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RESEARCH ARTICLE

Differential efficacy with epidural blood and fibrin patches for the treatment of post-dural puncture headache

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Abstract

Background: Accidental dural puncture (ADP) is the most frequent major complication when performing an epidural procedure in obstetrics. Consequently, loss of pressure in the cerebrospinal fluid (CSF) leads to the development of post-dural puncture headache (PDPH), which occurs in 16%–86% of cases. To date, the efficacy of epidural fibrin patches (EFP) has not been evaluated in a controlled clinical trial, nor in comparative studies with epidural blood patches (EBP).

Methods: The objective of the present study was to compare the efficacy of EFP with respect to EBP for the treatment of refractory accidental PDPH. This prospective, randomized, open-label, parallel, comparative study included 70 puerperal women who received an EBP or EFP (35 in each group) after failure of the conventional analgesic treatment for accidental PDPH in a hospital.

Results: A higher percentage of women with EFP than EBP achieved complete PDPH relief after 2 (97.1% vs. 54.3%) and 12 h (100.0% vs. 65.7%) of the patch injection. The percentage of patients who needed rescue analgesia was significantly lower with EFP after 2 (2.9% vs. 48.6%) and 12 h (0.0% vs. 37.1%). After 24 h, PDPH was resolved in all women who received EFP. The recurrence of PDPH was reported in one woman from the EBP group (2.9%), who subsequently required a second patch. The mean length of hospital stay was significantly lower with EFP (3.9 days) than EBP (5.9 days). Regarding satisfaction, the mean value (Likert scale) was significantly higher with EFP (4.7 vs. 3.0).

Conclusions: EFP provided better outcomes than EBP for the treatment of obstetric PDPH in terms of efficacy, safety, and patient satisfaction.

KEYWORDS
blood, dural, epidural, fibrin, headache, patch, puncture

INTRODUCTION

Accidental dural puncture (ADP) is the most frequent major complication when performing an epidural procedure in obstetrics.[1] The incidence of ADP ranges from 0.5% to 3.5% in university hospitals.[2] Consequently, the loss of pressure in the CSF leads to the development of post-dural puncture headache (PDPH), which occurs in as much as 16%–86% of cases[3] and higher than 70% according to other studies.[4,5] The severity of PDPH depends on the CSF volume lost via leakage, output flow speed, and the patient's features.[6] Gauge and needle type, the patient's age, or the physician's experience also contribute to PDPH incidence.[7,8] The pathognomonic characteristic of PDPH is its orthostatic component[9] sometimes associated with cranial nerve neurological symptoms.[10] The management of accidental PDPH requires conservative treatment: relative rest (avoiding Valsalva maneuvers), prevention of constipation (through diet), oral and intravenous hydration

