Discomfort and Pain in Newborns With Myelomeningocele: A Prospective Evaluation
Myrthe J. Ottenhoff, Ruben Dammers, Erwin J. O. Kompanje, Dick Tibboel and T. H. Rob de Jong
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Discomfort and Pain in Newborns With Myelomeningocele: A Prospective Evaluation

**OBJECTIVE:** In a worldwide debate on deliberately terminating the lives of newborns, proponents point at newborns with very severe forms of myelomeningocele (MMC) and their assumed suffering, claiming there are no effective means of alleviating their distress. Nevertheless, the degree of discomfort and pain in these newborns has never been assessed in a structured manner.

**METHODS:** In a prospective cohort study, 28 consecutive newborns with MMC were included over a 5-year period and were followed up throughout their hospital stay for initial treatment. We created 2 disease severity groups on the basis of the Lorber criteria. The primary outcomes were discomfort and pain, assessed by simultaneously scoring 2 validated scales: the visual analog scale for pain and the Comfort Behavioral Scale for discomfort. These scores were coupled to a validated and evidence-based analgesia algorithm.

**RESULTS:** Overall, discomfort related to pain was measured in 3.3% of the scores. This percentage differed little between the preoperative and postoperative periods and did not significantly differ between newborns with less severe MMC and severe MMC (3.9% vs 2.8%; \( P = .3 \)). The mean dosage of paracetamol was 35 mg/kg per day (95% confidence interval: 32–39); the mean dosage of morphine was 0.9 mg/kg per hour (95% confidence interval: 0.6 –1.2).

**CONCLUSION:** Over the length of their hospital stays for initial treatment, all newborns with MMC presented with low levels of discomfort and pain independent of disease severity and time frame. *Pediatrics* 2012;129:e741–e747

**WHAT’S KNOWN ON THIS SUBJECT:** Active termination of life in newborns with myelomeningocele because of assumed suffering in these newborns has been extensively discussed. However, the level of discomfort and pain in these newborns has never been substantially assessed.

**WHAT THIS STUDY ADDS:** This is the first study presenting quantitative data on discomfort and pain in newborns with myelomeningocele. Therefore, it can be of guidance in the choice of treatment: either active treatment or palliative care in the context of end-of-life decisions.

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**KEY WORDS**

decision-making, infant, newborn, pain measurements/standards, spinal dysraphism/therapy

**ABBREVIATIONS**

CI—confidence interval
COMFORT-B—Comfort Behavior Scale
MMC—myelomeningocele
VAS—visual analog scale

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; drafted the article or revised it critically for important intellectual content; and all authors provided final approval of the version to be published.

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Myelomeningocele (MMC) is a birth defect resulting from incomplete fusion of the neural folds and is therefore categorized as a neural tube defect. The recommended treatment is surgical closure of the defect and insertion of a ventriculoperitoneal shunt if hydrocephalus is diagnosed. However, surgery does not always seem feasible because some forms of MMC are considered to be too severe to be treated. Criteria for determining whether to proceed with treatment were developed by Lorber in the 1970s. These criteria are still being used today to distinguish between severe and less severe cases of MMC, as improvements in care have allowed many patients with MMC to reach their adult years with a nearly normal quality of life. Despite these improvements, decision-making on initiation of treatment in very severe forms of MMC, even prenatally, may be difficult. Even more difficult may be deciding on palliative treatment or active termination of life when surgical treatment is not started.

In 2005, a total of 22 cases of deliberate termination of life of newborns in the Netherlands were reported over the period 1997 to 2004. These 22 newborns were all born with MMC and suffered unbearably, without any proper medical means to alleviate their condition. This serious condition of these newborns was expected to continue on the long-term, without hope for the future. This debate was then extrapolated to all newborns with very severe conditions. In the Netherlands, this led to the development of The Groningen Protocol, which evoked an extensive international discussion. This protocol contains directives and criteria under which physicians can decide to deliberately terminate the lives of newborns without the prospect of legal prosecution. It was adopted by the Dutch Society of Pediatrics and was accepted by the Dutch Public Prosecution Service. Proponents of The Groningen Protocol used the assumption of unbearable and hopeless suffering in newborns with a very severe form of MMC as an argument in their favor. Opponents argued that newborns with MMC certainly can feel pain but that any discomfort and/or pain can be alleviated effectively and that newborns are not able to suffer to begin with.

