POPULATION STUDY ARTICLE

Perceived maternal information on premature infant's pain during hospitalization: the French EPIPAGE-2 national cohort study

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BACKGROUND: Parents of preterm neonates wish greater involvement in pain management; little is known about factors associated with this involvement. We aim to describe perceived maternal information on infants' pain during hospitalization (PMIP), to study associations between PMIP and mothers' attitudes during painful procedures, and to identify individual and contextual factors associated with PMIP.

METHODS: Analyses of questionnaires from the French national cohort study of preterm neonates, EPIPAGE-2. PMIP was derived from mothers' answers to questions about information perceived on both pain assessment and management.

RESULTS: Among 3056 eligible neonates born before 32 weeks, 1974, with available maternal reports, were included in the study. PMIP was classified as "sufficient," "little, not sufficient," or "insufficient, or none" for 22.7, 45.9, and 31.3% of neonates, respectively. Mothers reporting PMIP as "sufficient" were more frequently present and more likely comforting their child during painful procedures. Factors independently associated with "sufficient" PMIP were high maternal education, gestational age <29 weeks, daily maternal visits, perception of high team support, and implementation of the neonatal and individualized developmental care and assessment program.

CONCLUSION: Perceived maternal information on premature infants' pain reported as sufficient increased maternal involvement during painful procedures and was associated with some units' policies.

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INTRODUCTION

Parents of preterm neonates have described pain as the most stressful event during the stay in neonatal units¹ and have reported concerns about their infants' discomfort, their inability to respond to it, and the negative effect the experience might have on their parenting abilities.² Later on, parental presence in neonatal intensive care units (NICUs) was found to be associated with increased use of analgesia^{3–5} and lower pain scores during venipunctures.⁵ Parental involvement in pain management was also described as enhancing parental confidence in their parenting role after discharge.⁶ Nevertheless, despite the desire of parents to be involved in their babies' pain management² and the well-described benefits of their participation, parents were present during only 6.4% of 1884 venipunctures analyzed in EIPPAIN-2, a 2011 French cohort study.⁵ To our knowledge, factors affecting parental empowerment in pain management have been mainly studied through qualitative studies based on focus group interviews. These studies highlighted the positive role

of talking about neonatal pain with parents.^{7,8} One randomized controlled trial has shown that parents receiving an intervention targeted at increasing their understanding of pain management were better prepared to take an active role in infant pain care.⁶ An epidemiological approach might provide additional knowledge by quantifying the association between the level of perceived parental information on their infants' pain and their attitudes during painful procedures, and by identifying factors associated with the level of perceived information.

The French national EPIPAGE-2 cohort study was conducted to measure survival and morbidity after very preterm birth and to explore variations in the organization of care and medical practices.⁹ Pain assessment and treatment, and information mothers perceived about infants' pain (PMIP, perceived maternal information on infants' pain) were collected. In the present study, we aimed to describe (1) PMIP, including perceived information on infants' signs of pain and comforting techniques; (2) mothers' presence, involvement, and feelings during painful procedures

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and their association with PMIP; and (3) to identify individual and contextual factors associated with PMIP. We hypothesized that maternal participation to comfort and support the infant during painful procedures would be positively associated with the level of PMIP and that unit factors would play a major role in the perception of this information.

METHODS

EPIPAGE-2 study design

The EPIPAGE-2 study is a national population-based cohort study launched in France in 2011 and scheduled to follow children up to the age of 12 years.⁹ Eligible participants were all infants live born or stillborn and all terminations of pregnancy between 22 and 34 completed weeks gestation (WG) in all French maternity units.

Participants

Children included in the present study were part of the EPIPAGE-2 cohort. Inclusion criteria were birth between 22 and 31 WG, survival at discharge (the questionnaire for mothers to record information about pain was not proposed for infants who died), hospitalization between days 0 and 7 in only one level-III or level-IIb neonatal unit,¹⁰ and birth after a single or twin pregnancy. Mothers of twins completed the questionnaire for both infants. Neonates born after a triplet or a quadruplet pregnancy were excluded to avoid overrepresentation of some mothers in the study group. Infants born at 22 to 26 WG were recruited during an 8-month period, and those born at 27 to 31 WG during a 6-month period.

Data collection

Maternal and infant-related information. Data were collected by questionnaires completed at birth and in the neonatal period by perinatal teams. The birth questionnaire included the following variables used in this study: (1) maternal age; (2) birth in France (yes/no); (3) living in couple relationship (yes/no); (4) level of education (<secondary school, high school, university); (5) primipara (yes/no); and (6) multiple pregnancy (yes/no). Variables extracted from the neonatal questionnaire and used in this study were: (1) gestational age (GA) at birth; (2) small-for-gestational age (SGA) (birth weight less than the 10th percentile for GA and sex based on French intrauterine EPOPé growth curves);¹¹ (3) severe neonatal morbidity defined as any of severe bronchopulmonary dysplasia, necrotizing enterocolitis stage 2 to 3, severe retinopathy of prematurity stage >3, or any of the following severe cerebral abnormalities—intraventricular hemorrhage grade III or IV or cystic periventricular leukomalacia;¹² (4) exposure to opioids, sedatives-hypnotics, or general anesthetics (O-SH-GA)¹³ (yes/no); (5) assessment of acute and continuous pain or discomfort (at least one assessment during the first week of life, yes/no); and (6) use of a pain scale during hospital stay (yes/ no, and type of scale).