(3000 mL/day), 100 mg intravenous hydrocortisone, 50 mg/8 h intravenous dexketoprofen, 300 mg/8 h oral caffeine (if not breastfeeding), and 1 g/6 h oral paracetamol (as rescue medication).[11] Notwithstanding, in some cases, interventional therapy is needed.[12,13] This frequently involves the use of an autologous epidural blood patch (EBP) to assist in closing the CSF leakage as a definitive treatment.[14] Epidural blood patches have a variable rate of success. Prospective studies suggest complete and permanent headache relief after one EBP in up to one-third of women with PDPH following a dural puncture with an epidural needle, but 50%–80% of partial relief is included.[15] Frequently, the technique is partially effective or ineffective in providing complete pain relief.[16,17] EBP is a technique that is not exempt from the risk of developing adverse effects and complications, possibly related to the injected blood volume. Previous studies have reported lumbar discomfort (78%), lumbar pain (35%–54%), pain in the legs or buttocks (12%), fever (5%), sensory impairments and weakness in the legs (18%), or radicular pain in the sciatic nerve.[18-26] Less frequent are complications such as arachnoiditis, meningeal irritative reaction, paraparesis and cauda equina syndrome, facial nerve paralysis and partial brachial plexopathy, and subdural hematoma.[20,21,22,23,25] Epidural fibrin patches (EFP) represent an alternative to EBPs with persistent orthostatic headaches. The successful use of 3–5 mL fibrin glue, injected through an epidural needle in the treatment of PDPH and headaches associated with spontaneous intracranial hypotension, has been reported.[27-32] The EFP imitates the final stages of the coagulation cascade that leads to the development of the fibrin clot.[33] The EFP has been used to repair dura mater and close CSF leaks in neurosurgery. In neurology and anesthesiology, it has also been used in PDPH cases which are refractory to conventional treatment.[34,35] The volume of fibrin to achieve a satisfactory result is lower than that of blood, as it dispenses with the plasmatic volume. A volume of 1.4 mL of fibrin has been shown to be effective in animal models in stopping spinal fluid flow; the greater viscosity of this compound provides higher pressure than that caused by a larger blood volume.[36] By contrast with a larger volume of autologous blood to restore cerebrospinal pressure, we consider that the properties of fibrin support our hypothesis of adhesiveness and viscosity. Aseptic meningitis[35] and allergic reactions[37] associated with the administration of fibrin glue can occur exceptionally.

To our knowledge, the efficacy of EFP has not yet been elucidated in a controlled clinical trial or in a large series of obstetric patients. Also, none of the studies have been specifically designed to evaluate alternatives. Therefore, the objective of the present study was to compare the efficacy of EFP with respect to EBP for the treatment of refractory accidental PDPH in obstetric anesthesia.

METHODS

This prospective, randomized, open-label, parallel, comparative study included puerperal women who received an EBP or EFP, after failure of the conventional analgesic treatment for accidental PDPH, due to labor epidural in a public tertiary hospital. The study was approved by the hospital's Ethics Committee. Inclusion criteria to participate in the study were: women; aged 18–40; weighing 40–100 kg; vaginal delivery; diagnosis[38] and known localization of the ADP (done with an 18 G Tuohy needle or 19 G catheter); carrying out a preventive and conservative analgesic therapy without significant pain relief at 24 h; persistent moderate to severe PDPH; and signing an informed consent. Preventive treatment was applied to all patients. Conservative treatment was similar to the preventive one but adding 300 mg/8 h oral caffeine (if not breastfeeding), and 1 g/6 h oral paracetamol (as rescue medication). Exclusion criteria included: multiple dural punctures (or at different levels); combined epidural anesthesia; cesarean delivery; complementary intravenous opioid analgesia for delivery; allergy to any compound used in the study; fever (≥38°C); coagulation disorders; local or systemic infection; and history of neurological disease or major psychiatric disorder.

Patients were randomized (in blocks) to receive EBP (group A) or EFP (group B). Both patch injections were made under surgical conditions. A total of 15 mL fresh blood extracted from the patient antecubital vein and 6 mL fibrin sealant (Tissucol Duo®, Baxter S.L. Valencia, Spain) was administered at 0.3 and 1 mL/s speed flow in the EBP and EFP injections, respectively. Afterward, patients stayed in supine position in bed, and received 1 g/6 h paracetamol (as rescue analgesic medication, if required).

The primary endpoint was the comparison of efficacy between treatments regarding pain relief. The main variable included the identification of PDPH and its severity. It was classified on a multidimensional verbal scale divided into four categories,[10] from absence of PDPH (value 1) to mild (value 2), moderate (value 3), and severe PDPH (value 4). This approach considers not only the intensity of pain but also the functional status and the impact of pain on it. Mild PDPH was defined as an orthostatic headache that slightly restricts daily activities, does not confine the patient to bed, and is not associated with other symptoms. Moderate PDPH was defined as an orthostatic headache that forced the patient to stay in bed for most of the day and is not frequently associated with other symptoms. Severe PDPH was defined as an orthostatic headache that forced the patient to stay in bed the entire day, and was associated with symptoms such as nausea, vomiting, dizziness, hearing loss, hyperacusis, photophobia, photopsia, diplopia, neck stiffness, or neck pain.[10]

