

# Long-term subcutaneous morphine administration after surgery in newborns

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## Abstract

**Aim:** To analyze the management of newborns after major surgery receiving morphine subcutaneously and to identify possible side effects.

**Methods:** Morphine was administered via a subcutaneous catheter (Insuflon<sup>®</sup>) in 20 newborns after major surgery. Side effects like hypotension, pain during morphine administration and local infection were noted. Morphine dose was adjusted according to the hospital guidelines with the Neonatal Infant Pain Score (NIPS) and the Finnegan withdrawal score.

**Results:** Surgery was performed at the median age of 38 5/7 weeks (range: 32 1/7–49 5/7 weeks). Before starting subcutaneous morphine administration, patients received intravenous morphine for a median of two weeks (range six days to seven weeks). All patients showed good pain relief with no severe side effects. Three patients reacted with crying to the first dose of subcutaneous morphine. No other side effects occurred.

**Conclusion:** Subcutaneous application of morphine with the Insuflon<sup>®</sup> catheter is an alternative to intravenous treatment of postoperative pain in neonates. In this small group pain relief was good and side effects were harmless.

**Keywords:** Cannula; neonate; postoperative pain; subcutaneous injection.

## Introduction

Morphine therapy in newborns is a controversial issue in recent years because of the side effects of this drug and

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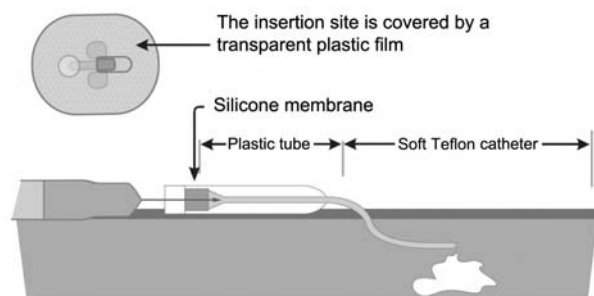
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outcome studies which showed that intermittent boluses of open-label morphine were associated with an increased rate of composite outcome (death, severe intraventricular haemorrhage, periventricular leukomalacia) [1, 4]. In addition, data from a recent study suggest that early surgery may lead to increased pain sensitivity in older children [9]. Whereas for short-term therapy, peripheral intravenous catheters are routinely used, central venous lines are usually required for long-term therapy, which notably increase the risk of catheter-related bloodstream infections and thrombosis [5, 7].

No published data exist so far on subcutaneous administration of morphine for postoperative pain treatment in newborns. The aim of this study was to analyse our data of newborns treated with morphine via a subcutaneous catheter.

## Materials and methods

A cohort of 20 consecutive newborns receiving morphine after complex visceral or cardiac surgery was analysed. Following removal of the central venous line, morphine was administered subcutaneously as a bolus injection via a subcutaneous catheter (Insuflon<sup>®</sup>; Unomedical A/S, Lyngø, Denmark) for a total of six doses daily. The Insuflon<sup>®</sup> consists of a Teflon catheter with a length of 19 mm (Figure 1). To make the insertion painless, EMLA<sup>®</sup> crème was used as a local anesthetic. Most devices were inserted in the ventral thigh, changing the side routinely once a week unless adverse effects were noted. The application was performed by the nursing staff according to the instruction of the manufacturer. Patient's pain was assessed by the neonatal infant pain scale (NIPS). This pain score was developed and validated for procedural pain and includes facial expression, crying, breathing pattern, arms, legs and state of arousal. We used this score because the nursing staff is very well trained in applying the score. In patients on morphine for longer than two weeks, the Finnegan score was applied as well [3, 7]. Morphine dose was adjusted if the pain score was above four, according to the guidelines, or the Finnegan score was above eight in three consecutive assessments. The subcutaneous doses of morphine were calculated by dividing the daily dose of intravenous morphine by six. Morphine doses were reduced by 25% every second day if the NIPS score was four or less, according to our hospital pain relief reduction guidelines. In our institution morphine treatment will stop in one step if the patient requires five or less days of treatment; otherwise the morphine will be gradually decreased. If the pain score was higher than four the dose was increased back to the previous level and left for the next 24 h before the next reduction. Blood pressure was monitored by peripheral measurements 15–20 min after injection during the first three times of subcutaneous morphine application and



**Figure 1** Principle of the subcutaneous catheter (Insufion®).

when the dose of morphine was increased. Side effects like hypotension, apnea, local infection or local bleeding were monitored.

