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Painless childbirth? Epidural and spinal techniques in obstetric anesthesia

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Chapter 8

Management practices for postdural puncture headache in obstetrics: a prospective, international, cohort study

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ABSTRACT

Background:

Accidental dural puncture is an uncommon complication of epidural analgesia and can cause postdural puncture headache (PDPH). We aimed to describe management practices and outcomes after PDPH treated by epidural blood patch (EBP) or no EBP.

Methods: Following ethics committee approval, patients who developed PDPH after accidental dural puncture were recruited from participating countries and divided into two groups, those receiving EBP or no EBP. Data registered included patient and procedure characteristics, headache symptoms and intensity, management practices, and complications. Follow-up was at 3 months.

Results

A total of 1001 patients from 24 countries were included, of which 647 (64.6%) received an EBP and 354 (35.4%) did not receive an EBP (no-EBP). Higher initial headache intensity was associated with greater use of EBP, odds ratio 1.29 (95% confidence interval 1.19-1.41) per pain intensity unit increase. Headache intensity declined sharply at 4 h after EBP and 127 (19.3%) patients received a second EBP. On average, no or mild headache (numeric rating score ≤ 3) was observed 7 days after diagnosis. Intracranial bleeding was diagnosed in three patients (0.46%), and backache, headache, and analgesic use were more common at 3 months in the EBP group.

Conclusions

Management practices vary between countries, but EBP was more often used in patients with greater initial headache intensity. EBP reduced headache intensity quickly, but about 20% of patients needed a second EBP. After 7 days, most patients had no or mild headache. Backache, headache, and analgesic use were more common at 3 months in patients receiving an EBP.

INTRODUCTION

The increased availability of safe and efficacious labour epidural analgesia in the Western world has contributed to an improved birth experience for many women, as it alleviates pain during labour. Unfortunately, there is a small (0.3-1.5%) risk of iatrogenic accidental dural puncture (ADP).[1,2] If it occurs, 50-88% of women will develop symptoms of postdural puncture headache (PDPH).[2,3] From a European perspective, with 5 million babies born in the EU in 2017 and an epidural labour analgesia rate between 20% and 80%, ADP results in approximately 10 000-15 000 women developing PDPH every year.[4] This may cause impaired ability to self-mobilise and breastfeed the baby, delays hospital discharge,[5] and sometimes chronic headache and backache may develop.[6] Also, a small but statistically significant increase in the incidence of intracranial bleeding (ICB) has been described in patients with PDPH, compared with those without a headache.[7] Therefore, ADP and subsequent PDPH add a cost and resource burden to an already strained healthcare system in Europe. Different management strategies for PDPH exist, ranging from conservative management to treatment with an epidural blood patch (EBP). So far, the best interventional therapy that has been demonstrated to immediately reduce the severity and duration of PDPH is an EBP.[8,9] Although EBPs are efficacious, some patients may experience rebound headache requiring a new EBP.[10] However, only limited evidence exists from small prospective randomised trials and systematic reviews as to the choice between continuing conservative management or applying an EBP for management of PDPH. Therefore, the aims of this multinational cohort study were to describe characteristics of PDPH and its management, to describe and identify factors related to physician treatment choices in the application of EBP or not, to describe intensity of headache over time in patients treated with EBP or no-EBP, and to record any complication after EBP or conservative management.

METHODS

This was a prospective, multicentre, international, pragmatic, observational, cohort study where 158 centres from 27 countries registered to participate. Data were collected during the period January 1, 2016, to December 31, 2018. The ethical committee in the countries/institutions approved the study and it was registered in clinicaltrials.gov (NCT: 02362828).

Signed, informed consent was obtained from each patient before inclusion if the ethics committee in the country/hospital stated this to be mandatory. All consenting women ≥ 18 yr admitted to the hospital and having epidural analgesia during labour were included in the study if confirmed/suspected ADP occurred and a clinical diagnosis of PDPH was made postpartum. When a combined spinal-epidural technique was used during labour or Caesarean section, CSF had to be seen in the epidural needle and PDPH had to occur to include the patient into the study. Exclusion criteria were: hospitals performing < 500 deliveries/yr, patients having PDPH after spinal anaesthesia alone, no definite evidence of ADP observed at epidural insertion when performing a combined spinal-epidural anaesthesia/

analgesia, language constraints, any medical disorder which may prevent compliance with the protocol, and patients presenting with PDPH >5 days after epidural anaesthesia or analgesia. At each site, a specialist anaesthesiologist evaluated the patients with a demonstrated/suspected ADP and characteristic symptoms of PDPH after epidural anaesthesia or analgesia, to confirm the diagnosis (definition below).[11] Headache intensity was measured using a numeric rating score (NRS) where 0=no pain and 10=worst imaginable pain. General data protection regulation guidelines were followed and patient and procedure characteristics, location of headache, and management strategies were collected through an internet-based program (OpenClinica). Patients recruited into the study were followed up until discharge from the hospital and subsequently at home at 3 months by telephone. Any readmission as a result of PDPH/EBP was recorded until 3 months.

Definitions

ADP was defined as visible CSF in the epidural needle, a positive aspiration test through an epidural catheter, or typical evidence of spinal anaesthesia after injection of local anaesthetic via the epidural catheter.

PDPH was defined as:[12]

1. Headache that worsens within 15 min after sitting or standing and improves within 15 min after lying down after dural puncture has occurred or is suspected.
2. The headache develops within 5 days after dural puncture (confirmed or possible).
3. The headache may or may not be accompanied by neck stiffness, vestibular, visual, or auditory symptoms.

