A Standardized Care Pathway following Mandibular Distraction in Infants Less Than 3 Months of Age

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Abstract

Objectives. To assess for differences in postoperative care following mandibular distraction osteogenesis (MDO) in infants before and after implementation of a standardized protocol.

Study Design. Retrospective chart review.

Setting. Urban tertiary pediatric hospital.

Subjects and Methods. The inpatient charts of infants who underwent MDO before 90 days of age were assessed for metrics such as postoperative length of stay (LOS), duration of mechanical ventilation, and the choice and duration of sedating medications.

Results. Over a 6-year period, 16 patients met inclusion criteria. The first 4 consecutive patients were managed at the discretion of the critical care staff. The remaining 12 infants were managed with a planned 4- to 6-day period of postoperative intubation, during which a standard protocol determined the choice, dosage, and duration of sedating medications. The mean age was similar between groups (preprotocol: mean, 26.5 days; protocol: mean, 20.3 days; \( P = .51 \)). The mean postoperative LOS was 13.3 days less among infants managed with the protocol (\( P = .06 \)), and the mean number of midazolam boluses was fewer among protocol patients (\( P < .01 \)). A more consistent postoperative LOS, duration of mechanical ventilation, and exposure to sedating medications was observed among protocol subjects (\( P < .01 \)). The LOS for 2 patients in the preprotocol group was extended due to iatrogenic withdrawal syndrome. There were no instances of accidental extubation or anoxia in either group.

Conclusions. Among infants undergoing MDO, standardizing postoperative airway and sedation practices may offer a more predictable postoperative course as compared with a case-by-case management philosophy.

Keywords

Pierre Robin sequence, mandibular distraction osteogenesis, pediatric otolaryngology, sedation protocol, standardized care pathway

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Pierre Robin sequence (PRS) is a triad of clinical abnormalities present at birth that includes micrognathia, glossoptosis, and airway obstruction, with or without an incomplete cleft palate. A relatively rare disorder, PRS is estimated to affect approximately 1 in 9000 live births.1 Airway obstruction, due to posterior displacement of the tongue in the context of micrognathia, contributes to respiratory distress and feeding difficulties, often experienced in the neonatal period. In infants with PRS, if surgical management of airway obstruction is necessary in early infancy, tongue lip adhesion (TLA), tracheotomy, or mandibular distraction osteogenesis (MDO) may be utilized. Recent data suggest that TLA may adequately address airway obstruction in select patients; however, this procedure invariably results in some degree of feeding impairment and may not allow for complete resolution of obstructive sleep apnea.2 While tracheotomy offers a definitive solution to chronic upper airway obstruction, this procedure is associated with significant risk of short- and long-term morbidity in the form of scarring, tracheal stenosis, and accidental decannulation.3,4 Current literature suggests that MDO offers a high success rate for addressing hypventilation and failure to thrive in even the most severely affected infants with PRS; however, achieving such outcomes requires an aggressive surgical intervention, the long-term effects of which are still unclear.5 Early literature pertaining to MDO was limited to case series focusing on basic clinical outcomes and short- and long-term complications.6-8 Although neonatal MDO has gained wider acceptance among plastic surgeons, oral surgeons, and

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Among those infants born with PRS who require early airway intervention with MDO, the risk of airway compromise and potential anoxic brain injury that may result from airway obstruction in the context of postoperative oropharyngeal edema cannot be overstated. The very nature of patients undergoing neonatal MDO ensures that these infants have an unstable airway preoperatively. Following placement of distraction hardware, there is a latency phase in which the mandibular segments are left undisturbed; during the first few days of activation, postoperative edema and analgesic requirements further jeopardize a tenuous airway in these patients. The challenge of providing adequate postoperative analgesia while assuring constant airway protection during this period is compounded by the many complications of prolonged sedation, including iatrogenic withdrawal syndromes, pulmonary complications, and prolonged hospital stays.9-11 These complications must be balanced with the adverse consequences of inadequate pain control in the pediatric population, such as long-term pain hypersensitivity and increased physiologic stress responses.12-14

No consensus has been reached regarding the optimal strategy for the immediate postoperative management of infants <3 months of age who have undergone MDO. To date, a 2010 study by Al-Samkari et al remains the largest study to report specific data regarding length of sedation and postoperative length of stay (LOS) following MDO.15 In that report, 12 infants received MDO with a mean postoperative LOS of 21.9 days and a mean duration of mechanical ventilation of 3.6 days. Anecdotally, current practice patterns vary widely, from extubation of infants shortly after the procedure to longer periods of postoperative sedation.

