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RESEARCH ARTICLE

Analysis of the changes in the management of preterm newborns born in a Spanish third-level hospital in the past 10 years

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Abstract

Background: *Preterm newborns require the use of the best and most current strategies to treat and prevent both acute pathology and associated sequelae. This study aimed to compare the differences in the management of preterm newborns over 10 years in a tertiary hospital in Spain and its impact on height, weight, and neurological development in the medium term.* **Methods:** *We conducted a retrospective, observational, and analytical study examining the management and clinical variables in preterm newborns under 32 weeks of gestational age who were born in our hospital in 2011 and 2021.* **Results:** *Twenty-six newborns were included in the study. Significant differences in magnesium sulfate use, continuous positive airway pressure immediately after birth, and non-invasive mechanical ventilation during hospitalization were observed. Differences were found in the use of parenteral nutrition and the timing of initiation of enteral feeding. We did not observe differences in the neurological or weight evolution in the medium term.* **Conclusions:** *Significant differences in managing preterm newborns in these 10 years were observed. Lower mortality and alterations in central nervous system ultrasound and, significantly, less growth retardation during admission in 2021 have been observed; however, it does not manifest with improvement in long-term somatometrics or neurological prognosis.*

Keywords: *Preterm newborn. Neonatology. Surfactant. Parenteral nutrition. Postnatal malnutrition.*

Análisis de los cambios en el manejo de recién nacidos prematuros nacidos en un hospital español de tercer nivel en los últimos 10 años

Resumen

Introducción: *La inmadurez de los recién nacidos pretérmino (RNP) requiere el empleo de las mejores y más actuales estrategias para tratar la patología aguda y prevenir sus eventuales secuelas asociadas. El objetivo planteado es comparar las diferencias en el manejo de RNP a lo largo de diez años en un hospital de tercer nivel en España y su impacto en el desarrollo neurológico y póndero-estatural a medio plazo.* **Métodos:** *Estudio retrospectivo, observacional y analítico examinando variables del manejo y clínicas de todos los RNP menores de 32 semanas de edad gestacional nacidos en nuestro hospital (nivel III-A) en 2011 y en 2021.* **Resultados:** *Se incluyeron 26 infantes (2011: 10 niños, 2021: 16 niños). Observamos diferencias significativas en el uso prenatal de sulfato de magnesio, mayor uso de presión positiva continua en la vía aérea (CPAP) al ingreso y ventilación mecánica no invasiva durante el ingreso, retraso en el uso de surfactante, empleo de alimentación intravenosa e inicio precoz de la alimentación enteral. Existe una menor tasa de mortalidad y desnutrición postnatal en 2021. No observamos diferencias en la evolución neurológica o ponderal a medio plazo.*

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Conclusiones: *Existen diferencias en el manejo de los prematuros en estos 10 años con mayor ajuste a las guías nacionales e internacionales vigentes. Esto se relaciona con menor mortalidad y alteraciones en la ecografía del sistema nervioso central y, significativamente, con un menor retraso en el crecimiento durante el ingreso en 2021; no se demostró mejoría del pronóstico somatométrico o neurológico a largo plazo.*

Palabras clave: *Recién nacido pretérmino. Neonatología. Surfactante. Nutrición parenteral. Desnutrición postnatal.*

Introduction

According to the World Health Organization, a preterm newborn (PNB) is born before 37 weeks of gestation[1,2]. Three categories are described that classify PNB based on their gestational age:

- Extreme preterm or extremely low birth weight preterm (< 1000 g): born before 28 weeks.
- Very preterm or very low birth weight preterm (< 1500 g): born between 28 and 32 weeks.
- Moderate and late preterm: born between 32 and 37 weeks.

Worldwide, an estimated 15 million neonates are born prematurely each year. Of those who survive, a significant number face lifelong cognitive, motor, or sensory disabilities[2].

