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## Evaluation of the protocol regarding the Neonatal Abstinence Syndrome by opioids in the Intensive Care Unit of Odete Valadares Maternity in Belo Horizonte

### Avaliação preliminar da abordagem da Síndrome de Abstinência Neonatal por opióides na Unidade de Terapia Intensiva da Maternidade Odete Valadares em Belo Horizonte

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**ABSTRACT:** *Introduction:* In order to treat pain and psychomotor agitation, which are common symptoms in Neonatal Intensive Care Units (NICU), sedatives/opioid analgesics are used. However, its prolonged use, mainly in the continuous base, can provoke the Neonatal Abstinence Syndrome (NAS). *Objectives:* Evaluate the approach of NAS by opioids in newborns (NB) admitted in a NICU of Odete Valadares Maternity (OVM) in Belo Horizonte. *Methods:* Analysis of the medical records from the OVM pharmacy of the NB who have used methadone in between June 2013 to July 2014, additionally with diagnosis or risk of abstinence by opioids, confirmed clinically by the Finnegan scoring system. *Results:* All of the NB who have received methadone during the study time were evaluated. From the total of 17 NB, 6 were eliminated as they have been transferred to other services or evolved towards death, making it impossible to complete the data analysis. From 11 NB included, 7 were premature with gestational age under 28 weeks. There was a prevalence of the male gender (72,7%). All the infants received fentanyl continuously, which period of use was 37 days in average

in the preterm NB, whereas being 25 days in the mature NB. The time spent to reach the control dose of methadone, meaning the sufficient dosage to avoid abstinence symptoms (Finnegan score < 8 in 3 consecutive evaluations) was in average 6 days and the time for drug suspension ranged from 10 to 159 days. From 11 NB, 8 presented signs of abstinence after the beginning of methadone with the need of dose adjustment. *Conclusion:* The study allowed a preliminary evaluation of the NAS protocol along with the use of methadone in the service where it was held. There was a relation between the use of methadone and continuous sedation, which duration was prolonged in the NB of male gender and premature ones. Although a more detailed approach should be accomplished, considering the amount of ventilated NB in the period (256 NB), the number of NB with possible abstinence was relatively small (6,6%), which may mean a judicious use of opioids in this population.

**Keywords:** Neonatal abstinence syndrome; Fentanyl; Methadone; Infant, newborn.

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**RESUMO:** *Introdução:* Para tratar a dor e a agitação psicomotora, sintomas comuns em unidades de cuidados intensivos neonatais, são utilizados sedativos/analgésicos opióides. Contudo, seu uso prolongado, principalmente na forma contínua, pode provocar a Síndrome de Abstinência Neonatal (SAN). *Objetivo:* Avaliar a abordagem da Síndrome de Abstinência Neonatal por opióides em recém nascidos (RN) internados na unidade neonatal da Maternidade Odete Valadares em Belo Horizonte. *Métodos:* Análise dos prontuários de RN que usaram metadona no período de junho de 2013 a junho de 2014, a partir do levantamento feito na Farmácia da unidade, portanto com diagnóstico ou risco de abstinência por opióide, confirmada clinicamente pela escala de Finnegan. *Resultados:* Foram avaliados todos os RN que, no período de estudo, receberam metadona. Do total de 17 RN, 6 foram eliminados pois receberam alta para outros serviços ou evoluíram para óbito, impossibilitando a análise completa dos dados. Dos 11 RN incluídos, 7 foram prematuros, com idade gestacional inferior a 28 semanas. Houve prevalência do sexo masculino (72,7%). Todos os RN receberam fentanil

continuamente, cujo período de uso foi, em média, 37 dias nos RN prematuros e 25 dias nos RN a termo. O tempo gasto para que se atingisse a dose controle da metadona, ou seja, dose suficiente para evitar os sintomas de abstinência (Escala de Finnegan <8 em 3 avaliações consecutivas), em média, foi de 6 dias e o tempo para suspensão da mesma variou de 10 a 159 dias. Dos 11 RN acompanhados, 8 apresentaram sinais de abstinência após o início da metadona com necessidade de ajuste da mesma. *Conclusão:* O estudo permitiu uma avaliação preliminar do protocolo de abordagem da SAN e do uso da metadona no serviço em questão. Houve relação do uso da metadona com a sedação contínua, cuja duração foi prolongada nestes RN, com o gênero masculino e com a prematuridade. Considerando o número total de RN ventilados no período (256 RN), o número de RN com possível S.A.N foi relativamente pequeno (6.6%), podendo significar um uso criterioso de opióides nesta população, embora uma abordagem mais detalhada deva ser realizada.

