Original Article

Comparing two techniques of performing an epidural catheter-assisted epidural blood patch using a 20 ml syringe versus a 5 ml syringe and its effect on clotting time, the strength of clot retraction and haemolysis – A prospective *in vitro* study (EC-EBP study)

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ABSTRACT

Background and Aims: Epidural blood patch (EBP) is performed by injecting autologous blood into the epidural space using a Tuohy needle. Certain clinical scenarios mandate an epidural catheter (EC)-assisted EBP. Collecting blood in a 20-ml versus 5-ml syringe appears to influence the quality of the clot. This *in vitro* study compared the techniques of performing the EC-assisted EBP using 20-ml versus 5-ml syringe on clotting time (CT), clot retraction (CR) and haemolysis. **Methods:** This *in vitro* study was performed in a haematology laboratory. Five consented adult healthy male volunteers donated blood. In the 5-ml syringe technique, blood was injected through an EC, and as it flowed out of the tip, it was collected at the beginning and the end of 1 min. With the 20-ml technique, blood was collected at the beginning and end of the first, second and third minute. The samples were tested for CT, CR and haemolysis by measuring the plasma-free haemoglobin (PFHb). **Results:** Five injections were made using a 5-ml syringe, and another five with a 20-ml syringe. Injection time was shorter in the 5-ml technique (80.80 ± 5.89 vs. 272 ± 28.4 s, $P < 0.0001$). With the 20-ml technique, CT progressively increased (>15 min), whereas, with the 5-ml syringe, the CT was normal. Both techniques caused mild, insignificant haemolysis (PFHb >0.005 g/dl), without affecting the quality of CR. **Conclusion:** EC-assisted EBP using a 5-ml syringe technique shortens the injection time and deposits fresh blood quickly without affecting CT and CR.

Key words: Blood coagulation, epidural blood patch, cerebrospinal fluid leak, clot retraction, haemolysis, intracranial hypotension

INTRODUCTION

Patients with intracranial hypotension (IH) often present with orthostatic headache, diplopia, tinnitus, vertigo, blurred vision, nausea and vomiting.[1,2] It is often due to cerebrospinal fluid (CSF) leak at the spinal level and occasionally from the skull base. For those who fail to show improvement with conservative treatment, an epidural blood patch (EBP) is performed to seal the CSF leak.[1,3,4] The EBP involves an injection of autologous blood into the epidural

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space. Certain clinical scenarios mandate an epidural catheter (EC)-assisted EBP.[5-9] We have observed in our clinical experience that injecting 20 ml of blood using a 20-ml syringe while performing the EC-assisted EBP for IH due to an occult CSF leak takes a long time and blood in the 20-ml syringe starts to clot towards the end of the injection.

Based on our experience, we hypothesised that depositing 20 ml of blood using a 20-ml plastic syringe accelerates the clotting process because of the long contact time and the larger surface area. Injection of partially clotted blood can cause consumption of coagulation factors, which can affect the clotting efficacy of the unclotted blood and prolongs the clotting time (CT). Also, injecting the partially clotted blood through the EC needs higher pressure to inject, causing haemolysis, which, in turn, affects the quality of the clot and can interfere with clot retraction (CR). Drawing blood using a 5-ml syringe (small surface area) and injecting it within a minute will reduce the contact time, and this can be repeated to achieve the same volume of blood. We performed an *in vitro* study in the haematology laboratory by simulating the scenario and compared the injection time, CT, the extent of haemolysis and the quality of CR between the two techniques of performing the EC-assisted EBP using a 20-ml syringe versus a 5-ml syringe.

METHODS

This article adheres to enhancing the quality and transparency of health and research (EQUATOR)-STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines. This prospective, observational, in-vitro study was approved by Institutional Research and Ethics Committee (vice approval number IRB No-. 13947 dated 28th April 2021). Written informed consent was obtained from all subjects who donated blood for the trial. This trial was registered in the Clinical Trial Registry - India (CTRI) before the enrollment of subjects (CTRI/2021/12/038365, dated 2nd December 2021, www.ctri.nic.in). The study was conducted in the Clinical Haematology Laboratory, Department of Transfusion Medicine and Immunohematology, in December 2021 over a period of 2 weeks.