In 2010, we performed our institution’s first neonatal mandibular distraction. In preparation for this, a nursing care pathway was created to improve communication between the surgical team and care providers at the bedside. However, guidelines for the administration of sedation medications were not provided to the medical staff, as the physicians involved felt that close interpersonal communication between the otolaryngology team and the neonatology (neonatal intensive care unit) or intensivist (pediatric intensive care unit) team would be sufficient. Over the 18-month period that followed, there were several instances of misunderstandings or miscommunications among the physicians who cared for the 6 infants and toddlers who underwent MDO. While there were no accidental extubations or serious safety events over this period, there was a clear lack of consistency among cases in regard to the dosage and frequency of sedating medications as well as the management of mechanical ventilation parameters. Once these children were extubated, some had an uneventful course, while others demonstrated prolonged symptoms of withdrawal from sedating medications. After the sixth such case of ad hoc management, the pediatric otolaryngology team convened a meeting with the neonatal intensive care unit and pediatric intensive care unit leadership with the shared goal of developing a standardized approach to the postoperative management of infants following MDO.

In developing this standardized care pathway, all parties conveyed a common desire to lower postoperative LOS, limit the frequency and duration of sedating medications, and reduce symptoms of withdrawal. The standardized clinical pathway referred to in this study was based on a previously published protocol for pediatric patients following complex airway procedures.6 With the input of the neonatology team, this protocol was modified and adapted for use in newborns undergoing neonatal MDO. The protocol was approved by the hospital safety committee in June 2012 and has been utilized exclusively since that time.

The purpose of this current study was to assess for differences in postoperative LOS, duration of mechanical ventilation, and the choice and duration of sedating medications following MDO in infants before and after implementation of this standardized postoperative sedation protocol.

**Materials and Methods**

**Overview of Protocol**

This protocol was developed for sedation requirements occurring while the patient is mechanically ventilated. Primary sedative agents included morphine and midazolam: infusions of these agents were started at 0.02 mg/kg/h, and boluses of 0.05 to 0.1 mg/kg/dose were given every 2 to 4 hours as needed, titrated to limit spontaneous movement or signs of pain (grimacing, tachycardia, tachypnea, etc). Substitution for midazolam with lorazepam was permitted at the discretion of the intensive care unit team. Dexametomidine was added if morphine, midazolam, or lorazepam infusions reached 0.06 mg/kg/h and the child continued to show symptoms of inadequate sedation (grimacing, excessive movement, tachycardia, tachypnea, etc). Neuromuscular blockade was achieved with vecuronium for the first 48 to 72 hours; infusions were initiated at 0.1 mg/kg/h and titrated to maintain minimal spontaneous movement. Continuation of vecuronium after 48 to 72 hours was considered only if significant residual airway obstruction remained and the pediatric otolaryngology and neonatology/critical care team considered the infant unlikely to tolerate extubation at that time.

A wean from sedating medications was initiated between postoperative days 3 and 5, with the goal to extubate infants from postoperative day 4 to 6. If vecuronium had not yet been discontinued, it was discontinued at least 6 hours prior to planned extubation. Midazolam and morphine infusions were discontinued at least 3 hours prior to planned extubation. All infants were extubated to nasal cannula in the unit. If there were any signs of intermittent obstruction, a nasopharyngeal airway was inserted by the otolaryngology team, and this was removed the following day when the child was more awake and active. Following extubation, boluses of sedation agents were given as needed for signs of withdrawal as determined by nursing staff. Dosages of these
agents were rapidly tapered; acetaminophen was given as needed for signs of pain (Figure 1).

Oral feeding was initiated, with nasogastric feeds for supplementation, starting 24 hours after extubation or at the discretion of the feeding team. Children were discharged home from the unit only when the parents were able to demonstrate a high level of comfort with oral feeding. All children had demonstrated 48 hours of consistent oral intake ≥100% of their calorice needs, and no child was discharged with supplemental feeds through a nasogastric or gastrostomy tube.

