

## Nicotine Withdrawal Symptoms in Newborns

Óscar García-Algar

Servicio de Pediatría, Hospital del Mar, Barcelona, Spain

Maternal smoking during pregnancy exposes the fetus to the potentially harmful effects of the components of tobacco smoke, and these can affect perinatal outcome and the health of the newborn.<sup>1,2</sup> Epidemiological data show a wide geographic variation in smoking during pregnancy. In some countries, such as the United States and Italy, the prevalence of smoking during pregnancy has fallen substantially over the last few years, although in many other countries it remains high (34% in Spain), and data on smoking during pregnancy are scarce.<sup>1,3-8</sup>

Some authors believe that prenatal exposure to the components of tobacco smoke leads to behavioral and neurological abnormalities after birth, and nicotine is thought to be a neuroteratogen.<sup>9</sup> For many years, reports on the possibility of nicotine withdrawal symptoms in newborns were scant and contradictory—while some authors admitted the possibility,<sup>2</sup> others rejected it.<sup>10</sup>

In an interesting study designed to evaluate short-term neurobehavioral effects among newborns exposed to tobacco consumption, Law et al<sup>11</sup> compared 29 nonexposed newborns with 27 exposed newborns. The mothers reported smoking an average of 6.7 cigarettes/d and this was confirmed by determining cotinine levels in the mothers' saliva. The newborns' neurobehavioral function was studied using the Newborn Neonatal Intensive Care Unit Network Neurobehavioral Scale<sup>12</sup> during the first 48 hours after delivery. The exposed newborns were significantly more excitable, reactive, and hypertonic than the nonexposed newborns. It was postulated that the effects of smoking on newborns could be indicative of long-term behavioral deficiencies, such as a lower intelligence quotient and attention deficit/hyperactivity disorder. Finally, the finding of signs of stress and withdrawal symptoms in exposed newborns, in addition to a dose-dependent relationship between exposure and neurobehavioral effects, led the authors to consider the possibility of neonatal withdrawal symptoms.

In fact, in much the same way as a fetus exposed to opiates in utero, newborns with prenatal exposure to nicotine have become passive addicts in utero and can

present withdrawal symptoms on birth. In 1975, Finnegan et al<sup>13</sup> developed a clinical scoring system to evaluate withdrawal symptoms in newborns. The score has 31 items that are monitored every 2 or 3 hours during the first days of life—2 consecutive scores above 8 indicate withdrawal symptoms. The Finnegan scoring system was specifically designed for opiates, although it has also been applied to newborns exposed to cocaine.<sup>14</sup>

Godding et al<sup>15</sup> compared nicotine withdrawal symptoms in 17 newborns whose mothers were heavy smokers with those observed in 16 newborns whose mothers were nonsmokers and had not been exposed to smoke. Exposure in utero was evaluated by determination of cotinine levels in neonatal urine and blood from the umbilical cord. The Finnegan score was different and even changed significantly according to the number of cigarettes smoked by the mother. The score also correlated with biochemical markers of exposure. Nevertheless, no scores indicating withdrawal symptoms (>8) were obtained for exposed newborns. In spite of this, the statistical difference between exposed newborns and controls in terms of biomarkers led the authors to conclude that the newborns of mothers who had smoked heavily during pregnancy experienced withdrawal symptoms.

Studies carried out by our group<sup>16-20</sup> using the Finnegan scoring system have revealed the existence of nicotine withdrawal symptoms in newborns exposed to tobacco consumption in utero. The Finnegan scores were recorded for 33 newborns whose mothers were smokers to evaluate the existence of withdrawal symptoms. Urine cotinine levels were also determined in the newborns as a biomarker of acute exposure to tobacco smoke.<sup>16</sup> The nicotine concentration in the newborns' hair was then determined to evaluate chronic exposure to the components of tobacco smoke during the third trimester of pregnancy.<sup>21</sup> No definitive positive results were obtained using the scoring system (2 consecutive scores >8); however, the newborns of mothers who smoked more than 20 cigarettes per day while pregnant scored between 0 and 8, especially with regard to irritability and tremor during the first 24 hours of life. In addition, increasing nicotine concentration in hair and urine was associated with higher scores.<sup>16,21</sup>