Five healthy adult volunteers aged above 18 years with normal complete blood count (CBC) were included. Volunteers with anaemia or thrombocytopenia and those with a history of red cell membrane disorder or platelet function defects were excluded. Two millilitres of blood was collected from five volunteers, and the baseline CBC was checked the day before the experiment. After confirming that the CBC values were within normal limits, the volunteers were included in the study.

For the 5-ml syringe technique, venipuncture was done on the volunteers under strict asepsis, and 5 ml of blood was collected in a 5-ml syringe. Blood was immediately injected through the 18-G EC by the same investigator (RM). As the blood flowed out from the EC tip, 1 ml was collected at two-time points, that is, at the beginning (immediate sample) and at the end of 1 min (1 minute sample). The time taken to inject 5 ml of blood through the EC was noted. The CT was measured using the standard method, and the extent of haemolysis was assessed by measuring plasma-free haemoglobin (PFHb) at both time points. The quality of CR was checked after 6 h and the following day.

For the 20-ml syringe technique, from the same volunteers, 20 ml of blood was collected in a 20-ml syringe using a 20-G scalp vein set, and the blood was injected through the 18-G EC by the same investigator (RM). As the blood flowed out of the EC tip, it was collected at different time points – at the beginning (immediate sample) and at the end of the first, second and third minute (1-min, 2-min and 3-min samples). The time taken to inject the 20-ml blood through the EC was noted. A total of four samples were collected, and CT was estimated. The extent of haemolysis was measured for the immediate, 1-min and 3-min samples by measuring PFHb. The quality of CR was analysed after 6 h and the following day.

CT was calculated from the time the blood reached the syringe (from the venipuncture needle) to the time the blood stopped flowing on the side of a glass tubing during the gentle tilt, which was made every 30 s. The CT between 8 and 15 min was considered within normal limits. The extent of haemolysis was assessed by measuring the PFHb using a HemoCue® plasma low haemoglobin analyser. PFHb less than 0.005 g/dl was considered within normal limits. PFHb of >0.005 g/dl was considered haemolysis, and PFHb of more than 0.25 g/dl was regarded as severe haemolysis. The quality of CR was assessed at the end of 6 h and the following day by looking at the clot size in all the collected samples.

The primary objective of our study was to compare the CT, and the secondary objectives were to compare the

extent of haemolysis and the quality of CR between the two techniques of performing EC-assisted EBP using a 20-ml versus 5-ml syringe technique. The following data were collected. The demographics (age, gender, body mass index) of the volunteers and their baseline haemoglobin and platelet counts were noted. The injection time, CT, PFHb (extent of haemolysis) and the size of a retracted clot (CR) were, recorded and compared between the two techniques.

The primary analysis compared the variables for the 5-ml syringe technique with the 20-ml syringe technique. Continuous quantitative variables were summarised using mean and standard deviation, and a *t*-test was carried out to assess the statistical difference between them. Statistical analysis was done using GraphPad Prism Version 5.0 (Graphpad Software, Boston, MA, USA).

RESULTS

A total of 10 injections were made; five injections using a 5-ml syringe technique and another five injections using a 20-ml syringe technique. The demographics (age, gender, body mass index) of the volunteers are presented in Table 1. The mean time taken to inject 5 ml of blood was 80.80 ± 5.89 s for the 5-ml syringe technique, while it was 272 ± 28.4 s for the 20-ml syringe technique ($P < 0.0001$). Using the 5-ml syringe technique, the CT for the immediate sample was 12.27 ± 3.59 min and for the 1-min sample was 11.36 ± 2.31 min; both were within normal limits. The CT progressively increased from the second (1-min sample) to the fourth sample (3-min sample) in the 20-ml syringe technique and exceeded the normal limits in the third and fourth samples (>15 min). The quality of CR was assessed visually by looking at the size of the retracted clot at 6 h and the following day. The retracted clot quality looked the same at both time points for both techniques; no clot lysis was noted in any of the samples in both technique.

The extent of haemolysis was measured using PFHb. Both the techniques (5-ml and 20-ml syringes) caused haemolysis in the immediate sample (first sample) [Table 2]. But no significant difference was noted between the two techniques ($P = 0.50$). The haemolysis reduced further in 1-min samples in both techniques [Table 2]. Very minimal haemolysis was noted in the 3-min sample in the 20-ml syringe technique (0.009 ± 0.03 g/dl). Though high pressure was needed to inject the partially clotted blood by the 20-ml syringe towards the end, it did not cause severe haemolysis. None of the samples had PFHb >0.25 g/dl at any time point in this study.