**Study Design**

This was a retrospective chart review study performed at a single tertiary urban academic medical center. Approval was provided by the Tufts University Health Sciences Institutional review board. All patients <90 days of age who underwent MDO between January 2009 and April 2016 were identified. The following inclusion criteria were applied: (1) isolated or syndromic PRS, with or without cleft palate, and (2) surgical intervention with bilateral MDO prior to 90 days of age. Exclusion criteria included prior surgical management of PRS with tracheostomy or TLA as well as gastrostomy tube dependence for nutritional support. These exclusion criteria were adopted as one of the outcome metrics of the study was postoperative LOS. Any need for procuring durable medical equipment (suction supplies, monitoring equipment, or tube feeding supplies) was therefore excluded as a factor affecting timing of discharge. Likewise, all children included in this study remained in the hospital until they had demonstrated >48 hours of sustained oral intake, fulfilling 100% of their calorice needs.

In accordance with the care team’s goals for the implementation of the standardized protocol, the following outcome metrics were chosen to assess the impact of protocol implementation: postoperative LOS, duration of postoperative sedation, total number of sedation and analgesic boluses while the patient was mechanically ventilated, and total number of sedation and analgesic boluses after extubation. Additional factors were assessed, such as accidental extubation and duration of sedation wean. For statistical analysis, patients were divided into 2 groups: the preprotocol group, which consisted of patients who underwent MDO prior to the 2012 implementation of our protocol, and the protocol group, which consisted of patients who underwent MDO after protocol implementation. Demographic characteristics were summarized with descriptive statistics. Statistical differences in outcome metrics between groups were calculated with Student’s t tests, and variances of the outcome metrics in the 2 groups were compared with an F test for equality of variances.

**Ethical Considerations**

A prospective randomized controlled study of the protocol did not seem feasible given the ethical considerations surrounding the shared consensus among surgeons, neonatologists, and pediatric intensivists that postoperative care of patients undergoing MDO merited a standardized approach. While no serious safety events occurred prior to the implementation of the protocol, iatrogenic neonatal withdrawal syndrome did occur in 2 infants in the preprotocol group during this time, with prolonged exposure to analgesic medications and a longer hospital stay related solely to the need for weaning off of narcotic medications. Since these occurrences were noted in 50% of our preprotocol patients, we did not think that it was ethical to continue ad hoc postoperative care practices as part of a prospective randomized trial.

**Results**

Between January 2009 and April 2016, a total of 26 patients underwent bilateral MDO at our institution. Six of these patients had surgery prior to creation of the standardized protocol, and 20 patients were managed after protocol implementation. Among the 6 patients in the preprotocol group, 2 were >3 months old at the time of surgery and did not meet inclusion criteria. Among the 20 children in the protocol group, 7 patients were also excluded for age. In
addition, 1 infant with significant medical comorbidities was excluded from the analysis because the patient died during the weeks that followed surgery while still in the hospital. In this case, the family elected to change goals of care midprotocol, when previously pending test results returned portending a poor neurologic prognosis. Overall, 16 patients met inclusion criteria of having undergone bilateral MDO at <3 months of age without prior TLA, tracheostomy, or dependence on a gastrostomy tube for supplemental feeding. The preprotocol group consisted of 4 infants who had been managed consecutively at the discretion of the neonatology or critical care staff on a case-by-case basis. The protocol group was composed of the remaining 12 infants who received postoperative care guided by the standardized clinical care pathway described earlier. The distribution of syndromic and isolated forms of PRS was identical in each group, with 75% of patients diagnosed with isolated PRS and 25% with syndromic PRS (Table 1).

Within the preprotocol group, 50% (n = 2) of the patients were female, and the mean age at the time of MDO was 26.5 days (range, 9-65 days). Within the protocol group, 42% (n = 5) of the patients were female, and the mean age at surgery was 20.3 days (range, 13-38 days).

The sedation agents utilized were similar in both groups; however, several differences were observed between the ad hoc and protocol strategies. Patients in the preprotocol group were sedated through narcotic infusions with or without concurrent midazolam infusion. These patients also received frequent boluses of narcotics, with additional boluses of benzodiazepines and vecuronium used on an as-needed basis. None of the preprotocol patients received a vecuronium infusion. Conversely, infants in the protocol group consistently received basal administration of vecuronium, narcotics, and benzodiazepines through continuous infusion at standardized weight-based rates, with additional boluses of sedating medications given only for breakthrough symptoms of pain and/or agitation.