**Descritores:** Síndrome de abstinência neonatal; Fentanila; Metadona; Recém-nascido.

## INTRODUCTION

This study evaluated the protocol concerning the Neonatal Abstinence Syndrome (NAS) by opioids instituted in *Odete Valadares Maternity (OVM)*, located in the city of Belo Horizonte, Minas Gerais state, in Brazil. This hospital provides comprehensive care to women's health and their newborns (NB), performing approximately 400 deliveries per month. It is equipped with a Neonatal Intensive Care Unit (NICU) including 20 hospital beds, accepting an average of 30 NB monthly. In June 2012 the standard operational procedure to the NAS approach was elaborated, since then the OVM has been having a positive outcome with the protocol implantation in the service.

The pain and psychomotor agitation are common disorders presented by the neonates hospitalized in NICU, especially the ones who have been submitted to surgical intervention or mechanical ventilation. The pharmacological therapy used to treat these clinical conditions includes anesthetics, sedatives and central and peripheral analgesic medicines.

In the NICU of OVM, the preferable drug to relieve these symptoms is fentanyl, taking into consideration its cost-effectiveness relation. It is a medication with great analgesic power, sedative and respiratory depression properties. When compared to morphine, standard drug in its category, fentanyl is 80 to 100 times more potent<sup>17</sup>, has a rapid onset of action and presents less hemodynamic impacts. It can be administered in continuous intravenous infusion or bolus. However, its prolonged use, predominantly in the uninterrupted scheme can lead to the Abstinence syndrome<sup>18</sup>, which is one of the most relevant complications of the extended treatment with opioids.

The risk of developing the NAS is proportional to the exposure time to opioids in intravenous administration<sup>4</sup>, beginning from the third day of medication. The clinical

manifestations of NAS include hyperirritability of the central nervous system (CNS), respiratory, gastrointestinal and autonomic expressions<sup>14</sup>. The symptoms may vary and are common to other neonatal pathologies, what makes it difficult to be recognized, being often an exclusion diagnosis. There are scoring systems such as the Finnegan one<sup>15</sup>, (Chart 1) that assists in identifying and determining the NAS signs, being essential in the therapeutic approach to this clinical condition. The syndrome should be suspected when the NB, deprived of the drug amount that was being offered to them, start developing symptoms, which nature was described above, that cease with the adjustment of the drug in question.

The service strategies conducted to minimize the risk of NAS include the methadone prescription and the judicious use of continuous infusion of opioids, which should be restricted to special occasions, when the agitation and stress of the NB impose a greater risk to their recovery and jeopardize ventilatory assistance. The vast majority of ventilated and post surgery infants, were successfully treated with bolus opiates. The gradual weaning and the use of methadone are other measures described in the protocol to prevent the NAS.

Therefore, considering the pain approach as an increasingly adopted measure by the multidisciplinary teams engaged in neonatal care, the NAS should demand the same concern pertaining to its adequately prevention and treatment, and it must receive the same consideration given to the pain protocols in the NICU.

In order to treat the NAS there is a wide variety of pharmacological and nonpharmacological therapies, adopted accordingly to the protocols of each institution. In OVM, the drug of choice is methadone, supported by international literature as first line therapy for NAS<sup>1,5</sup>, which can be justified as it is a potent opiate with a prolonged

half-life (26 hours)<sup>13</sup>, being this feature important when considering the drug removal as it allows the gradual raising of intervals in between administration what eases the drug withdraw. The nonpharmacological treatment has shown to