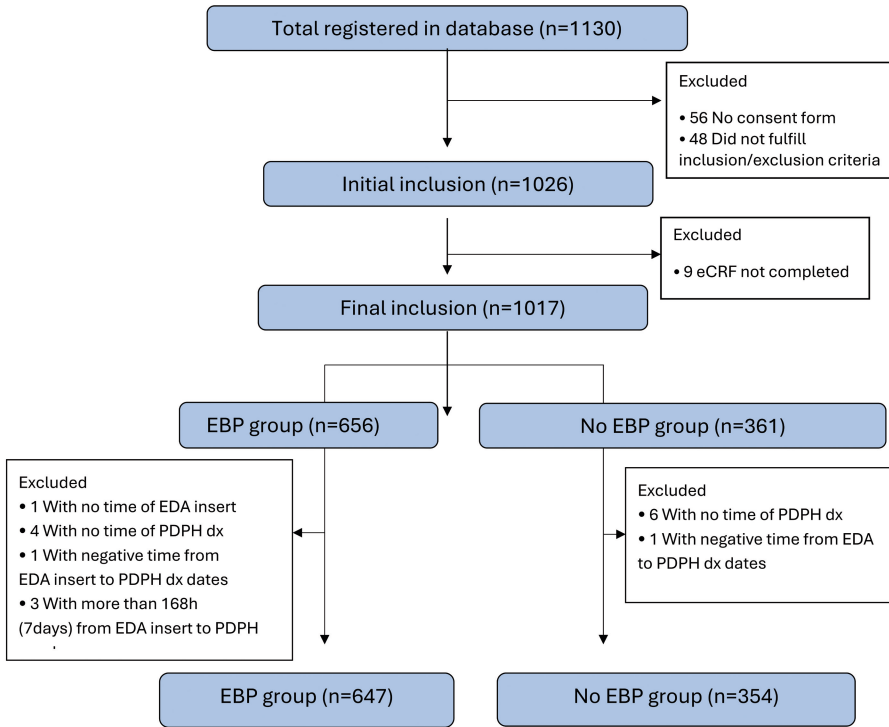
Persistent backache or headache was defined as NRS ≥ 3 at 3 months.

Spontaneous recovery of headache was defined as NRS <3 sitting/standing up at 24 h after PDPH diagnosis NRS <3 within 24 h after PDPH diagnosis.

PDPH with minimal orthostatic component was defined as a headache with <2 points difference in intensity on the NRS scale when comparing standing/sitting with lying position.

The European Society of Anaesthesiology was the sponsor and coordinated the study. The sponsor was responsible for implementing and maintaining quality assurance and quality control systems to ensure that the trial was conducted, and data were generated, documented, and reported in compliance with the protocol, Good Clinical Practice, and the applicable local regulatory requirements. Verification of data quality and registration was the responsibility of the local principal investigator, which was controlled by the sponsor with random assessments of centres to confirm correctness of data entered.

Fig 1. STROBE diagram for patient recruitment and data analyses.



Abbreviations: Dx, diagnosis; EBP, epidural blood patch; eCRF, electronic case record form; EDA, epidural analgesia; PDPH, postdural puncture headache.

Statistics

An unpaired t-test was used to compare continuous variables, the Mann-Whitney test was used to compare skewed variables, and the χ^2 test or Fischer exact test was used to compare categorical variables between EBP and no-EBP groups. Unless otherwise stated, results of NRS score (headache and backache) are presented in the sitting/upright position.

A stepwise logistic regression was used to identify independent variables to the choice of EBP/no-EBP treatment. All variables in Tables 1-3 were potential independent variables and modelled as categorical variables together with NRS pain intensity at diagnosis of PDPH as a continuous variable, and the significance level for the selection criteria was set to 0.20. This analysis was performed with full data available (complete cases), which resulted in 603 EBP and 342 no-EBP patients (total 945 patients).

Unadjusted and adjusted linear regression was used to evaluate the change in NRS pain intensity from PDPH diagnosis to 0-24 h, 7 days, and at 3 months post PDPH diagnosis between EBP and no-EBP groups. The adjusted models were further adjusted for NRS pain intensity at PDPH diagnosis, country of recruitment, and using a stepwise procedure with selection criteria 0.20 to adjust for independent variables to the outcome among the variables in Tables 1-3. As the mean pain intensity at PDPH diagnosis was different in the EBP and no-EBP groups, only patients with NRS ≥ 7 (resulting in 764 patients) and with complete information on all variables in Tables 1-3 were considered, resulting in 719 patients (498 EBP and 221 no-EBP patients). As there were missing outcome data on NRS pain intensity post PDPH diagnosis, the analysis was performed on the number of patients indicated in Table 4. To try to compensate for the missing outcome data, the adjusted models were also evaluated with the multiple imputation chained equations technique using the same variables for the imputation as were selected in the adjusted models described above. Statistical significance level was set to two-sided 5% and STATA release 14 and SPSS version 24 were used for the statistical computations.

RESULTS

A total of 1130 patients were included between January 2016 and December 2018 from 24 participating countries. However, after a complete data assessment, 1001 patients were included in the final analyses; 647 (64.6%) in the EBP group and 354 (35.4%) in the no-EBP group (Fig. 1). The distribution of the total number and percentage of patients who had EBP across the countries is shown in Figure 2. Fewer than 50% patients received an EBP in Spain, Portugal, Greece, and Italy.

Table 1. Patient characteristics and headache pain intensity as numeric rating score (NRS) on sitting up at the time of PDPH diagnosis.