Effectiveness was evaluated according to PDPH relief provided by the treatment. This relief was considered as

complete (when PDPH and associated symptoms were resolved), incomplete (if a mild, recurrent PDPH remained, but could be tolerated and thus a second patch was not required), or failure/null relief (when the intensity of the PDPH invariably remained, and a second patch was required). Recurrence of PDPH was defined as the development of a new headache after being previously resolved, or as an increase in severity after previous significant relief.

Secondary endpoints included additional efficacy outcomes (such as recurrence/persistence of the headache, need for rescue analgesia, length of hospital stay, and re-admission in the hospital), satisfaction with the treatment, and the safety profile of the treatments. Satisfaction was measured using a 0 to 5 Likert scale, ranging from 0 (not at all satisfied) to 5 (extremely satisfied). All variables were evaluated 2 h, 12 h, and 30 days after the patch injection.

Despite the fact that the study was not blinded for the patient and the specialist performing the patch injection, it is necessary to remark that the latter was always the same in all cases. Moreover, the specialist who evaluated the patients during the visits, the person who analyzed the data, and the statistical analyst were not aware of the group the patients belonged to.

Based on our previous clinical experience, to calculate the sample size, a statistical power at 80% and a two-sided confidence interval of 95% were considered to detect a difference >50% between groups (PDPH severity as dependent variable and EFP as independent variable). Continuous variables are expressed as mean and standard deviation (SD), whereas categorical ones as absolute and relative frequencies. Comparisons between groups regarding evaluated variables were analyzed using the chi-square test, *t*-test, or Pearson's chi-square test, as appropriate. Statistical significance was established with $p < 0.05$. All statistical procedures were carried out with SPSS© version 15.0 software, Chicago, SPSS Inc.

RESULTS

A total of 87 women were initially recruited; however, 70 finally agreed to participate in the study, 35 women in each group (Figure 1). The sample was homogeneous for age, weight, height, smoking habits, ASA physical

