*Research Article*

# *Continuous deep sedation until death in neonates and infants in Flanders: a post-mortem survey*

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# Abstract

**Background** The use of analgesics and sedatives to alleviate pain and discomfort is common in end-of-life care in neonates and infants. However, to what extent those drugs are used in that context with the specific aim of bringing the infant in a state of continuous deep sedation (CDS) is currently unknown.

**Methods** We performed a nationwide mortality follow-back survey based on all deaths under the age of one over a period of 16 months in Flanders, Belgium. Data on CDS were linked to sociodemographic information from death certificates. Physicians completed an anonymous questionnaire. Questions measured whether CDS preceded death, and which clinical characteristics were associated with the sedation (ex. type of drugs used, the duration of sedation).

**Results** Response rate was 83% (229/276). In 39% of all deceased neonates and infants, death was preceded by CDS. Physicians used a combination of morphine and benzodiazepines in 53%, or morphine alone in 45% of all sedation cases in order to continuously and deeply sedate the infant. In 89% of cases death occurred within one week after sedation was begun, and in 92% artificial nutrition and hydration were administered until death. In 49% of cases there was no intention to hasten death, and in 40% the possibility of hastening was taken into account.

**Conclusions** CDS precedes about two in five neonatal and infant deaths. Guidelines for CDS in this age group are non-existent and it is unclear whether the same recommendations as in the adult population apply and can be considered good practice.

## Introduction

Though infant mortality under the age of one is relatively low (e.g. 3.2 out of 1000 births in Flanders in 2016)[1], the impact on parents, family members and healthcare personnel is tremendous. In 77% of such deaths in Flanders, death was non-sudden[2] and thus complex discussions on commencing 'comfort care' and palliative care could have taken place[3]. Most infant deaths are preceded by an end-of-life decision, very often the withholding or withdrawing of treatment[4, 5]. When such decisions are made, it is common practice that analgesics and sedatives are initiated or increased within the context of palliative treatment. Managing pain is challenging, as pain cues in new-borns are difficult to discern and interpret[6]; it is often unclear at what point palliative care with adequate pain relief becomes the hastening of death[7]. This leads to an ethically, morally and even legally complex decision-making process that needs thoughtful deliberation between the parents and the medical professionals involved.

A recent literature review reveals that a majority of neonatal deaths are preceded by the administration of some form of pain and/or symptom relief medication[8]. In adults and minors, the term 'continuous deep sedation until death' is used to describe the specific practice of reducing consciousness by administering sedatives to treat pain and symptoms[9]. Although this practice occurs in neonates and infants, terminology varies[4, 8, 10, 11]. As the described objective is effective pain and symptom control by lowering consciousness at the end of life[8], the same terminology as in minors and adults i.e. continuous deep sedation until death (CDS) will be used throughout this paper.

Population data on the prevalence of CDS in neonates are scarce. To our knowledge, the only data is from the Netherlands in 2005 indicating that 19% of all deceased infants under the age of one were continuously and deeply sedated until death[12]. Despite the fact that literature on CDS in children is lacking, international guidelines in paediatric care consider it as a normal part of medical treatment at the end of life[10, 11, 13, 14]. The only available population estimates on CDS in minors are from Belgium, indicating that it occurs in about 1/5 of all deaths between one and 17 years old[15]. Data on the prevalence of CDS in neonates and infants under the age of one, and information on the type of drugs used, the duration of sedation or the provision of artificial nutrition and hydration are non-existent although they would be useful for physicians in daily practice.

This study aims to fill the current gap in knowledge regarding prevalence and characteristics of continuous deep sedation until death in neonates on a population-level. Furthermore, we will

examine whether neonates receiving CDS are different from those who die without it, based on clinical and demographic characteristics.

## Materials and Methods

### Design

We conducted a population-level mortality follow-back survey, including all infants under the age of one year of whom the mother resides in Flanders and who died between September 2016 and December 2017. STROBE guidelines for reporting cross-sectional research were used.