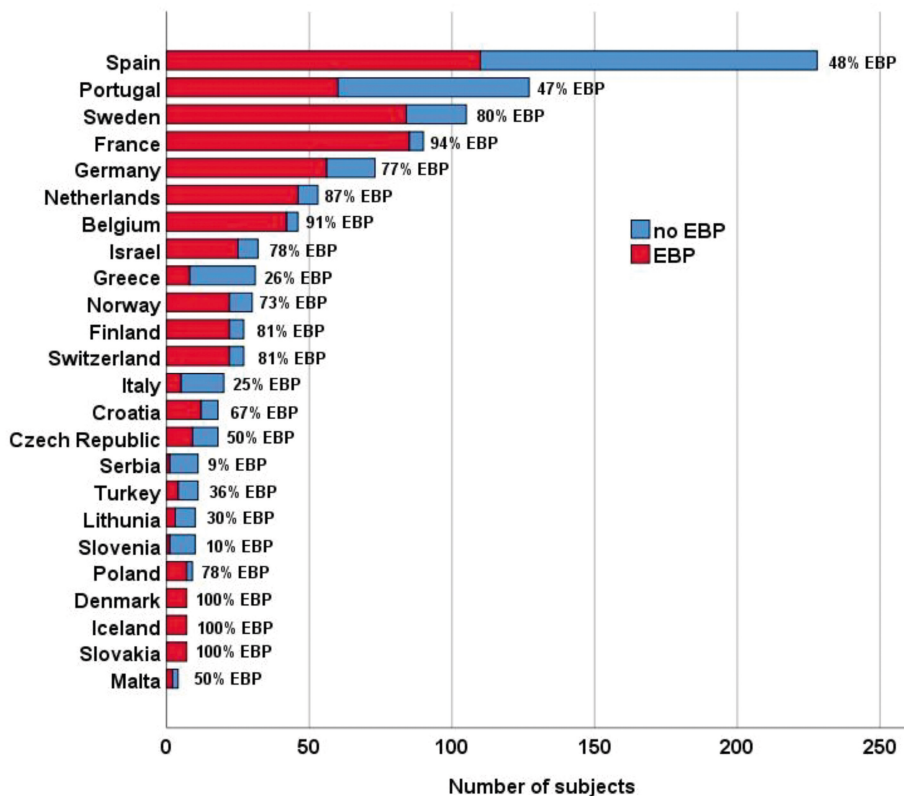
	Total (n=1001)	EBP (n=647)	No-EBP (n=354)	P-value
Mother's age				
Mean (SD, range)	31.0 (5.1. 18-46)	31.0 (4.9. 18-46)	31.0 (5.6. 18-44)	0.9
Parity				
Multipara, n (%)	510 (51)	337 (52)	173 (49)	0.33
BMI (kg/m ²)	(n=1000)	(n=646)	(n=354)	
Mean (SD)	27.7 (5.5)	27.4 (5.2)	28.1 (6.0)	0.077
Previous history, n (%)				
Neuraxial anaesthesia	266 (26)	162 (25)	104 (29)	0.14
Postdural puncture headache	31 (3)	17 (3)	14 (4)	0.25
Chronic headache	40 (4)	30 (5)	10 (3)	0.16

Table 1. Continued

	Total (n=1001)	EBP (n=647)	No-EBP (n=354)	P-value
Migraine	139 (14)	98 (15)	41 (12)	0.12
Vertebral column pathology	81 (8)	49 (8)	32 (9)	0.42
Chronic backache	61 (6)	41 (6)	20 (6)	0.66
Smoker	(n=1000)	(n=646)	(n=354)	
Yes, n (%)	119 (12)	64 (10)	55 (16)	0.009
Occupation, n (%)				
Administration	135 (13)	93 (14)	42 (12)	0.27
Teaching	81 (8)	60 (9)	21 (6)	0.064
Healthcare	147 (15)	110 (17)	37 (10)	0.005
Professional worker (no university education)	216 (22)	125 (19)	91 (26)	0.019
Professional worker (with university education)	214 (21)	149 (23)	65 (18)	0.085
None	208 (21)	110 (17)	98 (28)	<0.001
Highest education, n (%)	(n=998)	(n=645)	(n=353)	
Basic schooling	172 (17)	89 (14)	83 (24)	<0.001
High school	384 (38)	245 (38)	139 (39)	0.67
University	442 (44)	311 (48)	131 (37)	0.001
Mode of delivery, n (%)				
Spontaneous	688 (69)	455 (70)	233 (66)	0.14
Instrumental	120 (12)	79 (12)	41 (12)	0.77
Caesarean section	193 (19)	113 (17)	80 (23)	0.049

Abbreviations: EBP, epidural blood patch; PDPH, postdural puncture headache; SD, standard deviation.

Fig 2. The number of patients recruited from each country and percentage of epidural blood patches (EBP) performed.



Characteristics of patients and epidurals

Characteristics of patients, equipment, and methods used for performing epidurals in all patients are shown in Table 1. Patients in the EBP group had a significantly higher level of education, were more often healthcare workers, non-smokers, and had fewer Caesarean section deliveries compared with the no-EBP group. Characteristics of epidural technique, diagnostic symptoms and their location and management of PDPH are shown in Table 2. In 41% of patients ADP was diagnosed by classical signs of PDPH, without CSF in needle/catheter. An intrathecal catheter (ITC) was inserted after ADP in 18% of patients; 14% in EBP vs 25% in the no-EBP group, $P<0.001$. Significantly more patients could breastfeed in the no-EBP group (94% vs 84%, $P<0.001$).

Table 2. Characteristics of epidural technique, PDPH diagnosis, and management of PDPH.