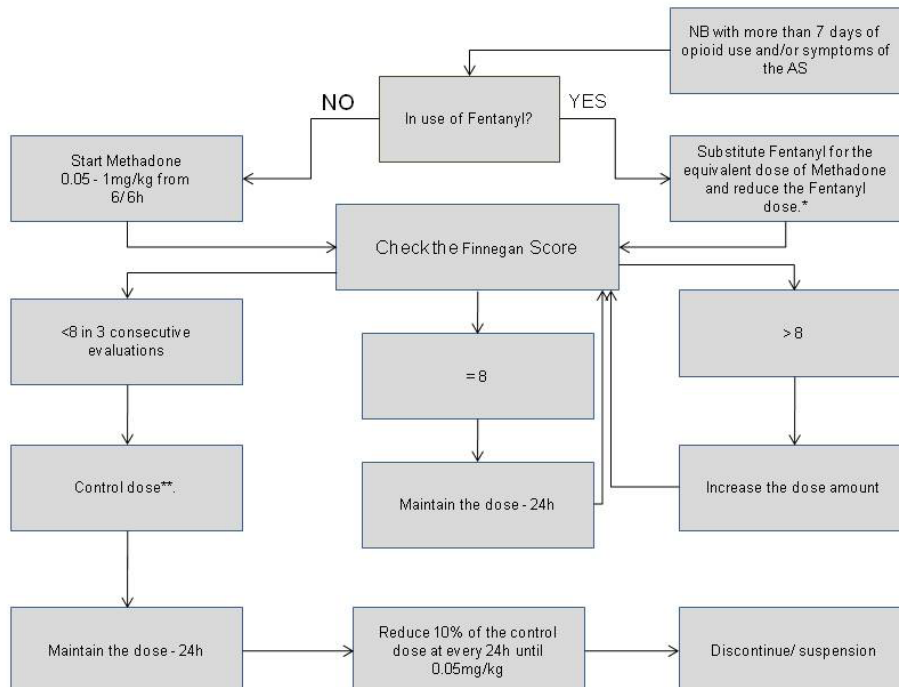
be supportive and an addition to the treatment.

The NAS protocol of OVM defines (Flowchart 1) the therapeutic conduct to be followed in NB with diagnosis

**Chart 1.** Finnegan Scoring System

Symptoms	Points	Symptoms	Points	Symptoms	Points
Excessive high pitched (or other) cry (< 5 min)	2	Moderate-severe tremors when undisturbed	4	Frequent sneezing (> 3-4/ interval)	1
Continuous high pitched (or other) cry (> 5 min)	3	Increased muscle tone	1	Nasal flaring	2
Sleep < 1 hour after feeding	3	Excoriation (eg. Chin, knees, elbows, toes, nose)	1	Respiratory rate > 60/min	1
Sleep < 2 hours after feeding	2	Myoclonic jerks (twitching/ jerking of limbs)	3	Respiratory rate > 60/min with retractions	2
Sleep < 3 hours after feeding	1	Generalized convulsions	5	Excessive sucking	1
Hyperactive Moro reflex	2	Sweating	1	Poor feeding (infrequent/ uncoordinated suck)	2
Moderately hyperactive Moro reflex	3	Hyperthermia (37.2 – 38.2°C)	1	Regurgitation (≥ 2 times during/past feed)	2
Mild tremors when disturbed	1	Hyperthermia (≥ 38.4°C)	2	Projectile vomiting	3
Moderate-severe tremors when disturbed	2	Molting	1	Loose stool	2
Mild tremors when undisturbed	3	Nasal stuffiness	1	Watery stool	3

**Flowchart 1.** Flowchart of management of the neonatal abstinence syndrome



Legend: \* Maximum dose of fentanyl in mcgr/hr multiplied by 60. The result is multiplied by 2. This last result refers to the Methadone dose in mg to be administered every 12 hours initially<sup>4</sup>

\*\*Dose capable of leaving the NB without abstinence signs and symptoms (Finnegan Score less than 8 in 3 consecutive evaluations).

or high clinical suspicion of NAS, as described below.

The NB who have used opioids continuously for a period < 3 days: the use should be interrupted abruptly. For the NB who have used opioid continuously from 3 to 7 days: the dose of the venous opioid should be reduced in 25 to 30 % per day and the suspension may occur according to tolerance in 72 hours, when it is essential to keep observing for possible signs of abstinence. For the NB who have used opioids for more than 7 days: convert the maximum dose of fentanyl infused to methadone and administer it every 12 hours. Perform the Finnegan scoring system every 12 hours until the control dose is reached (the one able of leaving the NB without abstinence manifestations - Finnegan score < 8 in 3 consecutive evaluations). Once the control dose has been achieved, prescribe it every 24 hours and start reducing 0.05 mg/kg/day, according to tolerance, until its removal. For the NB with suspicion of abstinence who are no longer under opioids: confirm the suspicion of NAS by the Finnegan scoring system, initiate methadone at the empirical dose of 0,05 to 0,1 mg/kg every 6 hours, what may be increased in 0,05 mg/kg until the symptoms control<sup>16</sup>. Once the control dose has been reached, the methadone interval should be raised until its administration is performed every 24 hours, when the reduction of 0.05 mg/kg/day can begin, according to tolerance, until its withdraw.