Most of these publications, however, are of an ethical, legal, or philosophical nature. Quantifying the assumed suffering therefore seems to be very important, not only in the light of the debate on deliberate termination of the life of newborns with MMC per se, but also of newborns with severe conditions in general. However, suffering should not be considered as an outcome measure for the following reasons: (1) suffering is a subjective term, which cannot be measured; and (2) suffering also includes future suffering in terms of hospital dependency, predicted inability to communicate, future quality of life, and predicted self-sufficiency. This broad idea of suffering cannot be experienced by newborns. Furthermore, if one suspects a newborn is currently suffering, thus excluding the future prospect of this distress, one should determine the actual causes for the suffering, such as discomfort or pain. Objective and validated scales are now available to measure both discomfort and pain; these tools include the Comfort Behavioral Scale (COMFORT-B) and the visual analog scale (VAS). In addition, the degree of discomfort and pain in newborns with MMC has never been assessed to our knowledge. We therefore conducted The Rotterdam Study on Discomfort and Pain in Newborns with Myelomeningocele, which we report here.

**METHODS**

**Study Design, Patients, and Setting**

We performed a prospective cohort study to characterize the discomfort and pain profiles of newborns with MMC. The study was approved by the local medical ethical review board of the Erasmus University Medical Center, Rotterdam, the Netherlands. Newborns with MMC were included when they were admitted for initial treatment to our hospital between January 1, 2005, and January 1, 2010. Patients were excluded when they were born with additional gross congenital anomalies or chromosomal anomalies not associated with MMC.

**Patient Demographic Characteristics and Lorber Criteria**

Routinely collected parameters included gender, postnatal and postmenstrual age, and the anatomic level of the MMC. In addition, clinical symptoms of meningitis, active hydrocephalus requiring surgical intervention, and the presence of a retention bladder were assessed along with types and doses of analgesics administered.

To investigate whether the discomfort and pain profile was dependent on the severity of the MMC, we distinguished between less severe MMC and severe MMC by using the Lorber criteria and accordingly created 2 groups, labeled the non–Lorber group and the Lorber group, respectively. Newborns were assigned to the Lorber group when 1 or more of the following conditions were met: thoracolumbar lesion, severe paraplegia (grade 5 paraplegia [at most the hip flexors acting] or grade 4 paraplegia [at most the hip adductors and the quadriceps acting in addition to the hip flexors]), gross enlargement of the head (2 cm above p90), kyphosis, additional gross congenital anomalies, and/or major birth injuries.

**Discomfort and Pain Measurements**

The COMFORT-B scale was applied to assess discomfort; the VAS was used to
assess pain. Purpose-trained ICU and pediatric nurses applied both scales in all patients for the duration of their treatment. These nurses previously demonstrated acceptable interrater reliability (linearly weighted Cohen’s $\kappa \approx 0.65$) with an already qualified scorer in 10 consecutive scoring sessions.22 The COMFORT-B scale measures discomfort by observation of behavior.23 The scale was validated by researchers at Sophia Children’s Hospital.22 The COMFORT-B scale includes 6 behaviors whose intensities are rated on a scale from 1 to 5: alertness; calmness/agitation; respiratory response in mechanically ventilated patients or crying in spontaneously breathing newborns; body movement; muscle tone; and facial tension. Rating is performed after 2 minutes of bedside observation. At the end of the observation period, a limb is carefully lifted to assess muscle tone. The scores on all 6 items are summed to produce a total score between 6 and 30. A COMFORT-B score $\geq 17$ indicates discomfort that should be alleviated.24

The VAS is a standard method of assessing pain in clinical settings and is generally considered as an overall assessment of pain. It is applied after the 2-minute COMFORT-B observation. The VAS is a 10-cm line on which the observer places a mark to rate pain from 0 (“no pain”) to 10 (“worst possible pain”). A VAS score $\geq 4$ is classified as “pain” and is an indication for (additional) analgesic treatment.22,25

Protocolized Pain Management
A series of studies at our institution have resulted in a validated algorithm for monitoring and treating discomfort and pain in newborns22,24,26–30 in line with nationwide guidelines.31 These guidelines have not changed in the last decade. This algorithm is based on the combined COMFORT-B and VAS scores for the following reason. When only the COMFORT-B scale exceeds a cutoff point, the discomfort could be caused by events other than pain, such as hunger or a wet diaper. However, when both COMFORT-B and VAS scores exceed their cutoff points simultaneously, the discomfort is most likely caused by the pain, which should then be treated.