	Total (n=1001)	EBP (n=647)	No-EBP (n=354)	P-value
Needle size, n (%)				
16G	63 (6)	40 (6)	23 (6)	0.84
17G	101 (10)	87 (13)	14 (4)	<0.001
18G	820 (82)	507 (78)	313 (88)	<0.001
19-20G	17 (2)	13 (2)	4 (1)	0.3
Media for detecting loss of resistance, n (%)	(n=1000)	(n=646)		
Air	169 (17)	71 (11)	98 (28)	<0.001
Saline	816 (82)	564 (87)	252 (71)	<0.001
Both	15 (2)	11 (2)	4 (1)	0.48
Position of patient inserting epidural, n (%)		(n=644)		
Lying	177 (18)	124 (19)	53 (15)	0.09
Sitting	821 (82)	520 (81)	301 (85)	
Level of insertion epidural, n (%)	(n=1000)	(n=646)		
L1-2	55 (6)	38 (6)	17 (5)	0.48
L2-3	255 (25)	184 (28)	71 (20)	<0.001
L3-4	557 (56)	338 (52)	219 (62)	0.003
L4-5	133 (13)	86 (13)	47 (13)	>0.99
Technical difficulties inserting epidural, n (%)	326 (33)	203 (31)	123 (35)	0.28
Multiple attempts inserting epidural, n (%)	452 (45)	307 (47)	145 (41)	0.049
Duration (h), median (IQR)				
Epidural insertion to PDPH diagnosis	31.0 (21.0-51.5)	32.7 (21.0-53.7)	29.9 (20.8-48.0)	0.02
Epidural insertion to EBP	NA	(n=646)	68.4 (47.7-96.8)	NA
Intrathecal catheter placed after ADP, n (%)	181 (18)	91 (14)	90 (25)	<0.001
Operator experience, n (%)				
<6 months	103 (10)	74 (11)	29 (8)	0.11
6 months to 1 yr	92 (9)	68 (11)	24 (7)	0.051
1-5 yr	400 (40)	244 (38)	156 (44)	0.05
>5 yr	406 (41)	261 (40)	145 (41)	0.85

Table 2. Continued

	Total (n=1001)	EBP (n=647)	No-EBP (n=354)	P-value
How was ADP determined, n (%)				
CSF in epidural needle	509 (51)	323 (50)	186 (52)	0.43
CSF in catheter/positive aspiration test	112 (11)	60 (9)	52 (15)	0.009
Spinal anaesthesia after test dose	96 (10)	56 (9)	40 (11)	0.17
Classical signs PDPH postpartum	408 (41)	291 (45)	117 (33)	<0.001
Other symptoms (addition to classical PDPH), n (%)				
Nausea/vomiting	221 (22)	158 (24)	63 (18)	0.016
Auditory symptoms	179 (18)	142 (22)	37 (10)	<0.001
Diplopia	18 (2)	15 (2)	3 (1)	0.094
Dizziness	240 (24)	162 (25)	78 (22)	0.29
Any other visual symptoms	126 (13)	90 (14)	36 (10)	0.088
Tinnitus	103 (10)	74 (11)	29 (8)	0.11
Other	155 (15)	108 (17)	47 (13)	0.15
Patient sent home before symptoms first presented, n (%)	80 (8)	61 (9)	19 (5)	0.023
Breastfeeding despite PDPH, n (%)	(n=954) 840 (88)	(n=611) 516 (84)	(n=343) 324 (94)	<0.001
Location of the headache, n (%)				
Temporal	243 (24)	182 (28)	61 (17)	<0.001
Occipital	571 (57)	386 (60)	185 (52)	0.024
Frontal	662 (66)	441 (68)	221 (62)	0.067
Neck	628 (63)	437 (68)	191 (54)	<0.001
Shoulder	234 (23)	163 (25)	71 (20)	0.066
Other	37 (4)	28 (4)	9 (2)	0.15
Type of conservative treatment before diagnosis, n (%)				
Paracetamol	654 (65)	462 (71)	192 (54)	<0.001
NSAID	521 (52)	356 (55)	165 (47)	0.011
Caffeine	249 (25)	166 (26)	83 (23)	0.44
Opioids	113 (11)	85 (13)	28 (8)	0.012
Fluids	339 (34)	225 (35)	114 (32)	0.41
Bed rest	363 (36)	244 (38)	119 (34)	0.2

Abbreviations: ADP, accidental dural puncture; EBP, epidural blood patch; IQR, inter-quartile range; PDPH, postdural puncture headache.

Results of stepwise logistic regression analysis are shown in Table 3. The following interesting factors were independently associated with a greater chance of receiving an EBP: pain intensity at diagnosis (odds ratio [OR] 1.29 per unit NRS increase), 17 G epidural needle (OR 5.43 compared with 18G), auditory symptoms (OR 1.64), and multiparity (OR 1.72). Interesting factors independently associated with a greater chance of not receiving an EBP were use of air as the medium for detecting loss of resistance (LoR) (OR 0.45), catheter placed intrathecally after ADP (OR 0.53), and a previous history of PDPH (OR 0.36).

Table 3. Results of stepwise logistic regression to identify independent variables for outcome EBP treatment choice (yes/no).

