

Neuraxial Techniques in Obstetric and Non-Obstetric Patients with Common Bleeding Diatheses

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BACKGROUND: There are few data in the literature regarding the safety of neuraxial techniques in patients with the most common bleeding diatheses, including hemophilia, von Willebrand's disease (vWD), and idiopathic thrombocytopenic purpura (ITP). Neuraxial techniques are not widely used in these populations because of concerns of potential hemorrhagic and/or subsequent neurologic complications. In this article, we review the available literature describing neuraxial techniques in patients with hemophilia, vWD, or ITP with the aim to assist anesthesiologists considering neuraxial techniques in these populations.

METHODS: After a systematic Pubmed, MEDLINE, and EMBASE search, we reviewed 30 articles published between January 1, 1975 and October 1, 2008 in which neuraxial techniques were performed in patients with hemophilia, vWD, or ITP to determine the perioperative management and evaluate the frequency of hemorrhagic complications.

RESULTS: We identified 507 neuraxial techniques (482 patients) performed in patients with hemophilia (107 neuraxial techniques, 85 patients), vWD (74 neuraxial techniques, 72 patients), or ITP (326 neuraxial techniques, 325 patients). Among the 507 neuraxial techniques performed, there were 371 lumbar epidural anesthetics, 78 spinal anesthetics, 53 lumbar punctures, 2 combined spinal epidural analgesia, 2 paravertebral blocks, and 1 thoracic epidural anesthetic. Four hundred six neuraxial techniques were placed in the obstetric population, 53 were performed in the emergency room for diagnostic lumbar puncture, 46 were performed for lower limb orthopedic surgery, 1 was performed for postoperative analgesia, and 1 was performed for an obstetric patient undergoing non-obstetric surgery. Factor replacement to normal levels ($>0.5 \text{ IU mL}^{-1}$) was initiated before block performance, though treatment was not standardized, in 105 of 107 patients with hemophilia and 10 of 74 with vWD. Sixty-four of the 74 patients with vWD had spontaneous normalization of factor levels before block performance. No hemorrhagic complications were reported when the diagnosis of hemophilia or vWD was known before the neuraxial technique. A single case of spinal hematoma (resulting in permanent paraplegia) was identified when the presence of hemophilia was not known before needle insertion and factor replacement had not been given. In all 326 cases of ITP, with or without systemic treatment of platelet transfusion, there were no reports of hemorrhagic complications associated with neuraxial techniques. Among the 326 neuraxial techniques placed in the setting of ITP, 9 patients had platelet counts of $<50 \times 10^9 \text{ L}^{-1}$, 19 had a platelet counts of $50\text{--}75 \times 10^9 \text{ L}^{-1}$, 204 had a platelet counts of $75\text{--}100 \times 10^9 \text{ L}^{-1}$, and 94 had a platelet count more than $100 \times 10^9 \text{ L}^{-1}$ before needle insertion.

CONCLUSIONS: There is a paucity of published data regarding the provision and safety of neuraxial techniques in patients with common bleeding diatheses. The minimum "safe" factor levels and platelet count for neuraxial techniques remain undefined in both the obstetric and general populations, and evidence-based recommendations in the setting of hemophilia, vWD, or ITP cannot be offered.

(Anesth Analg 2009;109:648-60)

Neuraxial blockade provides multiple benefits when compared with general anesthesia and/or systemic analgesia, including superior postoperative

analgesia,¹ decreased opioid-related side effects, improved rehabilitation,² and reduced morbidity and mortality.³⁻⁷ The advantages of neuraxial techniques in obstetric anesthesia are, further pronounced with

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Accepted for publication March 9, 2009.

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DOI: 10.1213/0131109.2009.03137

significant reductions in maternal morbidity and mortality, and improved pain relief and patient satisfaction.^{8–15} Consensus guidelines published by the American Society of Regional Anesthesia and Pain Medicine (ASRA) and the German Society of Anesthesiology and Intensive Care are available for anesthesiologists considering neuraxial techniques in patients receiving hemostasis-altering medications.^{16,17} However, there is little evidence in the literature regarding the application of neuraxial techniques in patients with common bleeding diatheses. These patients may safely and successfully undergo major surgery under general anesthesia provided that the defect is adequately corrected.^{18–29} The objectives of this review are to examine and summarize the reported perioperative management and assess the frequency of hemorrhagic complications in patients with the most common bleeding diatheses (hemophilia, von Willebrand's disease [vWD], and idiopathic thrombocytopenic purpura [ITP]) with the aim to assist anesthesiologists considering neuraxial techniques in these populations.

METHODS

A systematic search of the PubMed, MEDLINE, and EMBASE databases was performed using the medical subject heading words "regional anesthesia," "neuraxial blockade," "epidural," "spinal," "subarachnoid," "intrathecal," "lumbar puncture," "paravertebral," "steroid," and "caudal." Search results were then cross-referenced with each of the medical subject heading words "coagulopathy," "hemophilia," "von Willebrand," "thrombocytopenia," "ITP," "Immune," and "Idiopathic." Only studies in which neuraxial techniques were performed on patients with the aforementioned bleeding diatheses were included. Acquired forms of hemophilia were excluded. The references of all relevant publications were examined to capture any additional material suited for the present review. The quality of evidence for each identified article was independently graded by each of the authors (highest to lowest I–V) according to the criteria described by Wright et al. (Appendix).^{30,31}

Where possible, the pre- and posttreatment coagulation variables, platelet counts, treatment administered, needle gauge/type used for the block, difficulties noted with placement, and the source authors' recommendations regarding management of the bleeding diatheses were included in the summary tables. Complications were defined as hemorrhage related to the neuraxial technique procedure with or without subsequent neurologic compromise.