PNBs have pathologies inherent to their immaturity and require careful and specific management in the neonatal intensive care unit (NICU), as described in books and systematic reviews[2-8]. Medical advances continue to be made, some modified previous concepts, and others confirmed classical theories and approaches. Table 1 shows the established recommendations in 2011 and 2021, indicating the practices followed in those years[9-29].

The changes in management, improvements in the training of neonatal staff, and state-of-the-art medical equipment have led to a significant increase in the survival of preterm infants and a decrease in the prevalence of severe neurological disability[30,31]. However, other types of less severe neurological problems have increased, such as neuropsychological (autism spectrum disorder, attention deficit hyperactivity disorder, and conduct disorder), motor, and learning disorders. Nutritional support assessment is also relevant, as postnatal malnutrition correlates with future neurological, weight/height alterations. Mid- to long-term follow-up of preterm infants should be coordinated by a multidisciplinary team of pediatricians, rehabilitation specialists, physiotherapists, occupational therapists, and psychologists[31,32].

Therefore, the present study aimed to compare the differences in the management of PNBs born in a tertiary level hospital in 2011 and 2021 and to check whether the changes made have an impact on the neurological development and the weight/height of the children in the medium term.

Methods

We conducted a retrospective, observational, and analytical study to examine clinical and NICU management variables of all infants born before 32 weeks of gestation in a Level III-A hospital in 2011 and 2021. Data were obtained from medical record reviews and recorded in an anonymized database designed for the study. Families were contacted at hospital visits and provided verbal consent for review of their children's records. Those who were not followed up at the hospital were contacted by telephone.

Variables were described as mean and standard deviation, median and interquartile range or percentage according to their characteristics. Statistical tests were used according to the type of variable and according to whether the variables fit the normal (Student's t-test) or non-normal (Mann-Whitney's U) distribution. The χ^2 test was used for percentage analysis. The statistical analysis program SPSS v.22 was used. Significance was considered at $p < 0.05$.

The diagnosis of patent ductus arteriosus (PDA) and retinopathy of prematurity (ROP) required the involvement of pediatric cardiologists and ophthalmologists, respectively, using 2011[33,34] and 2021[35,36] guidelines. The diagnosis of bronchopulmonary dysplasia was based on dependence on oxygen or mechanical ventilation at 36 weeks of age corrected, according to the 2011[37] and 2021[38] definitions.

The percentiles of the somatometric data were obtained from http://www.webpediatrica.com[39] and adjusted for gestational age and sex. Data on post-discharge development were obtained from examinations at the hospital outpatient clinic and the health center. The diagnosis of behavioral disorders was based on DSM-5 criteria[40].

Results

All patients born in our hospital with gestational age < 32 weeks were included in the study: 10 born in 2011

Table 1. Comparison of PNB management and diagnoses in 2011 and 2021

Variable	2011 (n = 10)	2021 (n = 16)	p-value
Respiratory			
CPAP assistance at admission n (%)	5 (50%)	10 (62.5%)	0.420*
Surfactant administration n (%)	8 (80%)	8 (50%)	0.218*
LISA s n (%)	0%	2 (12.5%)	0.467†
Surfactant timing (hours of life) Mean ± SD	0.66 ± 0.73 h	1.8 ± 1.1 h	0.032‡
Duration of non-invasive ventilation (days) Mean ± SD	5.9 ± 6.11 days	7.46 ± 9.82 days	0.728‡
Median (p25-p75)	4 (0.5-8.75)	4 (0.62-9)	0.787§
Duration of any type of mechanical ventilation (days) Mean ± SD	5.9 ± 6.1 days	16.4 ± 25.2 days	0.452‡
Median (p25-p75)	6 (4-11)	4.1 (3-28)	0.783§
Hemodynamic			
PDA n (%)	1 (10%)	3 (20%)	0.626†
Medical or surgical treatment of PDA n (%)	0	1 (7.1%)	1†
Nutrition			
Intravenous feeding n (%)	1 (10%)	15 (93.7%)	0.001†
Start of IV feeding	24 h	9.86 ± 7 h	0.073‡
Start of enteral feeding (hours of life)	1.1 ± 0.56	2 ± 0.94	p = 0.02‡
Breastfeeding/mixed at discharge n (%)	6 (75%)	10 (64.3%)	0.394†
Neurological			
Altered cerebral ultrasound at admission n (%)	4 (40%)	3 (18.7%)	0.369†
Kangaroo care n (%)	0	15 (100%)	0†
Infectious			
Antibiotics at admission n (%)	9 (90%)	3 (18.7%)	0.001†
Nosocomial sepsis n (%)	6 (60%)	4 (28%)	0.211†
Hematological			
EPO n (%)	8 (80%)	5 (33%)	0.041†
Transfusions n (%)	5 (50%)	6 (40%)	0.622†
Ophthalmological			
ROP n (%)	0	1 (7.1%)	1†
Others			
Umbilical vein cannulation at admission n (%)	5 (50%)	14 (87.5%)	0.048†
Mortality n (%)	2 (20%)	2 (12.5%)	0.625†