Unit-related information. Unit questionnaires, completed by managers, collected general information on the NICU's activity and included the following variables used in this study: (1) number of neonates born before 32 WG admitted in 2011 (<50, ≥50); (2) availability of neonatal surgery in the hospital (yes/no); (3) neurodevelopmental care training (none, introductory course, sensory-motor program, or Neonatal Individualized Developmental Care and Assessment Program [NIDCAP]);¹⁴ Units were considered to have specific neurodevelopmental care training if formal training, with an identified trainer, was in progress or completed.

Declarative survey on perceived maternal information on their infants' pain. At their infant's discharge, mothers of surviving infants were invited to complete a questionnaire to report information about events arising during hospitalization,

distinguishing between the first and last unit of hospitalization in case of infant transfer. Data were collected on mothers' point of view on the amount of information they received about pain assessment and management, their presence and feelings during painful procedures, and their ability to comfort the baby during such procedures (Supplemental file S1, online). This questionnaire also included information on the presence of parents during hospitalization (self-reported daily maternal and paternal visits, yes/no), self-perceived team support (no/ yes, rather/ yes, fully), and maternal trait of anxiety (low/moderate/high), assessed with the Spielberger State-Trait Anxiety Inventory. Scores were calculated according to recommendations¹⁵ and classified into three classes: low (score ≤45), moderate (46–55), and high (>56).

Outcome assessment

The main outcome measure was level of PMIP derived from two questions on pain information given during hospitalization, as perceived by mothers (Supplemental file S1): (1) Were you shown how to recognize your baby's signs of pain and discomfort? (2) Were you shown how to calm and soothe your baby when he/she presented signs of pain and discomfort? Possible answers for both questions were: no, not at all/yes, a little/ yes, and sufficiently. A summary measure of PMIP, combining responses to these two questions, allowed for describing PMIP as: "sufficient," "little, not sufficient," or "insufficient, or none." When mothers answered "Yes, sufficiently" to both questions, perceived information was described as "sufficient." When they answered "yes, a little" to both questions, or "yes, sufficiently" to one question and "yes, a little" to the other one, perceived information was described as "little, not sufficient." Other combination of answers, excluding those with missing values, allowed for grouping mothers with "insufficient, or none" perceived information. Only responses related to the first unit of hospitalization were considered.

Statistical analysis

Descriptive statistics are reported as proportions or median (interquartile range [IQR]), as appropriate. We first compared the characteristics of included and excluded neonates. Second, to describe the French context of pain assessment and management during the study period, we reported proportions of assessments of continuous pain and discomfort and of procedural pain for neonates, and proportions of neonates receiving O-SH-GA by groups of GA (24–26, 27–28, and 29–31 WG). Third, we analyzed the association of PMIP with maternal presence, behavior, and feelings during painful procedures. Fourth, we studied the association of PMIP with mother-, infant-, and unit-related characteristics in a bivariate analysis. All these comparisons involved the χ^2 test. Finally, we performed multinomial multilevel regression to investigate the associations between levels of PMIP—in three levels—and individual and unit characteristics, taking into account the hierarchical nature of the database with infants (level 1) nested within units (level 2). At the individual level, variables were grouped as (1) individual characteristics of mothers (birthplace, living in a couple relationship, level of education, parity, single or twin pregnancy, and trait of anxiety) and infants (GA, SGA, and severe neonatal morbidity) and (2) characteristics dependent on both individual characteristics and unit organization (daily maternal and paternal visits, team support perceived by mothers, procedural pain assessment, exposure to O-SH-GA). At the unit level, characteristics entered into the model were number of neonates born before 32 WG admitted in 2011, availability of neonatal surgery, and neurodevelopmental care training.

Three sensitivity analyses were performed. First, we used multiple imputations by chained equations to impute missing data with the MI procedure in SAS. Imputation model variables included all individual and unit characteristics, and outcome. All variables were imputed by logistic regression. We generated 50 independent imputed datasets with 20 iterations each. Estimates

were pooled according to Rubin's rule.¹⁶ Two other sensitivity analyses were performed after excluding infants (1) born from twin pregnancies because their mothers were not independent and (2) transferred to another hospital, to account for a possible memorization bias.

Analyses were performed using SAS v9.4 (SAS Inst., Cary, NC, USA). The SAS GLIMMIX procedure was used for multivariate multilevel multinomial regression analyses. For analyses of the overall cohort, we used weighted percentages and tests, as well as GA adjustments in the multivariable analyses, to account for differences in sampling times between GA groups. All tests were two sided and $p < 0.05$ was considered statistically significant.