### Setting and participants

All infants under one year who died in the inclusion period in Flanders or Brussels whose mother was a Flemish resident. Flanders and Brussels are two of the three semi-autonomous regions of Belgium with autonomy over the quality of health care. All deaths occurring in both regions are processed by the same central administrative authority (the Flemish Agency for Care and Health). We included only deaths of Flemish residents to provide prevalence rates in a set population within one semi-autonomous region. The study design, mailing and anonymity procedure are described elsewhere[16]; an abbreviated overview can be found in the online supplementary material.

### Questionnaire and variables

We developed the first Belgian questionnaire on end-of-life care and end-of-life decision-making (including continuous deep sedation until death) in neonates based on a validated questionnaire in neonates[4] in the Netherlands, and validated Belgian questionnaires in minors[15] and adults[17]. The resulting questionnaire was thoroughly pilot tested and validated with eight neonatologists who represented all eight Flemish neonatal intensive care units, five researchers with extensive expertise in end-of-life care in neonates, minors and adults and an ethicist. The questionnaire included four descriptive questions regarding the death (place of death, death sudden and unexpected, presence of congenital anomalies, severity of congenital anomalies). Afterwards, questions regarding end-of-life decisions and end-of-life care were posed, including whether the infant was continuously and deeply sedated until death (CDS). The following question was used to indicate Continuous Deep Sedation: “Was the patient continuously kept in deep sedation or coma until death by means of one or more medications?”. If CDS was indicated, five questions followed regarding characteristics of this

sedation (drugs used, duration of sedation, whether artificial nutrition and hydration were provided and what the life-shortening intention of the physician was).

Demographic and clinical patient data (place of death, sex, age at death, gestational age at birth and cause of death (see Table 1)) were obtained from the death certificates. We used a deterministic linkage procedure to link death certificate with questionnaire data, and small cells analysis to ensure that linked death certificate data would prevent re-identification.

Statistical analysis

Descriptive statistics were calculated for demographic and clinical characteristics of the total population, and infants who did and did not receive CDS. Percentages of the characteristics of CDS (drugs used, duration of sedation, artificial nutrition and hydration provided, life-shortening intention of the physician) in all cases where sedation took place were calculated. A multivariable binary logistic regression model was fitted for the odds of receiving CDS based on demographic and clinical characteristics (sex, age at death, gestational age at birth, presence of congenital anomalies, and main cause of death) to determine whether or not neonates receiving CDS are significantly different from those who died without CDS. Non-significant predictors were excluded from the final model by means of a stepwise approach. Odds ratios (OR) and 95% confidence intervals (CI) were provided.

## Results

We received 229 completed questionnaires for 276 infants who died between 1 September 2016 and 31 December 2017 (83% response rate). No significant differences in demographic characteristics between deaths with and without a response was found, therefore no weighting of results was necessary.

In 183 out of the 229 cases (80%), death was non-sudden, indicating a possibility that medical decisions at the end of life were made. Eighty-nine infants had been continuously and deeply sedated until death (39% of all studied deaths, 49% of all non-sudden deaths). CDS was most prevalent among infants who died between day seven and day 27 of life (65%) compared with those who died within the first week of life (30%) or after day 27 (42%, p=0.02, Table 2). The percentage of CDS cases is high in infants born between 26-28 and 29-31 weeks of gestation (57% and 60% respectively), and in infants born at full term (51%), while in extremely preterm (< 26 weeks of gestation) and moderately preterm infants (32 - 36 weeks of gestation) the prevalence of CDS is significantly lower (27% and 32% respectively; p=0.02).