*χ^2.
†Fisher's exact test.
‡Student's t-test.
§Mann-Whitney's U-test.
p25-p75: 25th and 75th percentile.
CPAP: continuous positive airway pressure; EPO: erythropoietin; IV: intravenous; LISA: less invasive surfactant administration; N: number; PDA: patent ductus arteriosus; PNB: premature newborn; ROP: retinopathy of prematurity; SD: standard deviation.

and 16 born in 2021. The mean gestational age was 29.05 ± 2.4 weeks, varying between 24 and 32 weeks. The surviving lowest gestational-age infants were born in 2021 (their gestational ages were 24 and 25 weeks).

Table 2 shows the epidemiologic data and prenatal management of PNBs in our hospital in 2011 and 2021. We found significant differences between both groups only in the administration of magnesium sulfate.

Regarding respiratory management, we observed fewer infants treated with surfactant and a delay in its administration in 2021 (Fig. 1). Notably, two patients received surfactant in the delivery room in 2011 but none in 2021. Five of the seven infants with conventional mechanical ventilation in 2021 (84% of infants) were ventilated with volume control strategies, but none in 2011 ($p < 0.05$).

Since the breast milk bank of our Autonomous Community was inaugurated in 2017, no child born in 2011 received donated breast milk; instead, all children born in 2021, except for one patient at the expressed wish of the family, received donated breast milk during the first days of life. The analysis of weight development during admission showed no significant differences in the percentage of weight lost (14 ± 5.5% vs. 13 ± 8.2%, p = 0.72). However, we observed a higher mean percentile of weight (20.7 ± 27 vs. 6.3 ± 7.2, p = 0.081)

Table 2. Epidemiological data and prenatal management among premature newborns (PNBs) in 2011 and 2021

Variable	2011 (n = 10)	2021 (n = 16)	p-value
Gestational age Mean ± SD (min-max)	25 ± 2.4 weeks (25-32)	29.3 ± 2.5 weeks (24-32)	0.505‡
Birth weight Mean ± SD (min-max)	1206.5 ± 257.8 g (680-1490)	1246 ± 477 g (610-2320)	0.783‡
Height at birth Mean ± SD (min-max)	38.5 ± 4.4 cm (29-45)	37.8 ± 4.7 cm (29.5-44)	0.932‡
Cranial perimeter at birth Mean ± SD (min-max)	28 ± 4.7 cm (23-40)	28 ± 4.6 cm (22-41)	0.988‡
Gender (males)	90%	37.5%	0.014*
Lung maturity	80%	87.5%	0.625*
Magnesium sulfate	0%	75%	< 0.005†
Cesarean section	50%	56.2%	1
Intensive resuscitation at birth (orotracheal intubation, compressions and/or adrenaline)	50%	37%	0.689*
Apgar score at 1 min Mean ± SD	5.5 ± 2.4	5.5 ± 2.3	0.918‡
Apgar score at 5 min Mean ± SD	8.1 ± 1.45	7.5 ± 1.9	0.385‡

*χ^2.
†Fisher's exact test.
‡Student's t-test.
PNB: premature newborn; SD: standard deviation.