	OR (95%CI)	P-value
NRS pain intensity at PDPH, per unit	1.29 (1.19-1.41)	<0.001
Type of conservative treatment before diagnosis		
Paracetamol	1.90 (1.34-2.68)	<0.001
Caffeine	0.74 (0.49-1.10)	0.13
Media for detecting loss of resistance		
Air	0.45 (0.29-0.67)	<0.001
Saline	Ref	
Both	1.36 (0.33-5.58)	0.67
Catheter placed intrathecally after ADP	0.53 (0.36-0.78)	0.001
Needle size		
16G	0.92 (0.47-1.82)	0.82
17G	5.43 (2.64-11.1)	<0.001
18G	Ref	
19-20G	2.62 (0.61-11.3)	0.2
Occupation		
Administration	1.15 (0.70-1.90)	0.58
Teaching	1.03 (0.56-1.92)	0.91
Healthcare	1.47 (0.89-2.42)	0.13
Professional worker	Ref	
None	0.62 (0.40-0.96)	0.034
Breastfeeding despite PDPH	0.43 (0.24-0.76)	0.004
Location of the headache		
Temporal	1.59 (1.08-2.35)	0.019
Occipital	1.27 (0.91-1.75)	0.16
Frontal	1.57 (1.11-2.20)	0.01

Neck	1.50 (1.08-2.08)	0.014
Other	2.84 (1.13-7.11)	0.026
Other symptoms (addition to classical PDPH)		
Auditory symptoms	1.64 (1.05-2.56)	0.031
Medical history		
Neuraxial anaesthesia	0.73 (0.48-1.10)	0.13
PDPH	0.36 (0.14-0.88)	0.026
Chronic headache	1.93 (0.76-4.91)	0.17
Multipara	1.72 (1.18-2.51)	0.005
Patient sent home before symptoms first presented	1.88 (0.98-3.59)	0.056
Smoker	0.63 (0.39-1.02)	0.061
Level of insertion of epidural		
L1-2	1.18 (0.56-2.48)	0.66
L2-3	1.75 (1.18-2.61)	0.006
L3-4	Ref	
L4-5	1.22 (0.74-1.99)	0.43
Highest education		
Basic schooling	0.65 (0.39-1.08)	0.093
High school	0.64 (0.44-0.93)	0.019
University	Ref	
Mother's age (yr)		
≤24	0.88 (0.50-1.55)	0.66
25-29	1.11 (0.73-1.69)	0.63
30-34	Ref	
≥35	0.71 (0.48-1.05)	0.087

The potential independent variables were the patient characteristics variables (Table 1), the epidural technique variables and the PDPH symptoms and diagnosis variables (Table 2), and NRS intensity of headache at PDPH diagnosis.

Significance level for the variable selection criteria was 0.20. Complete cases analyses resulted in 945 subjects (603 EBP and 342 no-EBP). OR>1 indicates more patients to EBP treatment for the exposed category compared with nonexposed/reference.

Abbreviations: ADP, accidental dural puncture; CI, confidence interval; EBP, epidural blood patch; NRS, numeric rating score; OR, odds ratio; PDPH, postdural puncture headache.

Headache location, intensity, and time course

The location of the headache is shown in Table 2 and the intensity of headache at the time of diagnosis in different countries is shown in Supplementary table 1S. PDPH with only a minimal orthostatic component was reported by a total of 6.4% patients (8.8% vs 5.1% in the no-EBP vs the EBP group, $P=0.024$). The overall mean headache intensity (NRS, 0-10) was significantly higher in the EBP group, mean 8.0 (SD 1.8) compared with the no-EBP group, mean 6.9 (SD 2.3). Excluding Spain (that recruited many patients) from the analyses did not change the findings. Spontaneous recovery of headache after PDPH diagnosis and within 24 h occurred in 5.8% patients (12.2% vs 2.2% in the no-EBP vs the EBP group, $P<0.001$). The intensity of headache decreased significantly from PDPH diagnosis to 4 h after application of the EBP (mean 8.0 vs 1.5, $P<0.001$) (Fig. 3). However, 67/640 (10.5%) had a return of headache (NRS ≥ 7) within 24 h after the first EBP. On average, patients in both groups had mild headache (NRS < 3) after 7 days. When assessing all patients with severe headache at diagnosis (NRS ≥ 7), a significantly greater spontaneous reduction in NRS pain intensity from PDPH diagnosis was seen in favour of the no-EBP group compared with the EBP group within 24 h (adjusted mean difference 1.4, $P<0.001$) and after 7 days in favour of the EBP group (adjusted mean difference -1.0, $P<0.001$), but no significant difference was seen after 3 months (adjusted mean difference 0.2, $P=0.23$) (Table 4). These significant findings remained essentially the same with multiple imputation.

Table 4. Linear regressions comparing change in NRS pain intensity from PDPH diagnosis to 0–24 h, 7 days, and 3 months.

		NRS pain PDPH dx		NRS pain 0–24 h		Change of NRS pain			
	n	Mean (SD)	n	Mean (SD)	Mean change	Unadjusted (95% CI)	P-value	Adjusted**†‡§ (95% CI)	P-value
No-EBP	212	8.3 (1.1)	212	6.7 (2.6)	-1.5	Reference		Reference	
EBP	486	8.6 (1.1)	486	8.5 (1.7)	-0.1	1.4 (1.1–1.7)	<0.001	1.4 (1.0–1.7)	<0.001
		NRS pain PDPH dx		NRS pain 7 days		Change of NRS pain			
	n	Mean (SD)	n	Mean (SD)	Mean change	Unadjusted (95% CI)	P-value	Adjusted**†‡§ (95% CI)	P-value
No-EBP	202	8.3 (1.1)	202	1.8 (2.4)	-6.5	Reference		Reference	
EBP	420	8.6 (1.1)	420	1.0 (2.0)	-7.6	-1.1 (-1.5 to -0.7)	<0.001	-1.0 (-1.4 to -0.6)	<0.001
		NRS pain PDPH dx		NRS pain 3 months		Change of NRS pain			
	n	Mean (SD)	n	Mean (SD)	Mean change	Unadjusted (95% CI)	P-value	Adjusted**†‡§ (95% CI)	P-value
No-EBP	145	8.3 (1.1)	145	0.2 (0.7)	-8.2	Reference		Reference	
EBP	311	8.6 (1.1)	311	0.5 (1.7)	-8.1	0.1 (-0.2 to 0.4)	0.56	0.2 (-0.1 to 0.5)	0.23

Unadjusted and adjusted for NRS pain intensity at PDPH diagnosis, country, and other background variables selected from stepwise procedure (see statistical methods for details). Only subjects with complete information on NRS pain intensity, the background variables, and having NRS pain intensity ≥ 7 at PDPH diagnosis were included.