The multivariate binary logistic regression revealed two significant demographic predictors for receiving CDS, namely age at death and gestational age at birth (Table 3). Infants who died between

days seven and 27 are significantly more likely than those who died before the seventh day to receive CDS (adjusted OR=3.82, 95%CI=[1.71-8.50]). Furthermore, those born between 26 and 28 weeks' gestation (AOR=2.72, 95%CI=[1.03-7.19]), and those born at full-term (AOR=2.21, 95%CI=[1.03-4.73]) are more likely than extremely premature infants born at less than 26 weeks' gestation to receive CDS. Other predictors (sex, presence of congenital anomalies and cause of death) were non-significant and were thus excluded from the final model.

In 54% of all CDS cases, a combination of benzodiazepines and morphine was used; in 45% morphine alone was used. (Table 4). In 48% of infants who were sedated, death occurred between one and seven days after start of sedation. In 20% the infant died after 12-24 hours, and in another 20% sedation lasted for less than 12 hours. Only in a minority of cases was the duration of sedation between one and two weeks (6%) or more than two weeks (6%). Artificial nutrition and hydration were administered until death in 92% of cases. In 49% of cases the physician reported no intention of hastening death, whereas in 40% the possibility of hastening death was taken into account, although it was not the goal of the sedation. In 11% of cases hastening death was co-intended or explicitly intended.

## Discussion/Conclusion

This population-level mortality follow-back survey indicates that in four out of ten deceased neonates and infants death was preceded by continuous deep sedation until death (CDS). In the large majority, death occurred within one week of sedation beginning and artificial nutrition and hydration were administered until death. Physicians used a combination of morphine and benzodiazepines, or morphine alone. In 89% of cases there was no intention to hasten death although the possibility was taken into account (40%), though in 11% of cases hastening of death was co-intended or explicitly intended.

Strengths and limitations

Despite the sensitivity of the topic, we achieved a high response rate (83%) by using a robust design with a rigorous follow-up procedure, making conclusions valid for the entire population of deceased infants under the age of one irrespective of care setting or diagnosis. The questionnaire was developed based on existing and previously validated questionnaires on end-of-life decisions in neonates[4], minors[15] and adults[17], ensuring comparability over time, settings, countries and age groups. Socially desirable answers or unwillingness to participate were reduced by ensuring anonymity, however they cannot be completely avoided. Comparison of the response and non-

response groups revealed no significant differences, indicating that results are generalizable to the entire population of Flemish deceased neonates.

In a mortality follow-back study recall bias cannot be excluded since questionnaires were filled out about three months after death. However, a death certificate is the only available registration on a population level, making it the best method to study medical situations preceding death. Although other actors such as parents or nurses can provide useful information, we deemed the physician's perspective on the medical situation preceding death as the most important. Information regarding doses of medication or comfort assessments were not included in the questionnaire; this would have had a high clinical value but is very case-specific, difficult to interpret and often not noted in questionnaires. Detailed information regarding all CDS cases was limited by using questionnaires, further detailed (case) studies are recommended.

General discussion

We found that 39% of neonate and infant deaths were preceded by CDS. This practice in neonates and infants seems significantly higher than in adults (2.5-12%)[17, 18] and minors > one year old (22%)[15]. Treating pain in neonates is infinitely more complex than in minors or adults, as available non-verbal measures of assessment are much more difficult to interpret[19]. When death is expected in a neonate, a physician might be more inclined to resort to CDS in order to ensure adequate symptom control and peaceful death, as neonates themselves are unable to indicate when pain or symptom relief is sufficient. Interestingly, the prevalence of CDS in neonates in Flanders (39%) is much higher than in the Netherlands (19%)[12]. As identical questions were used in both countries, we might wonder whether this difference is due to actual differences in clinical decision-making between the countries, whether physicians interpret questions differently or whether our results reflect cultural differences. Additionally, as suggested in a paper from the Netherlands in 2005[12], a trend of increased use of CDS - similar to that in adults in the Netherlands from 8.2% in 2005 to 18.3% in 2015[20] – may be expected and thus the difference in prevalence might simply be due to a change in practice over time instead of a difference between countries. A new follow-up study in the Netherlands and/or a comparative study with Flanders is needed to test these hypotheses.