The study was approved by the hospital Ethics Committee. Data are expressed as median and range, as appropriate.

## Results

Baseline characteristics of the 20 newborns included in the study are summarized in Table 1. In 15 and 5 newborns complex cardiac surgery and visceral surgery, respectively, was performed at the median age of 38 5/7 weeks' gestation (range: 32 1/7–49 5/7 weeks). Underlying diseases were: in five patients hypoplastic left heart syndrome; six patients with transposition of the great vessels; one patient each with Ebstein's anomaly, double outlet left ventricle, hypoplastic aortic arch and truncus arteriosus; two with diaphragmatic hernia and one patient each with sacral teratoma, intestinal volvulus and esophageal atresia. The Insufion® catheter was placed in the thigh in 19 newborns and in the abdominal wall in the remaining newborn. One newborn developed a small amount of bleeding at the insertion site. No other local side effects, like swelling or inflammation, were observed. Three out of 20 newborns, requiring increased morphine doses, reacted with crying and retraction of the leg during application of the first subcutaneous injection. None of the newborns showed hypotension or apnea.

Withdrawal symptoms like sweating, nervousness, and crying were seen in three out of 20 patients and treated according to the guidelines described before.

## Discussion

Although morphine is the most important medication to treat postoperative pain in newborns, insufficient information exists on subcutaneous administration of this drug as compared to the intravenous administration. Results of this study show that subcutaneous morphine administration through the Insufion catheter was, in this small group of patients, easy and safe. Whereas pain treatment in newborns is still controversial, no doubts exist about the fact that newborns may well perceive pain, especially after surgery, and thus treatment is indicated in these young patients. Indeed, Nandi et al. [8] demonstrated that a considerable maturation of peripheral, spinal, and supraspinal afferent pain transmission occur in the early postnatal period. Besides ethical aspects, Anand et al. [2] showed that insufficient pain therapy causes increased morbidity and mortality in newborns. However, bolus administration in otherwise healthy preterm infants has been associated with increased side effects, particularly hypotension and IVH [1]. In a recent study by Simons et al. [10], however, blood pressure was not influenced by continuous intravenous morphine infusion. In agreement with these results, none of our newborns showed hypotension after subcutaneous injection. Our findings likely reflect possible pharmacodynamical similarities between continuous intravenous and subcutaneous administration of morphine, suggesting that these applications may be more appropriate than bolus intravenous injections. Long-term use of central venous catheters is associated with serious side effects like sepsis and thrombosis. Thus, subcutaneous administration could be of great advantages in this age group. Insufficient data on subcutaneous application of morphine in children are available, particularly when newborns are concerned. In one study by Lamacraft et al. [6], the effect of subcutaneous administration of morphine through a 22-gauge butterfly cannula for a median of 27 h was investigated in older children. Our study is the first to report successful long-term subcutaneous morphine administration in newborn patients. However, limitations of our study include the lack of a control group and the small number of patients. A number of our patients were certainly not suffering from pain any more but from withdrawal symptoms.

**Table 1** Baseline characteristics of the 20 patients.

	Median	Range
Birth weight (g)	3035	2020–4150
Age at first subcutaneous application (weeks gestation)	41.3	36–49 3/7
Duration of therapy (days)	7.5	2–17
IV Morphine therapy postoperative (weeks)	2	1–6.5
Initial dose (mg/kg/day)	0.1	0.01–0.3
Minimal dose before stop (mg/kg/day)	0.045	0.005–0.3
Application interval (h)	8	4–24

These symptoms were successfully treated with subcutaneous morphine as well. Another question might be why did we prefer this method instead of oral morphine treatment. A few of these patients showed malabsorption caused by either cardiac insufficiency or after abdominal operation. In our patient group the plasma concentration seems to be more stable. Another limitation of our study is that no pharmacokinetic studies were performed in these newborns and no ventilated patients were included.

In conclusion, subcutaneous administration of morphine using the Insuflon® catheter is a valid alternative to intravenous treatment of postoperative pain in newborns. Larger studies are required to further investigate the use of subcutaneous morphine administration in the treatment of pain in newborns, which will also focus on pharmacokinetics and on patients on mechanical ventilation.

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