Abbreviations: ADP, accidental dural puncture; CI, confidence interval; dx, diagnosis; EBP, epidural blood patch; NRS, numeric rating score; OR, odds ratio; PDPH, postdural puncture headache; SD, standard deviation.

Notes for table 4:

* Adjusted for NRS pain intensity at PDPH and country of residence.

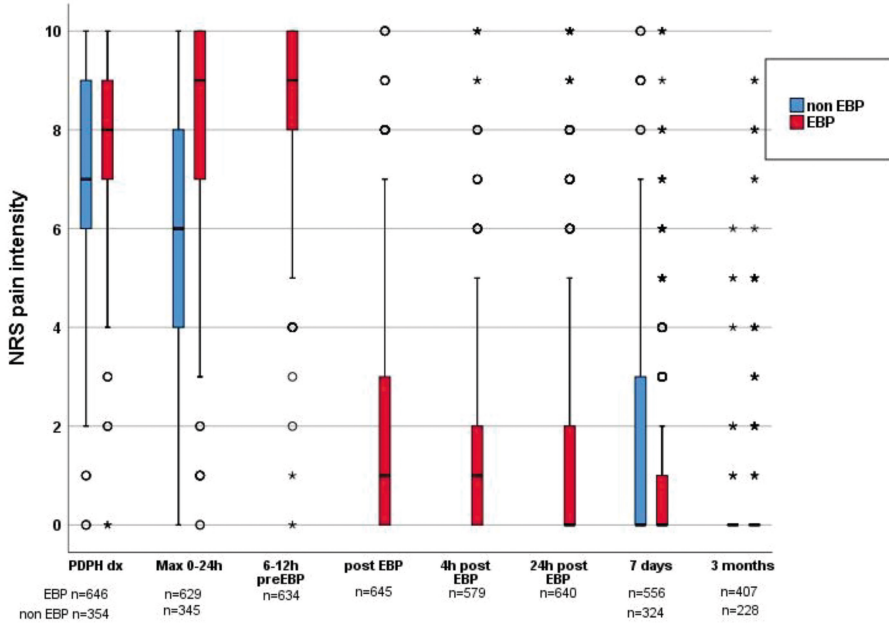
† Adjusted also for mother's BMI, occipital location of the headache at PDPH dx, other location of the headache at PDPH dx, patient sent home when first PDPH symptoms present, bed rest as conservative treatment before PDPH diagnosis, besides classical PDPH symptoms also nausea/vomiting symptoms present, besides classical PDPH symptoms also dizziness symptoms present, ADP was determined as classical signs of PDPH postpartum, ADP was determined as CSF in catheter or positive aspiration test, neuraxial anaesthesia as medical history, migraine as medical history, mother's occupation, and mode of delivery.

‡ Adjusted also for catheter placed intrathecally after ADP, besides classical PDPH symptoms also diplopia symptoms present, mode of delivery, temporal location of the headache at PDPH dx, neck location of the headache at PDPH dx, PDPH as medical history, and chronic headache as medical history.

§ Adjusted also for neck location of the headache at PDPH dx, mother can breastfeed her child, air or saline media for detecting loss of resistance, PDPH as medical history, occipital location of the headache at PDPH, smoking, education level, paracetamol as conservative treatment before PDPH diagnosis, besides classical PDPH symptoms also diplopia symptoms present, multiple attempts at inserting epidural needle at different levels.

§ Results from multiple imputation, adjusted NRS pain mean change from PDPH to 0–24 h 1.3 (95% CI 1.0 to 1.6) $P < 0.001$, to 7 days -1.1 (95% CI -1.5 to -0.7) $P < 0.001$ and to 3 months 0.1 (95% CI -0.2 to 0.4) $P = 0.54$.

Fig 3. Boxplot showing NRS pain intensity from PDPH diagnosis to 3 months in EBP and no-EBP groups.



In the EBP group, a significant decrease in NRS pain intensity was found from pre- to post-EBP ($P < 0.001$). The horizontal line in the box represents the median, the boxes inter-quartile range (IQR) and the whiskers min and max if no outlier present; outliers >1.5 times IQR are indicated as circles, outliers >3 times IQR are indicated as asterisks.

Abbreviations: dx, diagnosis; EBP, epidural blood patch; NRS, numeric rating score; PDPH, postdural puncture headache.

Management of PDPH after diagnosis

The median (IQR) time from epidural insertion to PDPH diagnosis was 31 (21-51.5) h and to EBP was 68.4 (47.7-96.8) h (Table 2). Other characteristics of epidural technique, diagnosis and management are also shown in Table 2. Sphenopalatine and/or occipital nerve block was performed in 3.3% patients, mostly from Portugal. From a total of 647/1001 (64.6%) who received an EBP, 127 women (19.6%) received a second blood patch because of recurrence of headache, and a further seven women (1.1%) received a third blood patch. When EBP was performed in <24 h from the PDPH diagnosis, a significantly greater number of patients received a second EBP (77/314, 24%) compared with when EBP was performed >24 h (50/321, 15%), $P = 0.002$.