We found that extremely premature infants (<26 weeks' gestation) and infants dying within the first week of life are less likely to receive CDS (27% and 31% respectively). From the moment they are born, extremely premature babies are often highly dependent on intensive care treatment, and pain medication is often offered to keep them as comfortable as possible. In some cases, however, the continuation of intensive care is considered to be futile or not in the child's best interest due to extreme suffering or reduced expected quality of life in future. When the decision is made to

withdraw treatment on which they are extremely dependent, there is neither the time nor the need for continuous and deep sedation as pain medication is often already provided[21], and death is expected to come quickly. Similarly to extremely preterm infants, those dying within the first week of life are also highly dependent on intensive care because of the extreme condition that led to admission to the neonatal ward immediately after birth, so again, the cessation of treatment is also likely to result in rapid death. Additionally, prevalence of CDS is also lower in infants older than 27 days, which is likely to be because of an increase in sudden deaths due to accidents or SIDs, which was confirmed by our data.

We found that sedation was administered more often in babies who were born between 26 and 28 weeks of gestation, those born full term and those who died between seven and 27 days old. These babies often receive intensive care in the first week of life which increases their chances of survival[22]. However, if after this crucial first week their quality of life then or in future is estimated to be very poor[23], it may be decided to discontinue life-saving treatment in order to end their (future) suffering. Typically, we hypothesize that these babies have a slower dying process than extremely premature babies, as they are less dependent on the treatment provided and can thus survive without it. Sedation is therefore indicated to keep them comfortable until death. This hypothesis is further supported by the fact that in half of all continuous deep sedation cases sedation lasts for between one and seven days, which is considered a slow dying process. In infants who died between seven and 27 days after birth, additional factors such as a slow diagnosis, a slow accumulation of comorbidities or delayed acceptance of imminent death by the parents might contribute to higher chances of a slow dying process, making CDS more likely.

In adults and minors, 'continuous deep sedation until death' is used to describe a practice of inducing unconsciousness as a last resort to treat unbearable, refractory symptoms in those close to death[24]. Although our results show that this practice often occurs in dying neonates, it is not labelled as such, and guidelines for CDS are to our knowledge non-existent, in stark contrast to CDS in adults[25, 26]. Our data cannot provide knowledge on whether clinical indications for this practice are similar to those of adults and minors as it is unclear from our survey data whether unbearable refractory symptoms were present. However, our data can provide insight into how CDS in neonates and infants is used in daily practice, which is vital for future guidelines and rules for best practice. In the majority of cases studied, the duration of CDS was only hours or days, and thus it is likely that it was used when death was imminent to reduce symptom burden. Additionally, loss of consciousness could also be caused by a gradual increase in pain and symptom management[15] rather than deliberate CDS. In our population, the physician reported the sole use of morphine (i.e. medication