Ethics

Recruitment and data collection occurred only after families had received information and agreed to participate. This study was approved by the National Data Protection Authority (CNIL no. 911009) and by appropriate ethics committees (Consultative Committee on the Treatment of Data on Personal Health for Research Purposes—no. 10.626, Committee for the Protection of People Participating in Biomedical Research—CPP SC-2873).

RESULTS

Population

During the study period, 3905 neonates were born alive at 22–31 WG, and 3274 survived to discharge. Only one survivor was born at 23 weeks and 6 days and was therefore included with those born at 24 WG. A total of 3056 neonates were eligible for the study and the maternal questionnaire was available for 1974 (64%) (Fig. 1). Characteristics of neonates included and those excluded because of missing maternal questionnaires are presented in Supplemental Table S1 (online). Responder mothers were older, more frequently born in France, lived in a couple relationship, and had a higher level of education than non-responders; infants were also slightly more mature, less often received O-SH-GA, and were more frequently hospitalized in units with available neonatal surgery and a neurodevelopmental care training program. Included neonates were admitted in 91 neonatal units: 1103 (56%) in a single neonatal unit and 871 (44%) in at least two units (median length of stay in the first unit for infants transferred: 29 days [IQR 17–48]).

Pain assessments and use of O-SH-GA

Assessments of continuous pain and discomfort and of procedural pain with neonatal scales during the first week of life were reported for 71.9 and 21.2% of infants, respectively (Table 1). O-SH-GAs were used in 36.9%.

Levels of perceived maternal information on their infants' pain

For a large majority of infants (82.3%), mothers reported having received some information on pain, either "sufficient" or "little, not sufficient" (Table 2). However, PMIP was reported as "sufficient" for 22.7%, "little, not sufficient" for 45.9%, and "insufficient, or none" for 31.3%; for 18.0% of infants, mothers declared that they did not receive any information to recognize pain nor comfort or soothe the child. Proportion of neonates with perceived maternal information described as "sufficient" varied from 8 to 60% between units.

The level of PMIP was associated with marked differences in maternal possibilities in supporting and comforting the child during painful procedures. A large proportion of mothers (81.9%) was allowed to stay with their infant during painful procedures and was satisfied to be present (96.8%). However, the presence of mothers increased with the level of PMIP as well as the possibility to comfort the child (Table 3). Although satisfied to be present, 70.4% of all mothers reported difficulties staying during painful

procedures, without significant differences among information groups.

Factors associated with PMIP

Factors associated with PMIP on bivariate analysis are presented in Table 4; multivariate multilevel multinomial regression analysis, performed with 1747 completed cases, in Table 5. The main individual factors significantly associated with PMIP were social characteristics of mothers, specifically level of education, as well as GA; factors depending on both individual characteristics and unit organization were daily visits of mothers and team support. We found no association between pain assessment, or use of O-SH-GA and PMIP. At the unit level, neonates hospitalized in units that were receiving NIDCAP training were more likely to have mothers who perceived the information on pain as "sufficient." Differences between the information groups "sufficient" vs. "insufficient, or none" and "little, not sufficient" vs. "insufficient, or none" were in the same direction.

Sensitivity analyses

Although 35.4% of mothers did not respond to the maternal questionnaire, results after multiple imputation were consistent with those of complete cases. However, increasing the power of the analysis appeared to reinforce the potential role of maternal individual characteristics (Supplemental Table S2, online). The exclusion of neonates born after multiple pregnancies did not modify the associations with PMIP (Supplemental Table S3, online). After excluding infants hospitalized in several units, the associations between individual characteristics and PMIP were no longer significant, but remained statistically significant for team support and neurodevelopmental care training.

DISCUSSION

In this French national cohort study of very preterm neonates, we have explored pain through the perspective of information perceived by mothers on pain assessment and management. Most of these neonates (82.3%) had mothers who reported that they received some information on pain, but perceived as "sufficient" for only 22.6%. When the information was perceived as "sufficient," units' policies were reported as more liberal to encourage mothers to be present during painful procedures and mothers appeared more likely able to soothe their babies during painful procedures. Nearly all mothers present during painful procedures declared being satisfied (96.8%), although most of them found it difficult, regardless of the level of PMIP. At the individual level, variables associated with higher levels of PMIP were maternal education beyond secondary school, and birth before 29 WG. At the unit level, associated variables were daily visits of mothers, mothers' perception of high team support, and hospitalization in units receiving NIDCAP training. Pain assessment and treatment with O-SH-GA were not associated with levels of PMIP.

Strengths and weaknesses of this study

The strengths of the study are its population-based design, at a national level, with data recorded simultaneously for mothers, infants, and units. At the maternal level we could describe PMIP but also associations between PMIP and maternal presence and involvement in soothing infants during procedures. The size of the cohort allowed for describing three levels of PMIP and a continuum in maternal presence and involvement during procedures. It also allowed describing subtle differences in variables associated with PMIP, such as level of education and team support perceived by mothers. Finally, simultaneously recording data at the individual and unit level allowed for studying both individual and unit factors associated with PMIP.