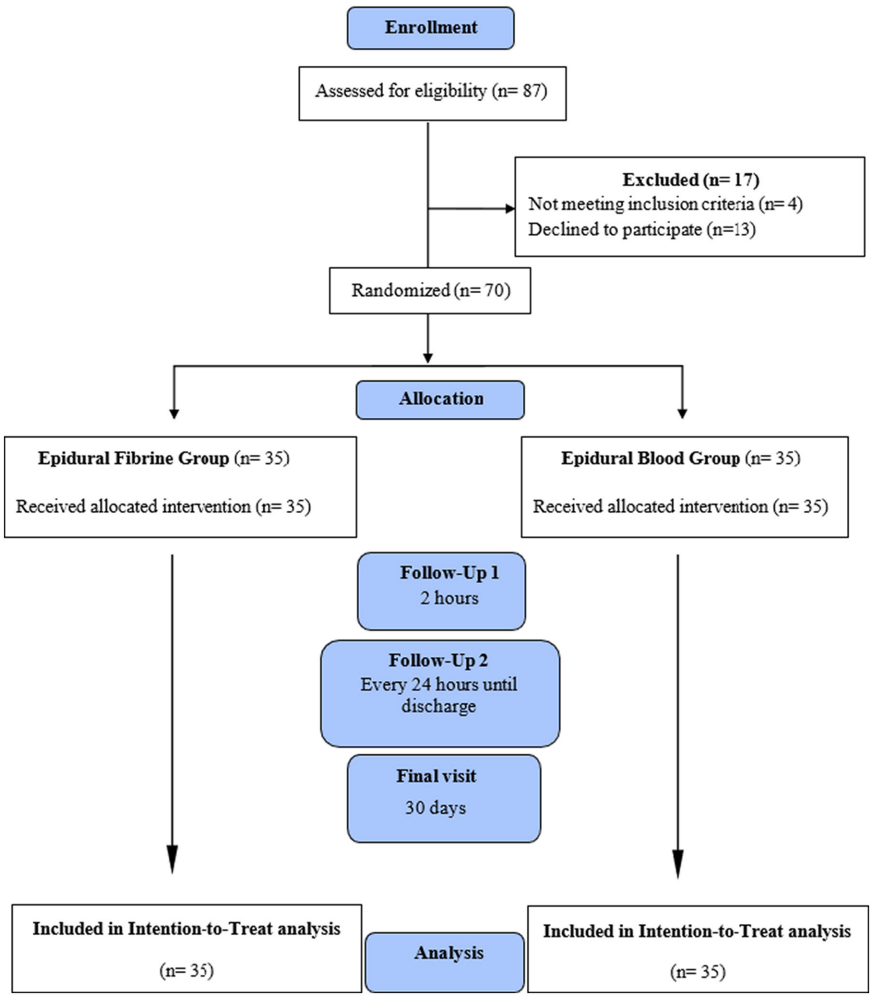

FIGURE 1 Patients flow diagram.

status, location of epidural puncture, type of delivery, and initial PDPH severity. Their mean age was 28.3 years (SD: 5.2), and body mass index was 28.0 kg/cm^2 (SD: 5.5; Table 1). The mean time between PDPH onset and the initiation of the treatment was 2.6 days (SD: 0.6). Most women had an American Society of Anesthesiologists (ASA) physical status of 1 (78.6%), and a spontaneous delivery (77.1%). The epidural puncture was predominantly located at L3-L4 (68.6% of cases). No women had a history of previous PDPH. Additional symptoms associated with PDPH included visual (35.7%), hearing (50.0%), cervical (48.6%), and vegetative ones (51.4%). Significant differences between groups were found regarding mean time between PDPH onset and initiation of the treatment (higher in EBP, 2.8 days vs. 2.4 days for EFP; $p=0.005$), hearing symptoms (greater in EFP; 28.6% vs. 71.4%; $p<0.001$), and mean number of additional symptoms that present with headache (1.5 vs. 2.2; $p=0.007$; Table 1).

A higher percentage of women with EFP achieved complete PDPH relief after 2 (97.1% vs. 54.3%) and 24 h (100.0% vs. 65.7%) of the patch injection (Table 2). The percentage of patients needing rescue analgesia was significantly lower with EFP after 2 (2.9% vs. 48.6%; $p<0.001$) and 24 h (0.0% vs. 37.1%; $p<0.001$) of the patch injection. Additionally, the number of rescue doses was also lower in the EFP group. After 2 h, 2.9% of patients

TABLE 1 Sociodemographic and clinical characteristics of patients.

	Epidural blood patch (*N*=35)	Epidural fibrin patch (*N*=35)	*p*-Value
Age, mean years (SD)	28.6 (5.0)	28.1 (5.5)	0.699
Weight, mean kg (SD)	75.4 (11.8)	76.5 (17.2)	0.765
Height, mean cm (SD)	163.5 (6.3)	165.1 (6.2)	0.260
Body mass index, mean kg/cm^2 (SD)	28.1 (4.1)	27.9 (6.7)	0.915
Smoking habits, *n* (%)			
No	32 (91.4)	31 (88.6)	0.690
Yes	3 (8.6)	4 (11.4)	
ASA physical status classification system, *n* (%)			
1	25 (71.4)	30 (85.7)	0.134
2	10 (28.6)	4 (11.4)	
3	0 (0.0)	1 (2.9)	
Location of epidural puncture, *n* (%)			
L2-L3	8 (22.9)	13 (37.1)	0.283
L3-L4	26 (74.3)	22 (62.9)	
L4-L5	1 (2.9)	0 (0.0)	
Type of delivery, *n* (%)			
Spontaneous	27 (77.1)	27 (77.1)	0.513
Assisted			
Vacuum	7 (20.0)	5 (14.3)	
Forceps	1 (2.9)	3 (8.6)	
Time between PDPH onset and initiation of treatment, mean days (SD)	2.8 (0.6)	2.4 (0.6)	0.005
Severity of the PDPH, *n* (%)			
Moderate	13 (37.1)	8 (22.9)	0.192
Severe	22 (62.9)	27 (77.1)	
Additional symptoms, *n* (%)[a]			
Visual	11 (31.4)	14 (40.0)	0.454
Hearing	10 (28.6)	25 (71.4)	<0.001
Cervical	18 (51.4)	16 (45.7)	0.632
Vegetative	14 (40.0)	22 (62.9)	0.056
Mean number of additional symptoms that present with headache (SD)	1.5 (0.9)	2.2 (1.2)	0.007