for pain) for sedation in 45% of cases, which supports this hypothesis. In 54% of continuous sedation cases within our study however, a combination of benzodiazepines (sedatives) and morphine (pain medication) was used, indicating that the sedative effect in these cases was intended[27]. CDS can also be used as a covert form of hastening death[15], which according to guidelines in adults should not be counted as CDS[9]. Since only a very small number (11%) of physicians reported a co-intention or an explicit intention to hasten death, we suspect that only a small number of cases could be considered as such. However, in two out of five reported cases, possible hastening of death was foreseen yet not intended. It is possible that some physicians in our study still stand behind the contentious doctrine of double effect[28, 29] where the wish to do something morally acceptable, such as relieving suffering, justifies the accompanying undesired effect of doing something morally questionable i.e. hastening death[30]. We can ask whether hastening death is indeed undesirable in extremely ill neonates, as we do in adults[9]; in treating infants, healthcare professionals and parents try to decide on what is best for the child[31], and when this is not possible or is unclear, they may make decisions that minimize suffering[32]. In cases of extreme suffering, the effect of hastening of death by providing increased doses of pain and/or symptom medication and lowering consciousness is often considered ethically and morally preferable. Lastly, though artificial hydration and nutrition provision is not recommended in CDS for adults, 92% of infants continued to receive them up until death. When 11% of CDS cases had a co- or explicit intention to hasten death to relieve suffering, providing fluid and nutrition seem contra intuitive. It is possible that physicians wanted to increase comfort by providing hydration and nutrition, as prognosis and estimated time until death in this population is hard to predict[33], however more research is needed. This information on the clinical characteristics of CDS in neonates and infants can be used as a starting point towards formulating guidelines in this population, which could aid healthcare providers in deciding when this type of sedation is warranted, and which due care criteria should be followed. However, further in-depth study is needed before such attempts toward guideline formation can be made.

**Conclusion**

The present study indicates that in neonates and infants who died under the age of one, continuous deep sedation until death is common (2/5 deaths <one year old). Continuous deep sedation is most prevalent in infants with a gestational age of between 26 and 31 weeks, and in infants between seven and 27 days old. In the large majority of cases, death occurred within one week of sedation beginning, and artificial nutrition and hydration were administered until death. Physicians used a combination of morphine and benzodiazepines, or morphine alone, in order to continuously and deeply sedate the infant. Guidelines for continuous deep sedation until death in neonates and

infants are non-existent and it is unclear whether the same recommendations as in the adult population apply and can be considered as good practice.

# Statements

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## Statement of Ethics

Study approval statement: For this study, approval was obtained from the Ethics Committee of Ghent University (Belgian Registration Number B670201628795), the Privacy Commission (CBPL, registration number SA3/VT005071970), the National Council of the Order of Physicians (registration number BD/wc/89997) and the Sectoral Committee of Social Security and health (registration number SCSZG/16/234).

Consent to participate statement: No written informed consent was asked, since filling out and sending back the filled-out questionnaire was seen as giving consent to participate in this study.

## Conflict of Interest Statement

The authors declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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## Author Contributions

All listed authors contributed to the writing and/or revision of the article and approved the final version of the manuscript.

Laure Dombrecht: literature search, conceptualization and study design, data collection, data analysis, data interpretation, writing of the manuscript

Kim Beernaert: supervision of the project, literature search, conceptualization and study design, data collection, data analysis, data interpretation, writing of the manuscript

Filip Cools, Gunnar Naulaers: funding acquisition, conceptualization and study design, data collection, data analysis, data interpretation, revision of manuscript

Linde Goossens: conceptualization and study design, data collection, data analysis, data interpretation, revision of manuscript

Kenneth Chambaere, Joachim Cohen, Luc Deliens: funding acquisition, conceptualization and study design, data collection, data analysis, data interpretation, writing of the manuscript

## Data Availability Statement

Questionnaires and detailed research protocols (in Dutch) are available upon written request to the corresponding author (Laure.Dombrecht@UGent.be). Data will not be made publicly available due to privacy constraints.

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**Table 1: Cause of death categories in neonatology**

A clinically relevant categorization for cause of death was developed to achieve homogenous groups with a similar cause without revealing detailed case-specific information. This categorization was evaluated, in terms of completeness to classify all possible causes of death and clarity of descriptions, by four physicians working in neonatal and prenatal care. Cases were sorted into one of seven categories by a neonatologist (FC) and a researcher with experience in neonatal end-of-life care research (LDm) based on the underlying cause of death, denoted by ICD-10 codes, on the death certificate. When main cause of death was inconclusive, ICD-10 codes of other associated causes of death were taken into account. Categories are mutually exclusive.