Fig. 1 Flow chart of the study population. ^aNo survivor at 22 weeks and only one survivor at 23 weeks and 6 days, included in those born at 24 weeks gestation. ^bAdmitted in the neonatal unit considered for inclusion within the first 48 h of life and during at least 7 days

Table 1. Pain assessments during the first week of life and use of opioids, sedatives-hypnotics, general anesthetics in each gestational age group

	Gestational age				<i>p</i> Value ^b
	Total 24–31 weeks ^a	24–26 weeks ^a	27–28 weeks	29–31 weeks	
	<i>n</i> = 1974	<i>n</i> = 301	<i>n</i> = 476	<i>n</i> = 1197	
Assessment of continuous pain and discomfort					
Yes, with a neonatal scale	1349/1869 (71.9)	225/288 (78.1)	338/449 (75.3)	786/1132 (69.4)	0.009
Yes, with a non-neonatal scale	2/1869 (0.1)	1/288 (0.3)	0/449 (0)	1/1132 (0.1)	
No, or without any scale	518/1869 (28.0)	62/288 (21.5)	111/449 (24.7)	345/1132 (30.5)	
Assessment of procedural pain					
Yes, with a neonatal scale	371/1757 (21.2)	55/275 (20.0)	94/422 (22.3)	222/1060 (20.9)	0.51
Yes, with a non-neonatal scale	254/1757 (14.3)	48/275 (17.5)	63/422 (14.9)	143/1060 (13.5)	
No, or without any scale	1132/1757 (64.5)	172/275 (62.5)	265/422 (62.8)	695/1060 (65.6)	
Use of O-SH-GA	736/1927 (36.9)	205/294 (69.7)	215/467 (46.0)	316/1166 (27.1)	<0.001

Data are *n* of events/*N* in each group and %. Denominators vary according to the number of missing data for each variable. Total 24–31 weeks percentages are weighted to account for differences in sampling process between gestational age groups

O-SH-GA opioids, sedatives-hypnotics, general anesthetics

^aIncluding one survivor born at 23 weeks + 6 days

^bComparison of gestational age groups 24–26 weeks/27–28 weeks/29–31 weeks, χ^2 test

Bold values are *p* < 0.05

Table 2. Main outcome measure: perceived maternal information on infants' pain

	Pain assessment (N = 1982)			
	Yes, sufficiently	Yes, a little	No, not at all	Missing
Pain management (N = 1981)				
Yes, sufficiently	449	184	44	5
Yes, a little	137	586	122	0
No, not at all	8	94	350	3
Missing	2	4	1	13

A summary measure of perceived maternal information on infants' pain was constructed by combining the answers to the two questions on pain assessment and management (Supplemental file 1, online). When mothers answered "Yes, sufficiently" to both questions, information was described as "sufficient" ($n = 449$). When they answered "yes, a little" to both questions, or "yes, sufficiently" to one question and "yes, a little" to the other one, information was described as "little, not sufficient" ($n = 907$). Other combination of answers, excluding those with missing values, allowed for grouping mothers with "insufficient, or none" information ($n = 618$).

There are some limitations. First, the number of non-responding mothers was high (35.4%), which may have underestimated the proportion of mothers who perceived the information as "insufficient, or none." However, scenarios with multiple imputations yielded associations that were consistent with results obtained with complete cases. Second, recording information on fathers' perceptions may have given interesting perspectives, as fathers are equally affected by the distress of a preterm birth as mothers, but maternal and paternal perceptions after a premature birth were reported as different.¹⁷ Recording information from mothers was already challenging in a cohort of this size, and it was assumed to be even more challenging for fathers, which is why paternal perception on pain information was not collected. Including fathers' perception in future research and investigating the potential differences between mothers and fathers (and/or significant others) would provide a more comprehensive understanding of parents' involvement in pain management and could allow to achieve a real family-centered pain management. Third, we were not able to quantify pain exposure or options of care for adequate pain relief, such as parental involvement in non-pharmacological pain-relieving intervention, and their possible relation with PMIP. This was not the main objective of EPIPAIN-2 and recording all these data at national level was too complex. Some of these variables were however recorded in EPIPAIN-2, an additional project of EPIPAIN-2 including infants born in Ile-de-France only and for a shorter period of time.⁹ The EPIPAIN-2 study reported that the mean numbers of venipunctures and heel sticks per patient-day among very preterm neonates were 3.8 (range 1–19)⁵ and 2.3 (range 0–20),¹⁸ respectively; further analyses of parental involvement in pain-relieving intervention are in progress. Fourth, the adequacy of a quantitative approach to describe levels of perceived maternal information about pain of their own preterm infant is questionable. This phenomenon is embedded in the deep human experience of distress of mothers being confronted with the suffering of their infant and a qualitative approach appears more suitable to explore all its aspects. However, this quantitative approach offers new insight, from a national point of view, and is interesting as a quality assessment process. Creating links between the vast amount of qualitative research in the field of parental information on pain^{2,7,8} and a quantitative approach may help to better define strategies to improve neonatal pain management. Although this study was