Note: Values are mean (SD) or number (proportion).

Abbreviations: ASA, American Society of Anesthesiologists; PDPH, post-dural puncture headache; SD, standard deviation.

[a]Additional symptoms included: hearing (tinnitus/hearing loss, and hyperacusis), visual (photophobia, photopsia, hemianopsia, and diplopia), cervical (stiffness and pain in neck), and vegetative (nausea, vomiting, and dizziness).

TABLE 2 Efficacy results of treatments during the follow-up.

	2 h after patch injection			24 h after patch injection			30 days after patch injection		
	Epidural blood patch ($N=35$)	Epidural fibrin patch ($N=35$)	*p*-Value	Epidural blood patch ($N=35$)	Epidural fibrin patch ($N=35$)	*p*-Value	Epidural blood patch ($N=35$)	Epidural fibrin patch ($N=35$)	*p*-Value
PDPH relief, *n* (%)			<0.001			0.001			NA
Complete	19 (54.3)	34 (97.1)		23 (65.7)	35 (100.0)		NA	NA	
Incomplete	15 (42.9)	1 (2.9)		11 (31.4)	0 (0.0)		NA	NA	
Failure	1 (2.9)	0 (0.0)		1 (2.9)	0 (0.0)		NA	NA	
Recurrence of headache, *n* (%)	0 (0.0)	0 (0.0)	NA	1 (2.9)	0 (0.0)	NA	1 (16.7)	0 (0.0)	NA
Intensity of PDPH, *n* (%)			0.001			0.006			0.029
Mild	7 (20.0)	1 (2.9)		3 (8.6)	0 (0.0)		6 (17.1)	0 (0.0)	
Moderate	9 (25.7)	0 (0.0)		6 (17.1)	0 (0.0)		1 (2.9)	0 (0.0)	
Severe	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)		1 (2.9)	0 (0.0)	
Need for rescue analgesia, *n* (%)	17 (48.6)	1 (2.9)	<0.001	13 (37.1)	0 (0.0)	<0.001	9 (25.7)	2 (5.7)	0.022

Note: Values are number (proportion).
Abbreviations: NA, not applicable; PDPH, post-dural puncture headache.

needed a rescue dose (consisting of two analgesic doses), compared to 42.8%, 8.6%, and 5.7% of patients in the EBP group that needed one, two, and three doses, respectively. After 24 h, only patients from the EBP group required one (5.7%), three (5.7%), or four doses (25.7%). After 2 h, 2.9% of the EFP group and 42.9% of patients of the EBP group achieved incomplete headache relief. After 24 h, all women receiving EFP resolved the PDPH and were discharged.

The recurrence of the PDPH was reported in one woman from the EBP group (2.9%), who subsequently required a second patch. After 30 days of the patch injection, all women who received EFP remained with no PDPH, whereas eight patients (22.9%) from the EBP group continued to experience it. The severity of the PDPH in these patients was predominantly mild (17.1%), followed by moderate (2.9%) and severe (2.9%). At this follow-up visit, the percentage of patients needing rescue analgesia was also significantly lower with EFP (5.7% vs. 25.7%; $p=0.022$).