Lorazepam was not used at all in the preprotocol group; however, this medication was utilized on occasion in the protocol group, although to a lesser extent than midazolam. Dexmedetomidine was not used in the preprotocol group; however, it was utilized in 1 patient within the protocol group as an alternative to further increases in the rates of morphine and midazolam infusions.

Among the 4 patients in the preprotocol group, the mean postoperative LOS was 30.8 days (range, 15-63 days; 95% CI, 8.6-52.9), while the mean postoperative LOS among the 12 patients in the protocol group was 17.4 days (range, 11-26 days; 95% CI, 14.8-20.0). Due to low numbers in the preprotocol cohort, statistically significant differences in mean LOS could not be established between the groups (P = .32).

The most dramatic difference in the utilization of sedating medication between groups was noted during sedation for mechanical ventilation. Patients in the preprotocol group received significantly more midazolam boluses than those in the protocol group (preprotocol: mean = 12.0 doses [95% CI, 6.8-17.2]); protocol: mean = 2.7 doses [95% CI, 0.6-4.7]; P = .03), even though the mean duration of benzodiazepine infusion was nearly identical between groups (preprotocol mean = 5.8 days [95% CI, 5.1-6.6] vs protocol mean = 5.4 days [95% CI, 4.9-6.0]). There were no differences between groups for the total number of morphine boluses or other sedatives or analgesics received during mechanical ventilation and after extubation (Table 2). Likewise, no differences were detected in the mean duration of mechanical ventilation, mean total narcotic requirement (duration and amount), or mean length of sedation wean after extubation.

An F test to compare 2 variances was performed between the groups, and this demonstrated significant variation in the consistency of LOS before and after protocol implementation (preprotocol: SD = 22.6 days; protocol: SD = 4.6 days; P < .01). Additionally, there was higher variability in the duration of mechanical ventilation (preprotocol: SD = 4.0 days; protocol: SD = 0.9 days; P < .01), as well as in the duration of continuous narcotic infusion (preprotocol: SD = 4.1 days; protocol: SD = 1.3 days; P < .01). Finally, greater variability in the total boluses of narcotic utilized

**Table 1.** Patient Demographics for Each Study Group.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Preprotocol (n = 4)</th>
<th>Protocol (n = 12)</th>
<th>P Valuea</th>
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<tbody>
<tr>
<td>Age, d</td>
<td>26.5 ± 16.8</td>
<td>20.3 ± 11.9</td>
<td>.51</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>3.30 ± 0.71</td>
<td>3.11 ± 0.32</td>
<td>.46</td>
</tr>
<tr>
<td>Gestational age at birth, wk</td>
<td>38.9 ± 2.78</td>
<td>37.7 ± 2.51</td>
<td>.45</td>
</tr>
<tr>
<td>Female</td>
<td>2 (50)</td>
<td>5 (42)</td>
<td>.77</td>
</tr>
<tr>
<td>PRS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolated</td>
<td>3 (75)</td>
<td>9 (75)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Syndromic</td>
<td>1 (25)</td>
<td>3 (25)</td>
<td>&gt;.99</td>
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Abbreviations: MDO, mandibular distraction osteogenesis; PRS, Pierre Robin sequence.

*Unpaired 2-sample t test.
after extubation was noted in the preprotocol group (preprotocol: SD = 42.9 doses; protocol: SD = 17.2 doses; $P = .02$; Table 3).

There were no incidences of accidental extubation or anoxia in either group. In the preprotocol group, 2 of the 4 patients exhibited a prolonged course of iatrogenic withdrawal syndrome following extubation. No child in either group was readmitted to a hospital within 30 days of discharge. All patients who underwent neonatal MDO avoided tracheostomy and gastrostomy placement during infancy. One child with Smith-Magenis syndrome who was in the protocol group required gastrostomy tube placement later in childhood. As for long-term follow-up, no child in either group has required repeat distraction or salvage tracheotomy as of the submission of this manuscript (duration of follow-up, 2.8-10 years).