not designed to understand why mothers considered PMIP as "sufficient," parents' suggestions for improving pain management obtained from qualitative studies include providing more information for parents, creating more opportunities for parental involvement, improving the timing of information, and increasing consistency in infant care together with increasing use of specific pain-relieving interventions given by NICU staff.² Finally, information was recorded at hospital discharge, and 44% of the neonates were hospitalized in more than one unit. Thus, we cannot exclude a memory bias. However, associations between unit factors and PMIP were consistent in the analysis of infants hospitalized in only one NICU, although associations between individual characteristics and PMIP were no more statistically significant. We hypothesize that hospitalization in a single unit could allow for greater collaborative relationships between parents and the team.

Context of the study

This study was launched in a country with large access to units for parents, with kangaroo care routinely proposed to parents in more than 50% of the units¹⁴—both acknowledged as enhancing parental involvement in pain control^{19,20}—but with less widespread architecture facilities to increase parental presence.¹⁴ The mean proportion of children treated with O-SH-GA was in a medium range with reference to the EUROPAIN study.¹³ In this survey from 18 European countries, 34% of infants born at a mean age of 29.4 WG received O-SH-GA, with disparities among units, from 33.3 to 89.3%. Assessment of continuous pain and discomfort can be considered as high in our study, compared to the same European survey²¹ with around 40% of neonates born <32 weeks being assessed, but evaluation of procedural pain was far less common. Nevertheless, pre-procedural analgesia for heel sticks increased from 62 to 75% in Ile-de-France between 2005 and 2011,¹⁸ and we may assume that trends did not differ greatly in the rest of the country, although a large variability between units probably exists.

Assessment of pain is considered of outmost importance to decrease analgesic complications,²² over sedation,²³ and tolerance/withdrawal,²⁴ but also to communicate about pain.²⁵ In this study, with high rates of pain assessment, a high proportion of mothers self-reported to have received some form of information on pain, although we cannot infer causality. However, less than one quarter of them described the information as "sufficient" and it appears useful to document factors associated with higher level of PMIP.

Maternal involvement in pain assessment and management

We found that both maternal presence and involvement in soothing infants during painful procedures increased when PMIP was reported as "sufficient" only. As we do not have data from professionals on the quality of information delivered to mothers, we cannot be sure that mothers "not sufficiently", or "not informed" were really less or not informed, or that the information was not cognitively understood. We were also not able to explore in detail mothers' emotional state, known to influence their ability to achieve their desire level of involvement.² Interestingly, associations between mothers' trait of anxiety and the level of PMIP were not significant. Nevertheless, information around pain should aim to help parents to soothe their child in an active way and their perception of the information, as an end-point, has a real value. Our results sustain, in the real life, those of a randomized controlled trial suggesting the positive effect of an intervention aiming to increase parental understanding of pain on parental involvement in pain management.⁶ Of interest, the level of education was significantly associated with the level of perceived information in the group of mothers who reported the information as "little, not sufficient," but this association was no more statistically significant for the group of mothers "sufficiently informed." Responding to the diversity of families is challenging

Table 3. Maternal involvement in supporting and comforting the infant during painful procedures by the level of perceived maternal information on infants' pain

	Total	Perceived maternal information on infants' pain						<i>p</i> Value ^a
		Sufficient		Little, not sufficient		Insufficient or none		
	<i>n</i> = 1974	<i>n</i> = 449	<i>n</i> = 907	<i>n</i> = 618				
If you were present in the unit during painful procedures...								
Did you have the possibility of staying next to your baby during a painful procedure (blood sampling, suctioning, etc.)?								
No, you were invited to leave	350/1943	(18.1)	33/444	(7.5)	132/898	(14.7)	185/601	(31.0) <0.0001
Yes, but you would have preferred not to be present	298/1943	(15.5)	72/444	(16.5)	132/898	(14.8)	94/601	(15.8)
Yes, and you were present	1295/1943	(66.4)	339/444	(76.0)	634/898	(70.6)	322/601	(53.2)
If you were next to your baby during a painful procedure...								
Were you able to support or soothe him/her during or after the procedure?								
Not at all, never/rarely	124/1285	(9.8)	9/335	(2.8)	54/632	(8.7)	61/318	(19.4) <0.001
Quite often	578/1285	(44.9)	115/335	(33.8)	331/632	(52.4)	132/318	(41.8)
All the time	583/1285	(45.2)	211/335	(63.4)	247/632	(38.9)	125/318	(38.8)
How did you feel about the situation?								
Without difficulty, and you were satisfied to be next to your child to support or comfort him/her	337/1286	(26.4)	100/334	(30.1)	156/632	(24.9)	81/320	(25.6) 0.14
With difficulties, but you were satisfied to be with your child to support or comfort him/her	908/1286	(70.4)	226/334	(67.7)	458/632	(72.2)	224/320	(69.6)
Very hard, you would have preferred to avoid it	41/1286	(3.2)	8/334	(2.2)	18/632	(2.8)	15/320	(4.8)