A total of 21 adverse events (AEs) immediately after the technique were reported. These AEs were mild and transient, especially lumbar discomfort/pain (86.4%) followed by nausea/vomiting (4.5%) and dizziness (4.5%). The main complication was lumbar radiculopathy that was six times more frequent in the EBP group (Table 3). The length of hospital stay was significantly lower with EFP (mean: 3.9 days, SD: 0.7) than EBP (mean: 5.9 days, SD: 2.6; $p<0.001$, Table 4). Moreover, three women from the EBP group (8.6%) were re-hospitalized.

Regarding satisfaction, the mean value (Likert scale) was significantly higher with EFP (mean: 4.7, SD: 0.5) than EBP (mean: 3.0, SD: 0.8; $p<0.001$). The percentage of women reporting "extreme satisfaction" with the treatment was greater with EFP (68.6% vs. 0.0%).

DISCUSSION

The EBP is the treatment of choice for PDPH with severe symptoms.[39] To date, the efficacy of EFP has not been evaluated in a controlled clinical trial, nor in comparative studies with EBP. According to the available literature, the efficacy of EBP ranges from 61% to 75%, and the failure rate is approximately 40%.[5,40,41] For obstetric patients, the failure rate of EBP in achieving complete pain relief varies between 65% and 75%, especially in the first 48 h after dural puncture.[15,42] Even a residual headache often remains in these cases. The recurrence rate (after a successful procedure) may reach 71% in some cases.[16]

The present study compared the analgesic efficacy of 6 mL EFP with respect to 15 mL EBP in patients with accidental PDPH and who were refractory to conventional analgesic therapy. After 2 h, the EFP achieved a complete PDPH relief rate of 97.1% (versus 42.9% with EBP), and after 24 h, of 100.0% vs. 65.7%. Efficacy results with

TABLE 3 Treatment-related adverse events and epidural procedure-related complications.

	Epidural blood patch (*N*=35)	Epidural fibrin patch (*N*=35)	*p*-Value
Adverse events, *n* (%)			
Lumbar discomfort/pain	15 (88.2)	4 (80.0)	0.259
Nausea/vomiting	1 (5.9)	0 (0.0)	
Dizziness	0 (0.0)	1 (20.0)	
Complications, *n* (%)			
Lumbar radiculopathy	6 (46.1)	1 (100.0)	0.939
Lumbar discomfort/pain	2 (15.2)	0 (0.0)	
Cervical radiculopathy	2 (15.2)	0 (0.0)	
Headache	1 (7.6)	0 (0.0)	
Fever	1 (7.6)	0 (0.0)	
Monoparesis	1 (7.6)	0 (0.0)	

Note: Values are number (proportion).

TABLE 4 Additional results at the end of the follow-up.

	Epidural blood patch (*N*=35)	Epidural fibrin patch (*N*=35)	*p*-Value
Hospital length of stay, mean days (SD)	5.9 (2.6)	3.9 (0.7)	<0.001
Unplanned consultations to the specialist, mean (SD)	0.4 (0.8)	0.0 (0.0)	NA
Re-admissions in the hospital, *n* (%)	3 (8.6)	0 (0.0)	NA
Degree of satisfaction, *n* (%)			
Not at all satisfied	1 (2.9)	0 (0.0)	<0.001
Slightly satisfied	9 (25.7)	0 (0.0)	
Moderately satisfied	15 (42.9)	1 (2.9)	
Very satisfied	10 (28.6)	10 (28.6)	
Extremely satisfied	0 (0.0)	24 (68.6)	
Mean (0–5 Likert) value (SD)	3.0 (0.8)	4.7 (0.5)	

Note: Values are mean (SD) or number (proportion).
Abbreviations: NA, not applicable; SD, standard deviation.