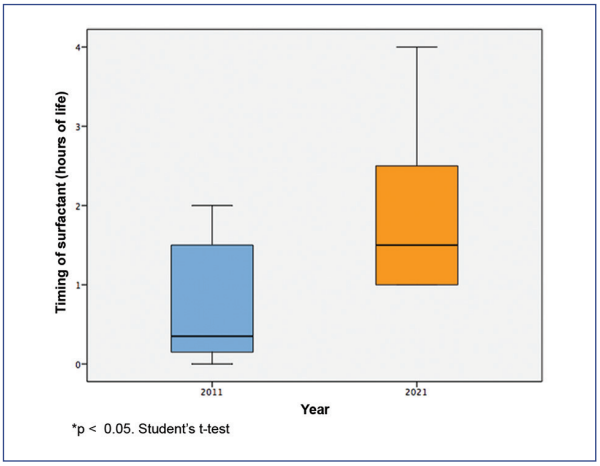

Figure 1. Comparison of the timing of surfactant administration (hours of life).

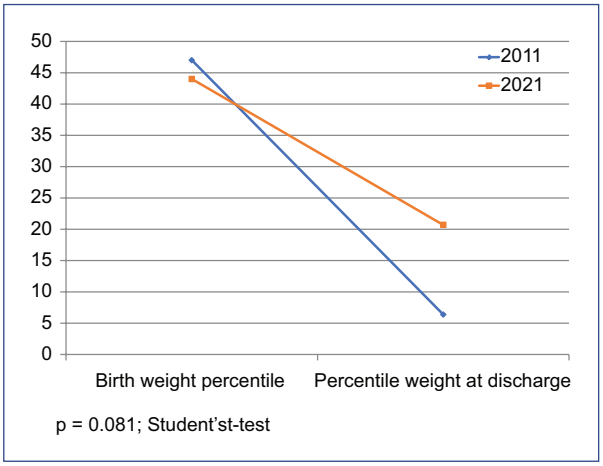

Figure 2. Comparison between birth and discharge weight percentiles in 2011 and 2021.

(Fig. 2) and height (13 ± 20 vs. 5 ± 4.5, p = 0.206) at discharge in 2021 compared to 2011.

Table 1 shows the percentage of children who required specific treatments and had specific diagnoses each year. Two patients died in each group, representing 20% of children in 2011 and 12.5% in 2021 (p = 0.625).

Regarding the evolution after discharge, we did not observe significant differences in weight development or a significant relationship between somatometric data at discharge from neonatology and subsequent evolution. Only six patients (27.3%) had alterations in psychomotor development (Table 3). No significant relationship was found between weight development

Table 3. Relationship between results of neonatal cerebral ultrasound performed during admission and neurological disorders developed by the children subsequently and age at diagnosis

Year	Neonatal cerebral ultrasound	Diagnosis	Age at diagnosis
2011	Germinal matrix hemorrhage.	Autism spectrum disorder Grade 2	18 m
2011	Right periventricular cystic leukomalacia	Spastic triplegic cerebral palsy	12-15 m
2011	Intraventricular hydrocephalus secondary to Grade III intraventricular hemorrhage and Grade II cystic leukomalacia.	Mild left hemiparesis	15 m
2021	Grade II periventricular leukomalacia+ex vacuo hydrocephalus	Spastic diplegic cerebral palsy	19 m
2021	Germinal matrix hemorrhage.	Mild global developmental delay	18 m
2021	Grade II intraventricular hemorrhage	Mild global developmental delay	18 m

Diagnoses according to DSM-5 criteria[39]. m: months.

at discharge and alterations in psychomotor development. However, it was observed that all children with altered psychomotor development had alterations in the central nervous system (CNS) ultrasound performed at admission.