Data are *n* of events/*N* in each group, percentages. Denominators vary according to the number of missing data for each variable. Percentages and *p* values were weighted to account for differences in sampling process between gestational age groups

^aComparison between the three levels of pain information, χ^2 test

Bold values are *p* < 0.05

for professionals, and the importance of an enhanced learning environment for professionals on communication with families has been highlighted.²⁶ The development of "potentially better practices" to improve neonatal pain management has also deserved attention.²⁷ NICU pain practices were found influenced by context²⁸ and teaching programs.²⁹ Overarching themes emerging²⁸ as positively affecting optimal pain management include a culture of collaboration between parents and professionals; barriers are threats to autonomous decision-making and complexities in care delivery. We hypothesize that responses of mothers "sufficiently informed" reflected a global strategy of units, promoting at the same time pain control, PMIP, maternal presence during procedures to alleviate pain, and communication with families. The positive associations between the daily presence of mothers, perceived team support, and neurodevelopmental care training and level of PMIP favors this hypothesis. Daily presence of mothers and perceived team support depend on mothers' characteristics but also on units' organization. We can assume that they were associated with contextual factors that we were not able to control for, such as leadership, staff attitudes and beliefs, which have been shown to play an important role in the successful implementation of parents' involvement in pain care.⁴ The presence of a local champion, whose duty is to facilitate the adoption of pain control measures, is the main reported factor closing the gap between evidence and clinical practice.²⁹ Unfortunately, this information was not available in EPIPAGE-2. Neurodevelopmental care may help increase parents' involvement in pain management, as pain, together with family-centered care, is considered as core measures of this approach.¹⁹ Nevertheless, implementing neurodevelopmental care is hotly debated because it is long and potentially costly. Consequently, information from cohort studies, collecting data in "real life," may add interesting perspectives. We found that PMIP was more often reported as "sufficient" for infants hospitalized in units implementing NIDCAP

than those in units without any training. No association was observed between PMIP and the introductory course, or the sensory-motor program. NIDCAP is based on the individual evaluation of the infant's behavior, shared with parents, with specific attention to withdrawal or approach signs around and during care procedures, potentially contributing to increase in PMIP. It also promotes family-centered care, a culture of collaboration between nurses and physicians, support for evidence-based practice, and partnering of the clinical staff with senior hospital management, so that changes can be truly integrated in daily care.³⁰ NIDCAP implementation may induce changes in staff attitudes, with a general atmosphere promoting neonatal pain management and parental involvement in daily care. However, even if the level of PMIP was higher in units receiving training on NIDCAP, only one-third of neonates hospitalized in these units had mothers perceiving the information as "sufficient." This may reflect different levels of implementation and deserves further attention. In addition, NIDCAP training is time intensive and new programs, built on the same theoretical framework such as the FINE program,³¹ may help fostering culture changes into the units.

Finally PMIP, whether "sufficient" or "little, no sufficient" was associated with GA between 24 and 26 WG, although infants born between 27 and 31 WG still experience several painful procedures.^{5,18} Paying an increased attention to pain information for mothers or parents of these less immature infants may help to disseminate best practices in NICUs and could have high impact on outcomes.

Perspectives

Our study is embedded in the complex process of parental involvement in pain management that has been conceptualized as evolving from a state of mind where parents view infant comfort as nurses and doctors roles only, to an end-point where they advocate for the infant and consider that the infant comfort

Table 4. Individual and units characteristics associated with perceived maternal information on infants' pain: bivariate analysis