The following cause of death categories were identified:

- Prematurity and related disorders: Death due to a direct cause of prematurity, immaturity or disorders related to prematurity. For example, necrotizing enterocolitis, intraventricular hemorrhage, respiratory distress syndrome, or death due to (extremely) low birth weight or low gestational age.
- Congenital anomalies - singular: Death due to a single congenital anomaly with a defect in one organ or organ system. For example, a congenital malformation of the heart or a spina bifida.
- Congenital anomalies - multiple or systemic disorders: Death due to the presence of multiple congenital anomalies in different organ systems, or due to a disorder that affects multiple organ systems. For example, chromosomal disorders, multiple congenital malformations diagnosed in one infant, or an inborn error of metabolism.
- Complications of pregnancy with repercussions on foetal growth or development: Infant died due to complications of pregnancy that had an influence on the growth or the health of the baby prenatally. For example, a cytomegalovirus infection with congenital infection of the foetus, or pre-eclampsia with severe intrauterine growth restriction.
- Acute complications of pregnancy and/or birth in a previously healthy foetus. For example, a placental abruption or birth trauma causing oxygen deprivation.
- Disorders acquired after birth: Death due to a non-congenital disorder, acquired after birth of a previously healthy baby. For example, infectious diseases resulting in multiple organ failure.
- Other: Cause of death was sudden, without previous diagnoses. Examples are sudden infant death syndrome, accidents or trauma.

## Table 2: Demographic and clinical characteristics

| | All deaths (n=229) N (% of all deaths) | Continuous deep sedation until death (n=89) N (% of sociodemographic group) | P-value |
|---|---|---|---|
| **Sex**[a] | | | 0.486 |
| Male | 135 (59%) | 55 (43%) | |
| Female | 94 (41%) | 34 (37%) | |
| **Place of death** | | | * |
| Hospital | 210 (92%) | 89 (44%) | |
| NICU | 115 (50%) | 73 (64%) | |
| Other hospital ward | 95 (42%) | 16 (18%) | |
| Home | 15 (7%) | 0 (0%) | |
| Other | 4 (2%) | 0 (0%) | |
| **Age at death**[c] | | | 0.017 |
| Early neonatal death (<7 days) | 125 (55%) | 36 (31%) | |
| Late neonatal death (7-27 days) | 43 (19%) | 28 (65%) | |
| Post neonatal death (>27 days) | 61 (27%) | 25 (42%) | |
| **Gestational age at birth**[c] | | | 0.017 |
| < 26 weeks | 72 (34%) | 18 (27%) | |
| 26-28 weeks | 28 (13%) | 16 (57%) | |
| 29-31 weeks | 10 (5%) | 6 (60%) | |
| 32-36 weeks | 25 (12%) | 8 (32%) | |
| ≥ 37 weeks | 76 (36%) | 37 (51%) | |
| **Congenital anomalies**[a] | | | 0.877 |
| Yes (single or multiple) | 73 (41%) | 36 (52%) | |
| No | 107 (59%) | 53 (51%) | |
| **Severity of congenital anomalies**[c,d] | | | 0.262 |
| Very serious | 41 (56%) | 18 (46%) | |
| Serious | 17 (23%) | 8 (50%) | |
| Moderate/mild[e] | 15 (19%) | 10 (69%) | |
| **Main cause of death**[b] | | | < 0.001 |
| Prematurity and related disorders | 47 (21%) | 22 (49%) | |
| Congenital anomalies singular | 38 (17%) | 21 (57%) | |
| Congenital anomalies multiple | 34 (15%) | 15 (47%) | |
| Complications of the pregnancy with repercussions for the foetus | 40 (18%) | 8 (21%) | |
| Acute complications of the pregnancy and/or birth in a healthy foetus | 34 (15%) | 12 (36%) | |
| Disorders acquired after birth | 19 (8%) | 11 (61%) | |
| Other | 17 (7%) | 0 (0%) | |

Missing values: Information on continuous deep sedation was missing in 9 cases (3.9%); gestational age was missing in 18 cases (7.9%); information on presence of congenital anomalies was missing due to the death being sudden and unexpected in 46 cases causing an immediate end of the questionnaire (20.1%) and in 3 additional cases without reason (1.3%). Percentages were calculated without these missing cases.
No continuous deep sedation until death includes sudden and unexpected deaths.