Because suffering is not an objective parameter, we considered this validated algorithm most suitable to assess the degrees of discomfort and pain of newborns with MMC before and after closure of the defect. Therefore, the primary outcome of this study was the concurrent COMFORT-B and VAS scores.

Statistical Analysis
Patient demographic characteristics are presented as mean values and 95% confidence intervals (CIs) or as frequencies and percentages where appropriate. The continuous variables of the Lorber group and the non–Lorber group were compared by using unpaired Student’s $t$ test when the variables were normally distributed or a Mann-Whitney $U$ test otherwise. Discrete variables were compared by using the $\chi^2$ test or Fisher’s exact test when at least 1 of the expected counts of the variable values was $< 5$. COMFORT-B, VAS scores, and combined COMFORT-B and VAS scores that exceeded the previous cutoff points are presented as frequencies and percentages. These percentages are treated as continuous variables and do not seem to be normally distributed. To evaluate time-dependent or surgery-related distress, we compared discomfort and pain during various time periods (preoperative, within 24 hours’ postoperative, 24–48 hours’ postoperative, and $>48$ hours’ postoperative) by using a Wilcoxon signed rank test.

To compare the discomfort and pain scores of the Lorber and the non–Lorber groups, the COMFORT-B, VAS scores, and combined COMFORT-B and VAS scores were treated as a discrete variable. Variables were compared by using the $\chi^2$ test or Fisher’s exact test. Statistical analysis was performed with SPSS 17.0 for Windows (SPSS Inc, Chicago, IL).

RESULTS

Patient Characteristics
We included 28 consecutive newborns with MMC. One patient was born with trisomy 18 (Edward’s syndrome) and was excluded. Twenty were born in the Sophia Children’s Hospital; 8 were admitted within 48 hours of birth. Of the 28 included patients, 14 were boys and 14 were girls. The mean gestational age was 39.1 weeks (95% CI: 33.3–39.9), with a range of 31.1 to 42.3 weeks. The mean birth weight was 3178 g (95% CI: 3041–3315). The Lorber group contained 8 newborns and the non–Lorber group 20 newborns. MMC at the lumbar-sacral level was most frequent (17 patients). Twenty-six patients (92.9%) had either congenital hydrocephalus or acquired hydrocephalus, which was eventually treated with a ventriculoperitoneal shunt. One patient developed meningitis postoperatively, which was treated with antibiotics with good results. None of these variables differed significantly between the Lorber and non–Lorber group, except level of MMC (Table 1). All patients were found to have a retention bladder that needed catheterization. After counseling of the parents and having obtained parental consent, surgical closure of the defect was performed, mostly in collaboration with a plastic surgeon.

COMFORT-B and VAS scores were collected over a mean of 317 hours (95% CI: 210–424). Individual follow-up times ranged from 8 to 1160 hours. The mean ICU stay for postoperative surveillance was 103 hours (95% CI: 14–190). Fourteen patients were discharged from the ICU within 36 hours. The follow-up
time and the time spent in the ICU did not differ significantly between the 2 groups (Table 1).

**COMFORT-B and VAS Scores**

Over a cumulative follow-up time of 9082 hours, we collected 1258 scores, of which 87% were concurrent COMFORT-B and VAS scores. Numbers and percentages of collected COMFORT-B, VAS, and concurrent scores are displayed per individual case in Supplemental Table 4 and per follow-up period in Supplemental Table 5.

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Patient Characteristics</th>
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<tbody>
<tr>
<td>Characteristic</td>
<td>Lorber Group</td>
</tr>
<tr>
<td>Less Severe (n = 20)</td>
<td>Severe (n = 8)</td>
</tr>
<tr>
<td>Gender, n (% male)</td>
<td>10 (50.0)</td>
</tr>
<tr>
<td>Birth weight, mean (95% CI), g</td>
<td>3160 (2993–3330)</td>
</tr>
<tr>
<td>Gestational age, mean (95% CI), wk</td>
<td>39.3 (38.2–40.3)</td>
</tr>
<tr>
<td>Follow-up, mean (95% CI), h</td>
<td>261 (194–327)</td>
</tr>
<tr>
<td>Time in ICU, mean (95% CI), h</td>
<td>68 (5–131)</td>
</tr>
<tr>
<td>Level of MMC, n</td>
<td></td>
</tr>
<tr>
<td>Thoracic</td>
<td>0</td>
</tr>
<tr>
<td>Thoracolumbar</td>
<td>0</td>
</tr>
<tr>
<td>Lumbar</td>
<td>5</td>
</tr>
<tr>
<td>Lumbosacral</td>
<td>15</td>
</tr>
<tr>
<td>Hydrocephalus, n (%)</td>
<td>18 (95.0)</td>
</tr>
<tr>
<td>Meningitis, n (%)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

