remifentanil to attenuate the increase in blood pressure and heart rate caused by orotracheal intubation, has been shown[27] and applies also to the pregnant population. Yoo et al. have specifically studied this in preeclamptic women[28], but we excluded these trials in our guideline-work to focus on the healthy parturients. Our included RCTs imply the same, the rise in blood pressure was less pronounced in the remifentanil group. Still, with 311 participants, the OIS is not met, which introduced imprecision, and we must downgrade the quality of evidence to low.

For women with preeclampsia undergoing CS, controlling the blood pressure is crucial to avoid intracranial haemorrhage, which can be fatal[29]. Some concern has also been raised that an increase in the concentration of

maternal catecholamines in healthy women during CS may adversely affect neonatal outcome[30]. Less rise in blood pressure after exposure to remifentanil can be interpreted as less circulation of catecholamines. We chose the outcome "maternal highest blood pressure during/after intubation" as important, but not critical, since this guideline covers healthy parturients, not women with hypertensive disorders in pregnancy or cardiovascular diseases. Which dangers a brisk rise in BP/SBP poses to healthy, pregnant women, is also not well studied or documented. But what we know from other groups of patients, is that a rise in blood pressure may cause failure of the heart´s left ventricle, stroke or angina/myocardial ischemia. We know that the physiology of pregnant women is altered compared to non-pregnant women. The coagulation system is affected; being pregnant is foremost a prothrombotic state, but thrombocytopenia develops in 5%-10% of women during pregnancy or in the immediate postpartum period[31]. This may have importance regarding cerebral haemorrhage. We also know that patients generally may well have hidden medical conditions that are not yet detected[32,33].
For the healthy parturient, reducing the risk for awareness is also an assumed benefit from the use of opioids[10]. We ranged maternal awareness as an important outcome when looking at the use of remifentanil in CS. Still, only one of our included RCTs, Noskova et al., presented maternal awareness as an outcome[24]. Their method to detect awareness was to measure the BIS-values in both groups during anaesthesia, defining BIS-values below 60 as sufficient depth of anaesthesia. They did not see BIS-values above this threshold in either group, or no difference between the groups. Yet, we have to recognize BIS as a pseudo-outcome for awareness. The patients' own reports of awareness weigh more heavily[10]. Omitting opioids for RSI can contribute to the awareness phenomenon, and we should keep that in mind when deciding whether to use opioids. Knowing about the overrepresentation of awareness in obstetric surgery, especially during CS[10], our goal must be to develop methods that diminish these incidences. The data available for the use of remifentanil to prevent awareness among women going through CS, are very scarce. Even when accepting BIS-values as a valid pseudo-outcome, the events are few and no difference of statistical significance has been detected between the groups. In fact, no suspected awareness was detected at all.

Our suggestion is to use a single shot of remifentanil for RSI in emergency CS to keep the mother haemodynamically stabile. This is also likely to reduce the risk of awareness, but the quality of evidence is low.

We examined the evidence available concerning neonatal outcomes after using remifentanil as a co-induction agent in CS. There have been only small and few trials looking at neonatal outcomes after a single shot of remifentanil at anaesthesia induction for CS. Yet, the fear of deleterious effects on the newborns is mostly what withhold us from using opioids in CS before delivery. Van de Velde et al. found that 50% of neonates were briefly respiratory depressed after using remifentanil in CS, but they also went on with a remifentanil infusion after induction[34]. We have included only trials looking at the use of a single shot of remifentanil to eliminate this extended effect of remifentanil on the neonates. The doses used in our included studies were mainly 0,5-1 µg/kg, and this is therefore also the dosing method we would suggest.
Our main finding was, that the overall incidence of neonatal affection after the use of remifentanil for RSI in CS was very low. This is reassuring when you have maternal indications for the use of fast acting opioids, such as remifentanil, for induction of general anaesthesia for CS. We did not see any statistically significant difference in the need for ventilatory support, in the form of CPAP or intubation, among neonates whose mother had received remifentanil for induction. The relative risk of needing neonatal respiratory support compared with an opioid-free induction technique was 1.159. Still, the results suffer from imprecision, due to few events and small sample sizes. We also found very little difference between the groups for the Apgar score at 5 minutes, which we rated as a critical outcome. Unfortunately, the result does not provide statistical significance.

Our suggestion is that a single shot of remifentanil can be used for RSI of general anaesthesia in emergency CS without compromising the safety of the neonate.

Using the GRADE system, we had to downgrade our evidence mostly due to imprecision of the outcomes. Imprecision occurs when there are few events or too small samples.
More well-powered studies are warranted in the field of induction opioids for CS. If a trial on single shot remifentanil for CS with large enough samples were conducted, we could get the precise evidence concerning both maternal and neonatal outcomes that we need. It would also be of great interest to look specifically at remifentanil use in emergency CS, maybe also when foetal asphyxia is suspected.
When it comes to awareness, the events are very few, and this is a hindrance to compare remifentanil in CS with placebo or no opioids. Undoubtfully, we would welcome future scientific work in this topic also.

5. Limitations

Limitations in the guideline work are foremost the lack of sufficiently powered studies, which leads to a low to moderate evidence level and a weak recommendation. Therefore, there is a risk that a potentially beneficial treatment is downgraded.
Furthermore, it is clearly a limitation that lack of evidence on remifentanil for RSI in emergency CSs caused us to extrapolate our findings from elective CSs to make recommendations for emergency CSs.

6. Conclusion

General anaesthesia for CS remains a challenge for the anaesthesiologist, although the risks have decreased significantly due to advances in obstetric anaesthesia[3,4].
There is increasing evidence that a single shot of remifentanil in a woman undergoing CS under general anaesthesia improves haemodynamic stability of the mother without compromising the safety of the newborn.
In this guideline we went through data from four RCTs that met our inclusion criteria.
We found no statistically significant difference in neonatal outcomes but a statistically lower maternal systolic blood pressure at/after intubation in the remifentanil group compared to no opioids.
As of today, there is little or no documentation looking at how healthy and vulnerable parturients may differ in their need and tolerance for opioids used during CS. There is also lack of trials to part emergency CSs from the elective ones.
The certainty of the evidence is low to moderate and further research is needed to make a strong recommendation.

7. References

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