	Perceived maternal information on infants' pain						<i>p</i> Value ^a
	Sufficient		Little, not sufficient		Insufficient or none		
	<i>n</i> = 449		<i>n</i> = 907		<i>n</i> = 618:		
Individual-level variables							
Maternal characteristics							
Age (years)							
<25	75/449	(16.7)	139/907	(15.2)	118/618	(18.8)	0.47
25–34	277/449	(61.8)	567/907	(62.6)	371/618	(60.2)	
≥35	97/449	(21.4)	201/907	(22.3)	129/618	(20.9)	
Birth in France	385/447	(86.5)	777/900	(86.4)	494/611	(81.0)	0.007
Living in a couple relationship	414/448	(92.5)	835/905	(92.4)	544/618	(88.2)	0.008
Level of education							
<Secondary school	126/446	(28.4)	202/901	(22.6)	205/613	(33.4)	<0.001
High school	86/446	(19.5)	201/901	(22.2)	137/613	(22.2)	
University	234/446	(52.1)	498/901	(55.2)	271/613	(44.5)	
Primiparous	237/439	(53.7)	517/903	(56.9)	345/613	(56.3)	0.53
Trait of anxiety ^b							
Low	133/449	(29.8)	348/907	(38.1)	203/618	(32.9)	0.012
Moderate	249/449	(55.3)	437/907	(48.3)	301/618	(48.7)	
High	31/449	(6.9)	49/907	(5.5)	53/618	(8.5)	
Missing	36/449	(8.1)	73/907	(8.1)	61/618	(9.8)	
Multiple pregnancy	138/449	(31.1)	291/907	(32.2)	183/618	(29.9)	0.63
Neonatal characteristics							
Gestational age (weeks)							
24–26	82/449	(14.2)	149/907	(12.7)	70/618	(8.7)	<0.001
27–28	113/449	(26.4)	236/907	(27.2)	127/618	(21.2)	
29–31	254/449	(59.4)	522/907	(60.1)	421/618	(70.2)	
Small-for-gestational age ^c	164/449	(37.4)	321/907	(36.2)	213/618	(34.8)	0.68
Severe neonatal morbidities ^d	85/421	(19.0)	159/857	(17.8)	71/594	(11.1)	<0.001
Associated to unit organization							
Daily maternal visits	414/447	(92.5)	819/897	(91.3)	509/613	(83.3)	<0.001
Daily paternal visits	266/439	(60.6)	546/895	(61.0)	330/604	(54.8)	0.043
Team support perceived by mothers							
No	3/446	(0.6)	23/899	(2.6)	51/608	(8.2)	<0.001
Yes, rather	63/446	(14.2)	273/899	(30.3)	249/608	(41.1)	
Yes, full	380/446	(85.2)	603/899	(67.2)	308/608	(50.7)	
Evaluation of procedural pain	164/449	(36.5)	279/907	(30.6)	182/618	(29.4)	0.037
Treatment with O-SH-GA	189/435	(41.7)	342/888	(37.3)	205/604	(33.0)	0.016
Units level variables							
<i>N</i> <32 weeks admitted/year <50	39/449	(8.9)	45/907	(5.1)	28/617	(4.7)	0.008
Neonatal surgery available	309/449	(69.0)	655/907	(72.1)	456/616	(74.0)	0.20
Neurodevelopmental care training							
Nidcap	139/449	(31.0)	198/907	(21.8)	98/618	(15.9)	<0.001
Sensory–motor	65/449	(14.5)	145/907	(15.9)	126/618	(20.1)	
Introductory course	103/449	(22.6)	241/907	(26.4)	167/618	(26.8)	
No training	142/449	(31.9)	323/907	(35.9)	227/618	(37.2)	

Data are *n* of events/*N* in each group (percentages). Denominators vary according to the number of missing data for each variable. Percentages and *p* value were weighted to account for differences in sampling process between gestational age groups

O-SH-GA opioids, sedatives-hypnotics, general anesthetics, NIDCAP neonatal individualized developmental care and assessment program

^aComparison between the three levels of information on pain, χ^2 test

^bAnxiety was assessed with the Spielberger State-Trait Anxiety Inventory and only the trait subscale was considered¹⁵

^cSmall-for-gestational age was defined as birth weight less than the 10th percentile for gestational age and sex based on French intrauterine growth curves¹¹

^dSevere neonatal morbidity was defined as severe bronchopulmonary dysplasia or necrotizing enterocolitis stage 2–3 or severe retinopathy of prematurity stage >3 or any of the following severe cerebral abnormalities on cranial ultrasonography: intraventricular hemorrhage grade III or IV or cystic periventricular leukomalacia¹²

Bold values are *p* < 0.05

Table 5. Individual and units characteristics associated with perceived maternal information on infants' pain: multinomial multilevel regression analysis

	Perceived maternal information on infants' pain		<i>p</i> Value
	"Sufficient" vs.	"little, not sufficient" vs.	
	"insufficient, or none"	"insufficient, or none"	
	aOR (95% CI)	aOR (95% CI)	
Individual-level variables			
Maternal characteristics			
Age (years)			
<25	1.2 (0.8–1.8)	1.1 (0.8–1.5)	0.80
25–34	1	1	
≥35	0.9 (0.6–1.3)	1.0 (0.8–1.4)	
Country of birth			
France	1.4 (1.0–2.2)	1.4 (1.0–2.0)	0.062
Other	1	1	
Living in a couple relationship			
No	1	1	0.130
Yes	1.6 (0.9–2.7)	1.5 (1.0–2.2)	
Level of education			
<Secondary school	1	1	0.007
High school	1.1 (0.8–1.7)	1.6 (1.2–2.3)	
University	1.2 (0.9–1.7)	1.7 (1.2–2.2)	
Parity			
Primiparous	1	1	0.10
Multiparous	1.4 (1.0–1.9)	1.3 (1.0–1.6)	
Trait of anxiety ^a			
Low	0.9 (0.6–1.2)	1.2 (0.9–1.6)	0.069
Moderate	1	1	
High	0.8 (0.5–1.4)	0.7 (0.4–1.1)	
Missing	1.1 (0.7–1.9)	1.0 (0.6–1.5)	
Type of pregnancy			
Singleton	1	1	0.60
Multiple	1.1 (0.8–1.5)	1.1 (0.9–1.5)	
Neonatal characteristics			
Gestational age (weeks)			
24–26	2.2 (1.4–3.6)	1.9 (1.3–2.9)	0.003
27–28	1.3 (0.9–1.9)	1.4 (1.0–1.8)	
29–31	1	1	
Small-for-gestational age ^b			
No	1	1	0.63
Yes	1.2 (0.9–1.6)	1.0 (0.8–1.3)	
Severe neonatal morbidities ^c			
No	1	1	0.093
Yes	1.5 (1.0–2.3)	1.4 (1.0–2.0)	
Associated with unit organization			
Daily maternal visits			
No	1	1	<0.001
Yes	3.0 (1.8–5.0)	2.1 (1.4–3.1)	
Daily paternal visits			
No	1	1	0.83
Yes	0.9 (0.7–1.3)	0.9 (0.7–1.2)	