Discussion

In this age of increased awareness of the negative consequences of prolonged sedation in children, this study seeks to determine if a standardized sedation protocol aimed at limiting patient exposure to opioids and benzodiazepines while still providing adequate pain control and a period of inactivity has advantages over the philosophy of managing these patients on a case-by-case basis. Additionally, given previously established associations between prolonged hospital stay and duration of sedation, this study seeks to better characterize the role of sedation protocols in optimizing postoperative LOS following neonatal MDO.

Our results suggest that postoperative LOS following MDO in infancy may be more consistent if patients are managed with a standardized postoperative sedation protocol. Likewise, standardizing the postoperative sedation of MDO patients may reduce benzodiazepine use in the postoperative period. Due to the small number of preprotocol patients, our study was not adequately powered to demonstrate statistically significant differences in mean LOS between groups; however, among the 12 patients managed after protocol implementation, the mean LOS was nearly half that of the 4 patients managed postoperatively prior to protocol utilization.

Wide variability in sedation and analgesic management after MDO poses a risk to the postoperative care of patients, as longer duration of sedation and receipt of more sedative agents are proven risk factors for precipitating iatrogenic withdrawal syndrome in pediatric patients.\(^\text{17}\) Therefore, it is our opinion that standardized postoperative sedation protocols may allow for more consistent use of sedative agents among infants recovering after MDO. Indeed, in our study, the wide variation in opiate exposure among the 4 infants managed on a case-by-case basis was also associated with an overall increase in duration and dosages of sedating medications (Tables 2 and 3).

Our study is limited primarily by the small number of patients in the preprotocol group, a shortcoming that leaves this report underpowered to determine statistical significance among many of the metrics assessed. In addition to the inherent limitations of any retrospective study, our cohort of patients possessed some potential confounding factors. Of our 16 patients, 5 were out-of-state residents, all of whom were in the protocol group. Discharge arrangements for these patients at times were complicated by logistical factors, such as arranging visiting nursing services through out-of-state networks, as well as arranging for transportation for families who needed to travel greater distances. Such influences may have increased the mean postoperative LOS in the protocol group. Additionally, at

<table>
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<tr>
<th>Table 2. Outcomes Related to Postoperative Course.</th>
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<tr>
<td>Group, Mean (95% CI)</td>
</tr>
<tr>
<td>Preprotocol (n = 4)</td>
</tr>
<tr>
<td>Postoperative</td>
</tr>
<tr>
<td>Length of stay, d</td>
</tr>
<tr>
<td>Day of last sedation bolus</td>
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<tr>
<td>Duration, d</td>
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<tr>
<td>Mechanical ventilation</td>
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<tr>
<td>Narcotic infusion</td>
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<td>Narcotic boluses, doses</td>
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<td>During mechanical ventilation</td>
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<td>After extubation</td>
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<tr>
<td>Duration of benzodiazepine infusion, d</td>
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<tr>
<td>Midazolam boluses, doses</td>
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<tr>
<td>During mechanical ventilation</td>
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<tr>
<td>After extubation</td>
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<tr>
<td>Acetaminophen boluses, doses</td>
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<tr>
<td>During mechanical ventilation</td>
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<td>After extubation</td>
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$^a$Unpaired 2-sample t test.
At least 1 patient in the preprotocol group was discharged on neonatal morphine sulfate with the goal of weaning off of this at local nursery. This occurrence may have favorably influenced the mean LOS for the preprotocol group.

The data presented in this study call for further research to evaluate current practices in the use of sedating medications following MDO in infants. Future studies that are more appropriately powered may provide data supporting or challenging the philosophy of standardizing postoperative sedation practices in this complex patient population. Additionally, future retrospective and prospective multicenter studies may be performed to shed light on potential regional variations in sedation practices and postoperative LOS following early MDO.

**Conclusion**

Our study suggests that among infants undergoing mandibular distraction, the use of a standardized sedation protocol for postoperative care may offer a more predictable postoperative course than sedation management strategies implemented on a case-by-case basis. Further research is needed to explore the effects that postoperative sedation protocols may have on reducing postoperative LOS and exposure to opioid and sedative agents in the pediatric population.

**Acknowledgments**

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**Author Contributions**

Grace R. Leu, collected data, analyzed, wrote article, final approval; Andrew R. Scott, designed study, analyzed data, revised, final approval.

**Disclosures**

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