Complications of epidurals, ADP and EBP

A total of 47/647 (7.3%) patients in the EBP group were further examined after failure of an EBP and 39/47 underwent CT/MRI examination. Five patients (0.8%) had the following

important findings: ICB (n=3), minimal subdural hematoma (n=1) (all seen on CT/MRI), intrathecal bleeding accompanied by the syndrome of reversible vasoconstriction (n=1) (seen on Doppler ultrasound), and probable aseptic meningitis (n=1) (classical symptoms with negative bacterial growth in CSF). Of the 635 patients (407 in the EBP group and 228 in the no-EBP group) who were followed up at 3 months, persistent backache was the commonest symptom reported by 14% (17% vs 8.8% in the EBP and no-EBP groups, respectively, $P=0.004$); the results continued to be statistically significant after excluding patients who had chronic backache before delivery (14.6% vs 7.5%, $P=0.01$). Persistent headache (NRS ≥ 3) at 3 months was reported by 5.0% patients (6.9% vs 1.7% in the EBP and no-EBP group, respectively, $P<0.001$). The commonest other symptoms included neck stiffness, auditory and visual symptoms, and nausea. In all, 10.1% patients were receiving medication (12.0% in EBP group and 6.6% in no-EBP group, $P=0.028$) for either headache or backache at 3 months.

DISCUSSION

ADP during initiation of epidural labour analgesia often causes PDPH affecting >10 000 women in Europe each year and affects postpartum maternal well-being, maternal-neonatal bonding and breastfeeding, and may delay hospital discharge. In this international, prospective, multicentre, cohort study, we were interested in determining the current practices in the management of PDPH, the factors that led the physician to choose between the application of EBP or conservative treatment only, and the outcome after 3 months for patients treated by EBP or conservatively. We found that, although EBP was the preferred method for management of PDPH, it was performed less frequently (<50%) in Spain, Portugal, Italy, and Greece. The precise explanation for this difference in observed practice between countries remains unclear from the present study, but institutional guidelines, obstetric anaesthesia practices, and individual physician preference may have contributed to these differences.[13]

Factors associated with conservative management (no-EBP) were the use of an ITC after ADP and the use of air as a medium for detection of LoR. There is mixed evidence from the literature regarding leaving an ITC in place after ADP on subsequent development of PDPH and the reduced need for an EBP.[14-16] This could be because of local inflammation or plugging of the dural hole which reduces CSF leakage, but this needs to be further evaluated in prospective, randomised studies.[17,18]

The use of air or saline for detection of LoR remains controversial, but a recent Cochrane review found no difference in several endpoints, including PDPH, using either technique. [19] Accidental injection of air intrathecally results in an almost immediate onset of PDPH (<1 h), with a shorter duration compared with PDPH after using saline for LoR.[20] This rapid onset and faster recovery of headache may explain the reduced application of an EBP for management of PDPH after the use of air for LoR.

Factors significantly related to physician choice for EBP included increasing intensity of PDPH after initial diagnosis ($\text{NRS} \geq 7$), use of a larger gauge epidural needle ($< 18\text{G}$), headache presenting dominantly in the frontotemporal or neck region, multiparity, and the presence of auditory symptoms. The intensity of headache is often a determining factor in treatment choice, which is confirmed in this study with stepwise regression analysis demonstrating the odds of receiving an EBP increase per unit increase in NRS headache intensity at PDPH diagnosis. Indeed, guidelines in France recommend that conservative management without EBP should preferably be used when the intensity of PDPH is mild to moderate.

Localisation of headache and the presence of auditory symptoms may influence the physician choice. It has been demonstrated before that large diameter epidural needles cause more severe headaches. The increased use of EBP in multiparous women is intriguing. It is likely that multiparas mobilise earlier, causing a more severe headache because of increased CSF leakage and therefore an increased use of EBP. One study, however, found that earlier mobilisation did not lead to more severe headache.[21]

In our present study, headache intensity declined significantly within 4 h after application of an EBP, which is important from a patient perspective. The speed of decline in the no-EBP group after the first 24 h is unknown, as we did not assess headache intensity daily. In both groups, headache at 7 days was, on average, either absent or mild ($\text{NRS} < 3$).

When assessing patients with only severe PDPH ($\text{NRS} \geq 7$) at diagnosis and comparing the EBP group and the no-EBP group, we found a small but statistically significant mean difference of 1 NRS unit in favour of the EBP group at 7 days. The clinical relevance of this small difference is disputable. In agreement with previous studies we found that about one in five patients had a recurrence of headache 24-48 h after the initial EBP requiring the application of a new EBP.[22] The reasons for this and an analysis of failure of EBP are not within the scope of the present study, but will be discussed in a later sub-analysis of data from European Practices in the Management of Accidental Dural Puncture (EPiMAP).

Towards the end of recruitment in 2018, some case reports and series were published describing the use of sphenopalatine ganglion or occipital nerve block as a management strategy for PDPH with favourable results.[9] Unfortunately, in our present study, there were very few cases reported since it was not an obligatory question, and mostly from Portugal, and therefore it is difficult to make any definite conclusions based on this data. Further studies are keenly awaited on this method of management of PDPH.

It is important to study the complications that may arise from administration of an EBP compared with conservative treatment. Although EBP is clearly efficacious, fear remains that its application may cause a new ADP, the headache may not resolve or there may be serious or persistent complications. In our study, five patients had serious complications, three of them being ICB, which were all identified in the EBP group (5 of 647 patients, 0.46%) when further

diagnostic methods such as CT/MRI were applied after the first or second EBP failure. These results are comparable to the known increased incidence of ICB in obstetric PDPH patients, but the relation with the EBP is not clear.[23] PDPH which does not recover spontaneously or after EBP, change character, or if there are new focal neurological signs should arouse suspicion of an intracranial complication and neuro-imaging, should then be considered.