[a] Two-tailed Fisher's exact tests were used to compare differences in sex and presence of congenital anomalies between groups with and without continuous deep sedation until death

[b] Pearson Chi-square test was used to compare differences in cause of death between groups with and without continuous deep sedation until death

[c] Kruskal Wallis tests were used to compare differences for age at death and gestational age at birth between groups with and without continuous deep sedation until death

[d] Could only be filled in for the 73 cases where a congenital anomaly was indicated.

[e] Moderate and mild were aggregated to protect the identity of the involved infants and to avoid small cells

**Table 3: relation between demographics and occurrence of continuous deep sedation until death**

| | | Odds of receiving continuous deep sedation until death[a] | | |
|---|---|---|---|---|
| | | | 95% CI | |
| | Sign. | OR | Lower | Upper |
| **Sex** | * | * | * | * |
| **Place of death** | * | * | * | * |
| **Age at death** | 0.004 | | | |
| Early neonatal death (<7 days)[b] | | | | |
| Late neonatal death (7-27 days) | 0.001 | **3.817** | **1.714** | **8.500** |
| Post neonatal death (>27 days) | 0.165 | 1.695 | 0.805 | 3.571 |
| **Gestational age at birth** | 0.130 | | | |
| < 26 weeks[b] | | | | |
| 26-28 weeks | 0.043 | **2.722** | **1.030** | **7.191** |
| 29-31 weeks | 0.352 | 2.033 | 0.457 | 9.041 |
| 32-36 weeks | 0.960 | 1.027 | 0.358 | 2.944 |
| ≥ 37 weeks | 0.041 | **2.209** | **1.031** | **4.731** |
| **Congenital anomalies** | * | * | * | * |
| **Severity of congenital anomalies** | * | * | * | * |
| **Main cause of death** | * | * | * | * |

Multivariable binary logistic regression, stepwise exclusion of nonsignificant variables

Nagelkerke $R^2$ = 0.155 for the final model. Sex, place of death, congenital anomalies, severity of congenital anomalies and main cause of death were not included in the final model due to their predictive value being nonsignificant (p-value > 0.05)

[a] Adjusted odds ratio

[b] The reference category

* Predictors were not significant and were thus removed from the final model stepwise.

**Table 4: Characteristics of the implementation of continuous deep sedation until death**

| | Infants who received continuous deep sedation until death N = 89 | % |
|---|---|---|
| **Drugs used** | | |
| Only benzodiazepines | 0 | 0 |
| Only morphine | 39 | 44.8 |
| Benzodiazepines and morphine (and other drugs) | 48 | 53.9 |
| **Duration of sedation before death** | | |
| < 12 hours | 17 | 19.5 |
| 12-24 hours | 18 | 20.7 |
| 1-7 days | 42 | 48.3 |
| 1-2 weeks | 5 | 5.7 |
| > 2 weeks | 5 | 5.7 |
| **Artificial nutrition and hydration administered?** | | |
| Until death | 81 | 92.0 |
| Not until death | 7 | 8.0 |
| **Intention of hastening death** | | |
| No intention | 43 | 48.9 |
| Taking into account possible hastening of death | 35 | 39.8 |
| Co-intention or explicit intention[a] | 10 | 11.4 |

Missing values: drugs used and duration of sedation was missing in 2 cases (2.2%); artificial nutrition and hydration, and intention of hastening death was missing in 1 case (1.1%). Percentages were calculated without these missing values.

[a] Co-intention and explicit intention were aggregated to protect the identity of the involved infants and avoid small cells