In a recent study, Mansi et al<sup>19</sup> studied 25 newborns whose mothers smoked at least 5 cigarettes per day and 25 newborns who had not been exposed to tobacco consumption. Neonatal behavior was evaluated using Brazelton's Neonatal Behavioral Assessment Scale<sup>22</sup> and prenatal exposure was studied by determining neonatal

Correspondence: Dr O. García-Algar  
Servicio de Pediatría, Hospital del Mar  
Pg. Marítim, 25-29  
08003 Barcelona, Spain  
E-mail: 90458@imas.imim.es

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urine cotinine levels. The newborns of smokers scored significantly lower than nonexposed newborns in several of the items. A significant correlation was observed between irritability and urine cotinine levels in the newborns of mothers who smoked and the newborns of mothers who did not. A significant correlation was also observed between the smokers according to the number of cigarettes smoked per day. The main conclusion of the study was that neonatal behavior can be considerably affected by the level of exposure, even after moderate smoking by the mother during pregnancy.

In a 12-week double-blind placebo-controlled clinical trial with nicotine patches, Selby et al<sup>23</sup> described nicotine withdrawal symptoms in the fetus of a heavy smoker who reported increased fetal movements accompanied by abdominal pain when she quit and began to use a placebo patch.

Furthermore, Vagnarelli et al<sup>20</sup> recently reported the case of a newborn whose mother smoked heavily during pregnancy and breastfeeding. During the immediate neonatal period the newborn presented tremor, hypertonia, and irritability, although these symptoms did not fulfill the Finnegan criteria for withdrawal symptoms. The suspicion of nicotine withdrawal symptoms was confirmed by the detection of extremely high nicotine and cotinine levels in the newborn's hair and in several segments of the mother's hair. The presence of detectable levels of nicotine and cotinine in breast milk confirmed that the mother had not quit smoking after delivery. The infant, who was breast fed, presented several episodes of tremor and muscle stiffness, similar to those of colic, when breastfeeding was stopped. This raised the possibility of postnatal nicotine withdrawal symptoms.

The above data allow us to draw the following conclusions:

1. Nicotine seems to alter the normal neurologic development of newborns and infants at least during the early stages of life.

2. Exposure in utero to the components of maternal tobacco smoke leads to nicotine withdrawal symptoms in newborns. Clinically, this is characterized by an early onset (within the first 12 or 24 hours of life), given that labor and delivery interrupt the continuous exposure to nicotine, with mild short-lasting symptoms. In general, symptoms do not require treatment and remit quickly during the following 36 hours.

3. In the case of breastfeeding, withdrawal symptoms can appear shortly after feeding is stopped and can be confused with colic.

4. At present, nicotine withdrawal symptoms in newborns cannot be characterized accurately because a specific test is not yet available. The Finnegan scoring system is the most widely used tool, although it was designed to measure opiate withdrawal symptoms in newborns. Therefore, a new scoring system based on irritability, tremor, and sleep disorders should be developed, as these are the symptoms that are most commonly observed in the newborns of women who smoke heavily during pregnancy. Such a system would be useful in future investigations on the effects of passive exposure to nicotine in utero.

5. A more objective clinical estimation of nicotine withdrawal symptoms in newborns could help to identify those women who have smoked during pregnancy and who would therefore be candidates for cessation programs during the breastfeeding period.

6. Smoking cessation programs during pregnancy and breastfeeding should include nicotine replacement therapy, which provides exposure to small and constant amounts of nicotine but not the other toxic components of cigarette smoke.<sup>18,20,24,25</sup>

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