a P-value calculated by using Fisher’s exact test.
b P-value calculated by using an unpaired t-test.
c Thoracic and thoracolumbar levels compared with lumbar and lumbosacral levels.
d Thoracic and thoracolumbar levels compared with lumbar and lumbosacral levels.

Overall, 7.9% of the COMFORT-B scores were ≥17; 3.7% of VAS scores were ≥4. Overall, 3.3% of all concurrent COMFORT-B and VAS scores exceeded both cutoff points. These percentages varied over time (Table 2). COMFORT-B scores exceeded their cutoff point significantly less frequently during the 24–48-hour postoperative period compared with all other time periods. VAS and concurrent scores exceeded their cutoff points significantly less frequently during the 24–48-hour postoperative period compared with the 0–24-hour postoperative period only.

Percentages of COMFORT-B, VAS, and concurrent scores exceeding their cutoff points in the Lorber group were higher than in the non–Lorber group, with no significant differences (P = .13, P = .08, and P = .3, respectively; Table 3).

**Administration of Analgesics**

All patients received paracetamol via rectal administration to alleviate pain at some time; 21 patients received morphine via infusion (75%). Paracetamol and morphine were being administered 59.4% and 13.9%, respectively, of the total follow-up time. Paracetamol was administered most often during the 24- to 48-hour postoperative period (82.8%), which corresponds to the highest mean dosages in this period (Table 2), followed by the >48-hour postoperative period (59.8%). Morphine was more frequently administered during the 0- to 24-hour postoperative period (64.6%), which corresponds to the highest mean dosage of all periods, followed by the 24- to 48-hour postoperative period (18.9%).

The overall mean dosage of paracetamol was 35 mg/kg per day (95% CI: 32–39), with a range of 0 to 102 mg/kg per day. Unfortunately, the upper limit of this range indicates an overdose, which reflects a single 33 mg/kg dosage over 6 hours followed by 3 single 23 mg/kg distributed over the rest of the day in 1 patient. This finding is considered a calculation error during the treatment of this newborn, as there were no high COMFORT-B or VAS scores at the time. This was the only overdose registered in our study. The overall mean dosage of morphine was 0.9 µg/kg per hour (95% CI: 0.6–1.2), with a range of 0 to 25 µg/kg per hour. The mean analgesic dosages are presented according to follow-up period in Table 2.
Newborns in the Lorber group did not consume significantly more paracetamol than newborns in the non-Lorber group \( (P = .21) \), but they did consume significantly more morphine \( (P = .02) \). However, the median morphine dosage in both groups was 0 mg/kg per hour, with an interquartile range of 0 to 0 (Table 3).

Figure 1 illustrates the mean dosages of paracetamol and morphine over the follow-up period, compared between the 2 groups. Only in the preoperative period did the Lorber group consume more paracetamol than the non-Lorber group \( (P = .01) \), in the >48-hour postoperative period, the Lorber group consumed significantly less paracetamol \( (P = .003) \). As for the daily morphine dosage, the Lorber group required significantly more in the 24- to 48-hour period and the >48-hour postoperative period \( (P = .007 \) and \( P = .002 \), respectively).

DISCUSSION

The findings from this study show that routine analgesic treatment\(^{22,24,26–30} \) resulted in low levels of discomfort and pain in all newborns with MMC, independent of the severity of the disease and over the whole preoperative and postoperative periods. Only the 24- to 48-hour postoperative period was different, as the 0- to 24-hour postoperative period showed higher percentages of exceeding VAS and concurrent scores compared with this period. In addition, the percentage of exceeding COMFORT-B scores in the 24- to 48-hour period was lower compared with all other periods. Disease severity was not associated with paracetamol consumption, except in the preoperative period. The more severely affected patients consumed more morphine, however. Nevertheless, morphine was rarely administered overall, as the median morphine dosage was 0 mg/kg per hour, with an interquartile range of 0 to 0.