EBP were in concordance with previous reports. Banks et al.[15] reported that, in a series of 100 women with ADP, 81% experienced PDPH, and 72% received EBP (7–25 mL of autologous blood). Of them, 67% and 95% achieved complete or partial relief, respectively.

The low efficacy of EBP could be attributed to the blood volume, as diverse studies have recommended the administration of a volume not lower than 20 mL,[3] and the way we measured pain relief using a categorical scale. Paech et al.[43] observed less pain relief when administering 15 mL of EBP than 20–30 mL, within the first 48 h of the epidural injection. By contrast, Taivanen et al.[17] did not show any additional benefit in the immediate relief of the headache by increasing the blood volume. Moreover, Szeinfeld et al. also considered 15 mL of blood as an ideal volume in EBP, while avoiding an increase in lumbar discomfort.[44] The recurrence rate of PDPH was 31%, lower than in previous studies, which used 16 G epidural needles[16]; or a recurrence attributed to a blood volume lower than 20 mL.[17] In our study, a second patch was only required in one patient from the EBP group (2.9%) after 24 h. This observation is also lower than in other reports. According to Taivainen et al.,[17] the incidence of PDPH in obstetric cases with 18 G Tuohy epidural needles ranges between 37% and 50%, due to inefficacy of EBP or recurrence of the PDPH after hospital discharge. Van de Velde et al.,[45] in a 10-year experience study on PDPH, reported 15% of cases requiring a second EBP (involving diverse types of needles and epidural procedures). Yet, 17.1% of our patients receiving EBP showed moderate PDPH 24 h after the injection, but they preferred not to repeat the procedure. Therefore, the decision to undergo, or not, a second EBP was subject to diverse factors.

Overall, the good results achieved in the EBP group might derive from the homogeneity of the sample in terms of age, and unique epidural injection, as well as the time between PDPH onset and initiation of the treatment (48 h later, not within the first 24 h), having received analgesic treatment. Moreover, according to McArthur et al.,[46] the presence of hearing symptoms might be a factor contributing to positive outcomes, which is higher in the EBP group.

The time from PDPH onset to the patch injection has been demonstrated to exert an influence over the subsequent outcome. Loeser et al.,[40] in a retrospective, controlled study revealed poorer outcomes when patients received the EBP 24 h prior to PDPH onset. Authors indeed recommended delaying the patch injection at least until the second day. Similarly, Kokki et al.[47] reported better outcomes with the EBP when injected within 24 h of PDPH onset. This observation could be related to higher CSF flow during initial hours, especially when caused by high-gauge needles like the 18 G Tuohy. Moreover, none of our patients experienced an ADP during the EBP.

It was also not necessary to limit the substance volume to be injected due to AEs, some of them associated with larger volumes. In our study, the most frequent AE and complication were lumbar discomfort/pain (27.1% of cases) and lumbar radiculopathy (50.0%), respectively; all were resolved spontaneously within 24 h. These were mild and transient AEs, and complications are possibly related to the injected blood volume, which can be up to 30 mL. In our case, 15 mL of EBP was well tolerated, however, AE and complication rates were significantly lower when using 6 mL of EFP. Despite it being complicated to evaluate the safety of the technique,[48] we can state that major complications were registered in none of the groups. Aseptic meningitis[35] and allergic reactions[37] associated with the administration of fibrin glue can occur, although we have not observed any of them in our experience. After a month of follow-up, no long-term side effects related to the fibrin patch were observed. Fibrin glue has been used as a dural sealant in both cranial and spinal cases. The glue is subsequently degraded by natural fibrinolysis for several weeks.[49]