Table 5 continued

	Perceived maternal information on infants' pain		<i>p</i> Value
	"Sufficient" vs. "insufficient, or none" aOR (95% CI)	"little, not sufficient" vs. "insufficient, or none" aOR (95% CI)	
Team support perceived by mothers			
No	1	1	<0.001
Yes, rather	4.7 (1.4–16.1)	2.4 (1.4–4.4)	
Yes, full	21.7 (6.4–73.1)	4.5 (2.5–8.1)	
Evaluation of procedural pain			
No	1	1	0.66
Yes	1.1 (0.8–1.5)	1.0 (0.7–1.3)	
Treatment with O-SH-GA			
No	1	1	0.19
Yes	1.3 (1.0–1.8)	1.0 (0.8–1.4)	
Unit-level variables			
<i>N</i> <32 weeks admitted/year			
<50 infants	1.5 (0.8–2.9)	0.9 (0.5–1.7)	0.27
≥50 infants	1	1	
Neonatal surgery available			
No	1.4 (1.0–2.1)	1.2 (0.9–1.7)	0.18
Yes	1	1	
Neurodevelopmental care training			
NIDCAP	2.6 (1.7–4.1)	1.6 (1.1–2.3)	<0.001
Sensory–motor	0.8 (0.5–1.3)	0.7 (0.5–1.1)	
Introductory course	1.1 (0.7–1.6)	1.1 (0.8–1.5)	
No training	1	1	

Complete cases analyses, *N* = 1747. Pain information is reported in three levels: sufficient/little, not sufficient/insufficient or none. Insufficient or none was the reference category

O-SH-GA opioids, sedatives-hypnotics, general anesthetics, NIDCAP neonatal individualized developmental care and assessment program, aOR adjusted odds ratio, CI confidence interval

^aAnxiety was assessed with the Spielberger State-Trait Anxiety Inventory and only the trait subscale was considered¹⁵

^bSmall-for-gestational age was defined as birth weight less than the 10th percentile for gestational age and sex based on French intrauterine EPOpé growth curves¹¹

^cSevere neonatal morbidities were defined as severe bronchopulmonary dysplasia or necrotizing enterocolitis stage 2–3 or severe retinopathy of prematurity stage >3 or any of the following severe cerebral abnormalities on cranial ultrasonography: intraventricular hemorrhage grade III or IV or cystic periventricular leukomalacia¹²

Bold values are *p* < 0.05

is of their primary responsibility in partnership with clinical care team.² We have tried to explore the first steps of this process (being informed, present, and provide comfort). Having a more comprehensive understanding of the next steps (being informant for NICU staff, active decision maker, and advocating for the infant) could help to better define strategies increasing parental involvement and satisfaction in pain management. In addition, NICUs stressful environment, during critically sensitive periods, affects brain development^{32,33} and may contribute to adverse outcomes.^{34–36} Analysis of the outcome at 5½ years of children included in this cohort is in progress and will help to investigate if maternal information on pain with increased involvement in soothing the infants is associated with long-term benefits.

CONCLUSION

In this national cohort study of very preterm neonates, information mothers perceive on infants' pain was common, but unfrequently described as "sufficient." Maternal involvement in soothing the infants during painful procedures was increased only when the information was perceived as "sufficient." Enhancing the information on pain for parents of preterm neonates could have significant clinical implications in terms of pain management for the neonate and parental well-being. A positive perception of information was higher in units caring for infants with a family-centered approach. Further research might focus on strategies enhancing staff attitudes and beliefs to inform parents on infants' pain and comforting techniques

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AUTHOR CONTRIBUTIONS

V.P., L.M.-M., L.V., and P.-Y.A. had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. V.P., L.M.-M., L.V., M.K., R.C., and P.-Y.A. conceptualized the study and wrote the manuscript. L.M.M. and L.V. performed the statistical analysis. M.D. coordinated data collection and had responsibility for technical support. P.-Y.A. obtained funding and supervised the study. All authors contributed to the plan analysis and interpretation of the results, and reviewed and approved the final manuscript. All members of the neurodevelopmental care study group were involved in the regional organization for data collection, reviewed, and approved the final manuscript.

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ADDITIONAL INFORMATION

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