Table 1: Demographics and baseline parameters

Demographics and baseline parameters	Values
Gender: male, *n*	5
Age in years, Mean±SD	25±6.0
BMI in kg/m^2, Mean±SD	21.3±0.8
Haemoglobin in g/dl, Mean±SD	15.9±0.9
Platelet count in count×10^3, Mean±SD	282.4±69.4

BMI=body mass index, SD=standard deviation

DISCUSSION

This *in vitro* study showed that performing an EBP with EC using a 5-ml syringe technique decreases the injection time, thereby reducing the contact time of blood on the plastic surface with a smaller surface area. Hence, this technique helps to deposit fresh whole blood as quickly as possible without increasing the CT.

In our study, we did not perform platelet count or platelet function tests in the blood that flowed out of the EC tip. Since we assessed the CR, which depends on platelet function, we did not measure platelet count. But the CT increased when the blood was injected using a 20-ml syringe as it took a long time to inject (272 vs. 81 s). This prolongation could be due to the partially clotted blood, causing consumption of coagulation factors.

Though both techniques (20-ml and 5-ml syringe techniques) of EC-assisted EBP injection caused haemolysis (PFHb >0.005 g/dl), it did not affect the CR which is essential for sealing the CSF leak. Studies have shown that PFHb above 0.25 g/dl is considered to be toxic because the kidneys cannot eliminate the haemoglobin breakdown products in such quantities.[10] In this study, none of the samples had PFHb of >0.25 g/dl. Since this was the first study to compare the CT, CR and clot lysis between the 20-ml versus 5-ml syringe techniques, we could not compare our results with others.

The results of our study revealed that performing an EC-assisted EBP using a 5-ml syringe technique reduced the contact time on the plastic syringe, thereby maintaining the integrity of the clotting process, which resulted in normal CT and CR with minimal haemolysis. While performing the EC-assisted EBP, the larger-diameter EC (18 G) offers less resistance than the smaller catheter (20 G). Hence, we recommend

Table 2: Injection time, clotting time and plasma free haemoglobin between the two techniques

Parameter	5-ml syringe technique, Mean±SD (95% CI)	20-ml syringe technique, Mean±SD (95% CI)	*P*
Injection time (s)	80.80±5.89 (73.49,88.11)	272±28.4 (236.7,307.3)	*P*<0.0001
Clotting time (min and s)			
Immediate	12.27±3.59 (7.81,16.73)	14.54±5.16 (8.24,21.04)	0.424
At 1 min	11.36±2.31 (8.49,14.22)	14.37±4.18 (9.18,19.57)	0.196
At the second minute		15.36±3.68 (10.79,19.94)	NA
At the third minute		17.27±3.86 (12.48,22.06)	NA
Extent of haemolysis (plasma-free haemoglobin) (g/dl)			
Immediate	0.13±0.09 (0.02,0.24)	0.12±0.04 (0.07,0.16)	0.747
At the first minute	0.12±0.05 (0.06,0.19)	0.10±0.04 (0.06,0.15)	0.492
At the third minute		0.09±0.03 (0.05,0.13)	NA

CI=confidence interval, SD=standard deviation

using an 18-G catheter for performing EC-assisted EBP. As the needle size is larger (16 G) for this catheter, one must be extremely careful to avoid dural puncture.

There are some limitations associated with this study, the first being we did not perform platelet count or other conventional coagulation tests or coagulation factor assay from the blood that flowed out of the EC. The second limitation was that the test was conducted in the haematology laboratory (room temperature 21°C–23°C), which could have influenced the CT slightly. Hypothermia-induced mild platelet dysfunction causing mild prolongation of the CT is a possibility.

CONCLUSION

Performing an EC-assisted EBP using a 5-ml syringe technique shortens the injection time. In addition, because of a smaller surface area and shorter contact time, the 5-ml syringe technique helps to deposit fresh whole blood without affecting the CT or the quality of CR. Hence, we recommend using this technique while performing EC-assisted EBP injection.

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Conflicts of interest

There are no conflicts of interest.

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