Of patients with EBP, 25.7% continued requiring rescue analgesic medication after 30 days from the patch injection, especially non-steroidal anti-inflammatory drugs (NSAIDs) (28.6%). MacArthur et al.[46] followed up 4700 women who required epidural analgesia for labor (74 of them suffering an ADP), from 13 months to 9 years. The authors reported 23% with headaches, neck pain, or migraine 3 months after the delivery (and lasting at least 6 weeks) in patients who experienced an ADP versus 7.1% of those who did not. The duration of the headache varied between 9 weeks and 8 years.[46] Although the follow-up of our patients was limited to 1 month, the persistence of the PDPH relief in the EFP group could be relevant to the incidence of chronic PDPH, in the long-term. The lower initial efficacy of EBP in obstetric PDPH (especially when administered early), the high rate of recurrence and the AEs associated with the increased volume used, could be correlated with inefficacy of EBP for high gradients of pressure.[50] Rosenberg et al.[51] demonstrated in vitro that EBP resists pressure lower than 54.38 cm H_2O with a 25G needle; however, it did not do so with 19G Tuohy needles (causing leakage with a pressure of up to 40 cm H_2O). By contrast, García-Aguado et al.[52] revealed that 1.4 mL EFP can cease the continuous CSF flow through a dural hole (with a pressure of 24.5 cm H_2O) in 87.5% of cases. Despite EFP having been successfully used to seal CSF leaks in patients with intrathecal catheters and ADP,[27,53] EBP remains the gold standard therapy in obstetrics.

In certain indications, especially in autologous blood refractory cases, the efficacy of the EFP might be associated with a synergic effect from the previously administered EBP.[30,32] Nevertheless, Lee et al.[54] reported a case in which the patient received 15 autologous blood and three fibrin glue patches before achieving successful relief in a case of spontaneous intracranial hypotension. It is a common practice to use fibrin, instead of blood, for an epidural injection in the treatment of this type of hypotension.[55] Moreover, the fibrin volume is lower than blood volume when it comes to achieving a satisfactory outcome. The epidural patch pursues both the sealing of the dural gap and the raising of CSF pressure in the patient. The effect of the blood volume in the epidural space is correlated to the proportional increase in the CSF pressure, but it has a limited effect in headache relief.[44,56] On the other hand, it has been observed that low blood volumes might reach 9–10 metameres, allowing the closure of the dural gap but not the reaching of an adequate CSF pressure at a cisterna magna level.[57] The closure of the dural gap does not explain the immediate pain relief that occurs with the blood patch, since the recovery of the CSF pressure would not be complete 24 h after its administration.[58] A higher fibrin concentration in the infusion would be achieved thanks to the greater viscosity of this compound, providing a higher pressure than the one caused by a larger blood volume.[37] Additionally, that pressure could be maintained for a longer time due to superior stickiness.[52] The closure of the dural gap could be a necessary but not sufficient requirement for significant and immediate relief. This observation is based on the successful relief that the administration of a blood patch provokes in patients with spontaneous intracranial hypotension syndrome with dural gaps localized at a thoracic or cervical level.[59,60] This outcome favors the hypothesis of pressure gradient re-establishment over the increase of the volume, which is triggered due to an increment of the viscosity of the injected volume and not to the rise of the volume per se.[37,61,62] Fibrin provides diverse advantages for the epidural injection over autologous blood including uncomfortable, and sometimes tricky, extraction of blood is required; faster blood clotting; lower potential risk for infection; and decreased diffusion into the epidural space (from the injection site).[61,63]

The main limitation of the study was the absence of a control (placebo or no-treatment) group, and of a blind, or double-blind design. Moreover, the single-center nature of the study limits the extrapolation

of results to the nationwide level. Despite this, these results are valuable for the management of accidental PDPH.

CONCLUSION

The EFP provides better outcomes than EBP for the treatment of obstetric PDPH in terms of efficacy, safety, and patient satisfaction. Despite EFP being able to be considered as a first-line treatment, further methodologically robust studies are still needed.

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DATA AVAILABILITY STATEMENT
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PATIENT CONSENT STATEMENT
Patients signed an informed consent.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES
This permission is not required.

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