Discussion

The medical records of 26 neonates born at a gestational age of < 32 weeks and admitted to the NICU of our hospital (level III-A) between 2011 and 2021 were analyzed. Although the sample size is small, the analysis of the records showed the changes that have occurred in the care of preterm infants over a decade.

Although we did not find significant differences between the two groups in gestational age and somatometric data, we observed that infants of lower gestational age (24 and 25 weeks) who survived were born in 2021. These patients had a high number of complications, longer mechanical ventilation duration, and longer hospital stays. It is noteworthy the high rate of males born in 2011, when, according to data from the Spanish National Statistics Institute (*Instituto Nacional de Estadística español*), the percentage of males born that year in our Autonomous Community was similar to that of females (51.9% males vs. 48.1% females)[41]. The analysis of prenatal management showed only differences in the administration of magnesium sulfate, which was expected since it was not until the mid-2010s that its use became widespread in Spain following the publication of its role as a neuroprotectant[42].

There are three fundamental points in which we have observed changes in the management of these patients in our NICU that have allowed greater harmonization with international guidelines. First, we observed differences in several aspects of respiratory management, particularly in the reduced use of surfactant, a significant delay in administering the first dose, and the generalization of less invasive administration techniques such as surfactant administration[16]. Similarly, we observed a trend toward greater use of noninvasive ventilation, especially continuous positive airway pressure, at admission and during hospitalization, and modalities with tidal volume control in the case of invasive mechanical ventilation, both strategies in line with the latest published evidence[16,43]. It is noteworthy that the duration of mechanical ventilation was longer in neonates born in 2021. This is secondary to the fact that this year, there were two patients of extreme gestational age (24 and 25 weeks) who required respiratory support for 85 and 61 days, respectively.

Second, we noted the early and widespread initiation of optimized parenteral nutrition in 2021, as indicated by national and international recommendations[20,22,23], in addition to the significantly earlier initiation of enteral nutrition based on breastfeeding from the milk bank. Both factors have allowed these neonates' weight and height percentiles at discharge to be higher than in 2011. However, we could not demonstrate a relationship between weight development and neurological development as has been published[44].

Third, thanks to the internationally recommended rational use of antibiotics[26,27], rates of empiric antibiotic therapy decreased significantly in 2021 without an increase in early mortality due to sepsis of vertical transmission or an increase in the rate of nosocomial sepsis. In this context, the reduced use of erythropoietin, as

recommended[27,29], was also confirmed, being used only in selected patients without an increase in transfusion rates.

In contrast, we did not observe significant differences in the rates of PDA, ROP, and brain lesions, problems that are very common in the first weeks of life of extremely preterm infants[6-8]. As for PDA and ROP, there were more cases of both in 2021 because the youngest gestational-age infants in the study were born in that year, although their incidence was lower than that published in the literature[32]. The rate of brain lesions observed at each stage was also lower than other reports[30,31,45-47], but has a subsequent neurological impact. Based on our results and large international series[30-47], we can correlate the alteration of the neonatal cerebral ultrasound with alterations in psychomotor development during early childhood. In this sense, although the differences are not significant, the most severe pictures correspond to children born in 2011 and are characterized by severe motor problems secondary to intraventricular hemorrhage.

Finally, although not statistically significant, the mortality rate is much lower in 2021, which is consistent with review articles relating improved care to increased survival of patients, especially those with extreme gestational age[45-47].

As limitations, we consider that despite including all preterm infants born in our hospital in 2011 and 2021, the total sample size was small. This fact has limited the achievement of statistical significance in some comparisons but gives more value to those comparisons that have achieved it. Although there is a decade between both years studied, the changes may need more time to be evaluated. Therefore, in subsequent studies, we will consider analyzing years that are further apart in time.

There are differences in the management of preterm infants over 10 years, with greater adherence to current national and international guidelines.

Lower mortality and fewer CNS ultrasound changes, and significantly less growth retardation were observed in neonates born in 2021; however, no improvement in long-term somatometrics or neurological prognosis were demonstrated so far.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author has this document.

Conflicts of interest

The authors declare no conflicts of interest.

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