Some limitations of this study should be addressed. First, because it was a single–center study, the level of reproducibility at other centers cannot

### TABLE 3 Scores and Analgesics According to Lorber Group

<table>
<thead>
<tr>
<th>Scale</th>
<th>Lorber Group</th>
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<tr>
<td></td>
<td>Less Severe</td>
<td>Severe</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>P</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VAS Median (interquartile range)</td>
<td>0 (0–0)</td>
<td>0 (0–1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scores (≥4), n (%)</td>
<td>18 (2.9)</td>
<td>25 (4.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>.15*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COMFORT-B Median (interquartile range)</td>
<td>11 (10–12)</td>
<td>11 (10–15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scores (≥17), n (%)</td>
<td>47 (6.7)</td>
<td>49 (9.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>.08*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concurrent VAS and COMFORT-B Median (interquartile range)</td>
<td>17 (2.8)</td>
<td>20 (3.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scores (≥4 and ≥17), n (%)</td>
<td>.3*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paracetamol dosage, mg/kg per day Mean (95% CI)</td>
<td>37 (33–42)</td>
<td>33 (28–38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (interquartile range)</td>
<td>52 (0–67)</td>
<td>53 (0–58)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine dosage, µg/kg per h Mean (95% CI)</td>
<td>0.5 (0.2–0.7)</td>
<td>1.5 (0.9–2.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (interquartile range)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
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</table>

* P value calculated by using a \( \chi^2 \) test.

\( P \) value calculated by using an unpaired \( t \) test.

\( P \) value calculated by using a Mann-Whitney \( U \) test.

**FIGURE 1** Comparison of paracetamol and morphine dosage between Lorber groups according to follow-up period. \( P \) values were calculated by using a Mann-Whitney \( U \) test.
be established. However, our center has extensive experience in the treatment of children with MMC; for example, our multidisciplinary MMC team was established 25 years ago. Furthermore, great attention is paid to the diagnosis and treatment of pain and discomfort in newborns and children.\(^{22,24,27}\) Second, there may be some selection bias, because nurses are more likely to assess the newborns whenever discomfort or pain is suspected. Both inconsistencies are due to daily practice on a pediatric ward.

Third, the follow-up ended at discharge, and the follow-up period therefore differed between the children. Assuming that the length of the hospital stay is related to the severity and complications of the disease, the discomfort and pain levels could have been overestimated. Still, we found no relationship between these variables (\(P = .7\)) and therefore consider our conclusions to be valid and justified by the data.

Our findings indicate that discomfort and pain in newborns with MMC can be adequately managed. In all patients, any possible level of discomfort and pain measured was treated with an evidence-based algorithm for analgesic treatment, except for 1 patient who received a single overdose of paracetamol. Concurrent COMFORT-B and VAS scores indicated the need of extra analgesic treatment only rarely (3.7% of cases). Moreover, during much of the follow-up period only paracetamol was administered, indicating mild pain.\(^{32}\) In addition, surgical closure of the defect seems to be an effective means of producing stable well-being in these newborns, given that pain and discomfort scores in the postoperative periods were not significantly higher than those in the preoperative period.

The doses of morphine administered in the postoperative periods were consistent with standards for newborns who have undergone surgery.\(^{27,28}\) In addition, severity of the congenital malformations had no influence on levels of discomfort and pain. We concluded, therefore, that treatment of more severely affected patients is as feasible as that of less severely affected patients.

Our results fit into internationally accepted consensus on the treatment of critically ill children, as levels of discomfort and pain overall are low and any exceptional high levels are easily treatable with a routine analgesic algorithm. For example, one review article concluded that “multi-disciplinary consensus guidelines for maintenance of sedation and analgesia in critically ill children have been successfully produced and are supported by levels of evidence.”\(^{32}\) However, the authors acknowledged the shortage of properly designed trials in this particular group of patients.\(^{33}\)

**CONCLUSIONS**

In this representative cohort of newborns with MMC, we detected low levels of discomfort and pain in newborns independent of disease severity and time frame. Any discomfort and pain could be routinely treated by using a validated analgesic algorithm. This study naturally suggests future research.

As the degree of discomfort and pain in these 28 newborns with MMC is now clearly described, the quality of life of these patients in childhood, adolescence, and adulthood should be further investigated. Factors in addition to discomfort and pain that could be explored include: cognitive development, motor problems, bladder dysfunctions, shunt deficiencies, total number of operations, chronic pain, and dependency on medical and/or supportive care.

**ACKNOWLEDGMENTS**

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**REFERENCES**


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