## OBJECTIVES

The present study has as an objective to evaluate the protocol regarding the approach of the NAS by opioids in NB who were hospitalized in the NIUC/OVM, by means of identification and study of the NB who have used methadone in the period of June 2013 to July 2014.

## MATERIALS AND METHODS

This study was based on a retrospective research conducted between the period of June 2013 to July 2014. The inclusion criteria were: NB admitted in the NICU/OVM who were prescribed methadone and have been discharged from this medical service until the end of June 2014. The research excluded all NB who have been dismissed to another service or that evolved towards death, in that one year and one month time course. To execute the study, it was analyzed the medical records from the NB who achieved the inclusion principle, by the raising made in the OVM pharmacy. The control of methadone use was accurately recorded beginning in June 2013. It was collected the following data: NB identification, medical record number, birth date, gestational age, weight from the NB birth, gender, total time of opioid use, maximum dosage administered, time necessary in order to reach

the methadone control dose, signs observed before and after the beginning of methadone, interval spent until the methadone suspension, opioid indication, total duration of mechanical ventilation (MV), if the NB was still under MV when beginning the methadone, besides the main diagnostics of these NB.

## RESULTS/DISCUSSION

The risk of developing the NAS by opioids is proportional to the exposure time to these drugs in venous administration<sup>1</sup>. The Finnegan Scoring System<sup>15</sup> (Chart 2) is the tool used in the institution, and supported by literature, to guide with the diagnostic and in monitoring infants with the suspicion of this affection. It should be performed every 8 hours<sup>15</sup>. This method keeps score considering four different systems already described above, which are included in the clinical manifestations of the NAS. Abstinence is considered when the score is higher than 8 in 3 consecutive evaluations, if there is not another better clinical explanation to justify the symptoms, and if these ones disappear immediately after restarting or raising drug amount<sup>15</sup>.

The NAS protocol of OVM aims to define the therapeutic conduct to be followed in NB with diagnosis or high clinical suspicion of the syndrome, being fentanyl (FNT), the most used opioid in OVM and the most indicated one due to its pharmacological properties<sup>1</sup>.

The diagnostic suspicion is raised by the presence of abstinence signs in NB who have used opioids for more than 7 days.

The strategies used in NICU/OVM to minimize the risk of NAS include the judicious use of continuous infusion of opioids, which are restricted to certain instances, when the NB agitation and stress impose risk to their recovery and jeopardize the ventilatory assistance. The majority of the NB who are ventilated or post-surgery are treated successfully with bolus opioids. The gradual weaning of opioids and the use of methadone are essential measures to the NB who used the continuous scheme.

In this work all of the NB who were using methadone in the study period were evaluated:

From the total of 17 NB, 6 were disqualified since they have either been dismissed from the service or have evolved towards death, making it impossible to analyze the data entirely. From 11 NB included, 7 were premature with gestational age under 28 weeks and there was a prevalence of male gender (72.7%). The birth weight varied between 470 grams to 3920 grams. According to Jansson et al.<sup>7</sup> the male gender and prematurity are characteristics that make the NB vulnerable to the NAS by opioids. Every NB received fentanyl continuously and the period of use was in average 37 days in the premature NB, and 25 days in the mature ones. The fentanyl dosage ranged between 2 to 7

mcgr/kg/hour. Six NB were been submitted to mechanical ventilation when they initiated the methadone. The time spent to reach the control dose was in general 6 days and the time for drug suspension varied between 10 to 159 days. From the 11NB, 8 presented signs of abstinence once the methadone was introduced, with the need of dose adjustment. From the total of 256 NB who have been ventilated in the period of the study in OVM, only 6.6% of them showed a probability of abstinence.

The main signs of abstinence noticed in the study were: agitation, tremors, excessive high pitched crying, drop in oxygen saturation, tachypnea, hypertonicity of the members and photo reactive pupils. These symptoms concur with the ones described in the reference literature<sup>15</sup>. It was not possible to establish a connection between the previous pathologies and the methadone need, however, there was a relation including prolonged MV, which comprehended 100% of the cases studied.

## CONCLUSION

This study allowed a preliminary evaluation of the protocol regarding the NAS approach and the use of

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