Patients receiving an EBP showed a statistically higher incidence of chronic headache and backache and an increased use of analgesics at 3 months, compared with the no-EBP group. This finding contradicts results from several retrospective case-control series, which reported lower or unchanged incidences in patients who received an EBP.[24,25] The overall incidence of both chronic headache and backache was lower though in our prospective cohort, which measured only moderate to severe headache (NRS \geq 3) instead of any headache or backache.

STUDY LIMITATIONS

Although the data presented are robust and the conclusions meaningful, many countries and centres were involved in data collection, and there may be physician or centre bias in patient management. We did not enquire about headache intensity each day during the first 7 days, which did not allow comparisons of headache dynamics over time between the EBP and no-EBP group. The results of maximal headache intensity 0-24 h after PDPH diagnosis (shown in Fig. 3 and Table 4) should be interpreted with caution because only half the patients had received an EBP within 24 h after PDPH diagnosis and the maximum 0-24 h intensity was assessed. Since this is a cohort study, the EBP intervention was not randomised, and therefore the mean pain intensity comparison between the EBP and no-EBP groups over time should be interpreted with some caution. The diagnostic criteria for PDPH also changed during the study period. The description of the orthostatic component of PDPH changed from 'headache that worsens within 15 min of sitting/standing and improves within 15 min of lying down' to 'usually but not invariably orthostatic and therefore cannot be relied upon as the diagnostic criteria'. [12,26] However, we used the criteria suggested by Amorim and colleagues[11] in 2012, which were based on the diagnostic criteria of PDPH by the International Headache Society from 2004. Another limitation of our study is that we did not collect baseline data on the number of epidurals performed, the actual number of dural punctures during the study period (including patients not recruited into the study), or the clinical course of patients having an ADP but not developing PDPH. Although these data would be interesting to determine the precise incidence of PDPH in different countries, they may not add any further relevant information regarding risk factors, management, and time course of PDPH. Finally, we did not include smaller centres (<500 deliveries/year) since experience in performing EBP at these centres may be limited.

CONCLUSIONS

In this pragmatic, observational study, 65% of patients received an EBP with large geographical variation. A greater headache intensity appeared to favour application of EBP by physicians, while the use of an ITC favoured a conservative approach. Patients treated with an EBP had rapid relief of symptoms, but about one in five patients required a second EBP. Almost all

patients had only mild headache at 7 days. Intracranial bleeding occurred in three patients and, although rare, should be a differential diagnosis in non-resolving headaches.

SUPPLEMENTARY DATA

Table 1S. Intensity of headache in different countries at the time of post-dural puncture headache (PDPH) diagnosis is shown.

Country	Total (n=1001)		EBP (n=647)		Non-EBP (n=354)		P-value
	n	Mean NRS (SD)	n	Mean NRS (SD)	n	Mean NRS (SD)	
Spain	228	7.6 (2.1)	110	8.1 (1.6)	118	7.1 (2.3)	<0.001
Portugal	127	7.3 (1.9)	60	7.7 (1.8)	67	7.0 (2.0)	0.035
Sweden	105	7.9 (1.8)	84	8.1 (1.8)	21	7.0 (1.9)	0.017
France	90	7.6 (2.2)	85	7.8 (2.0)	5	4.6 (2.1)	0.001
Germany	73	7.6 (1.7)	56	7.7 (1.7)	17	7.2 (1.8)	0.29
Netherlands	53	8.0 (2.1)	46	8.0 (2.2)	7	8.0 (1.3)	0.96
Belgium	46	8.0 (1.8)	42	8.2 (1.7)	4	6.5 (1.9)	0.064
Israel	32	8.4 (1.9)	25	8.8 (1.1)	7	6.8 (3.2)	0.013
Greece	31	7.0 (2.5)	8	7.2 (2.0)	23	6.9 (2.7)	0.72
Norway	30	7.5 (1.9)	22	7.6 (2.2)	8	7.1 (0.6)	0.52
Finland	27	8.1 (1.5)	22	8.1 (1.6)	5	8.0 (1.2)	0.86
Switzerland	27	8.4 (1.6)	22	8.5 (1.6)	5	7.8 (1.8)	0.38
Italy	30	7.4 (2.0)	5	9.4 (0.5)	15	6.7 (1.8)	0.003
Croatia	18	7.7 (2.5)	12	8.7 (1.4)	6	5.7 (3.1)	0.012
Czech Rep	18	6.9 (1.6)	9	7.1 (1.6)	9	6.8 (0.5)	0.67
Serbia	11	8.4 (1.4)	1	7.0 (0.0)	10	8.5 (1.4)	NA
Turkey	11	7.9 (2.0)	4	8.5 (1.3)	7	7.6 (2.3)	0.48
Lithuania	10	4.3 (2.9)	3	7.7 (1.2)	7	2.8 (2.0)	0.006
Slovenia	10	5.9 (2.8)	1	7.0 (0.0)	9	5.8 (3.0)	NA
Poland	9	7.1 (2.0)	7	7.8 (1.2)	2	4.5 (2.1)	0.019
Denmark	7	8.1 (1.8)	7	8.1 (1.8)	0	NA	NA
Iceland	7	7.4 (1.7)	7	7.4 (1.7)	0	NA	NA
Slovakia	7	8.1 (1.3)	7	8.1 (1.3)	0	NA	NA
Malta	4	7.0 (1.8)	2	7.0 (1.4)	2	7.0 (2.8)	>0.99
All patients	1.001	7.6 (2.0)	647	8.0 (1.8)	354	6.9 (2.3)	<0.001

Abbreviations: NRS, numeric rating scale; SD, standard deviation.

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