RESULTS

Our search yielded 86 articles of which 30 met our inclusion criteria. The quality of evidence score for the

30 source articles in this review was Level IV (Appendix). Sixteen of the 30 articles cited were case reports.^{32–47} Fourteen of the 30 articles were case series.^{48–61} Tables 1–3 summarize the articles according to bleeding defect and by type of neuraxial technique.

Hemophilia

Among six articles, we identified 107 neuraxial techniques performed on 85 patients with hemophilia, and there were no reports of spinal hematoma when the diagnosis of hemophilia was known before the procedure.^{32,37,38,51,52,58} Of these 107 neuraxial techniques, there were 53 diagnostic lumbar punctures in the emergency room, 35 spinal anesthetics for lower limb orthopedic surgery, 11 lumbar epidural anesthetics for lower limb orthopedic surgery, 7 lumbar epidural anesthetics for labor, and 1 lumbar epidural anesthetic for abdominal surgery. In the 105 neuraxial techniques in which the coagulopathy was known before the block, factor levels were replaced to normal (>0.5 IU mL⁻¹) before needle insertion, and no hemorrhagic complications were reported. Two neuraxial techniques were performed in patients with undiagnosed hemophilia prior to needle insertion,^{32,38} one of which resulted in the lone complication identified in this review, a catastrophic spinal hematoma³⁸ (Table 1).

The management of hemophilia in the patients reviewed herein was not standardized (Table 1). However, factor VIII/IX levels were normalized (>0.5 IU mL⁻¹) in all cases in which the diagnosis of hemophilia was known before needle insertion. Treatment most often included specific factor replacement (plasma derived or recombinant)^{37,58} with or without 1-deamino-8-D-arginine vasopressin.³² Two authors did not specify the type or dosage of factor replacement but reported that factor levels were normal before needle insertion.^{51,52}

The authors of three of the six source articles specified that removal of the epidural catheter after lumbar epidural analgesia was attempted or intended to be attempted only when factor levels were normalized (>0.5 IU mL⁻¹).^{32,37,51}

vWD

Among 10 articles, we identified 74 neuraxial techniques performed on 72 patients with vWD ranging from mild to severe (Type I, $n = 71$; Type IIA, $n = 2$; Type III, $n = 1$).^{33,34,36,41,42,45,53,54,59,60} There were no complications reported among these 72 patients, all of whom received neuraxial techniques for labor analgesia. Of the 74 neuraxial techniques, 72 were for lumbar epidural analgesia, and 2 were combined spinal epidurals. In 64 of the 74 neuraxial techniques, vWD indices were normal before needle insertion and treatment was not initiated.^{36,42,53,54,60} Treatment before needle insertion was initiated for 10 of the 74 neuraxial techniques.^{33,34,41,45,59}

Treatment for vWD was dependent on the severity and subtype of vWD (Table 2). In 5 of the 10 source articles previously abnormal vWD indices spontaneously returned to normal or near normal at term

Table 1. Data Summary of Neuraxial Techniques in the Setting of Hemophilia A or B

Author/reference	Type/N	Surgical population	No. of blocks	Pretreatment coagulation parameters	Treatment
<i>Lumbar epidural</i>					
Bernhardt et al. ³²	A N = 1	GEN	1	FVIII activity = 37% aPTT = 46s	None
Dhar et al. ³⁷	A N = 1	OB	1	FVIII <0.01 IU mL ⁻¹	Helixate FS® 3 IU kg ⁻¹ h ⁻¹
Kadir et al. ⁵²	A/B N = 6	OB	6	FVIII/IX levels >50% in 5 out of 6 LEAs	N/A
Hack et al. ⁵¹	A/B N = 11	ORTHO	11	N/A	N/A
<i>Spinal</i>					
Hack et al. ⁵¹	A/B N = 35	ORTHO	35	N/A	N/A
<i>Lumbar puncture</i>					
Silverman et al. ⁵⁸	A N = 28 B N = 5	ER	52	FVIII/IX <0.01 IU mL ⁻¹ (N = 30) 0.01–0.05 IU mL ⁻¹ (N = 2) 0.05–0.1 IU mL ⁻¹ (N = 1)	FVIII/FIX transfused at 40 IU kg ⁻¹ PCC in cases of AFI (N = 2)
Faillace et al. ³⁸	A N = 1	ER	1	FVIII activity <1% aPTT = 156s	None

Numeric values presented as $\times 10^9 \text{ L}^{-1}$.

Hemophilia severity: Mild = 10 to 50% FVIII activity; Moderate = 2 to 10% FVIII activity; Severe = <1% FVIII activity.

AFI = acquired factor inhibitor; aPTT = acquired thromboplastin time; DDAVP = 1-deamino-8-D-arginine vasopressin; ER = emergency room lumbar puncture; FIX = Factor 9 (Normal = 0.5–1.5 IU mL⁻¹); FVIII = Factor 8 (Normal = 0.5–1.5 IU mL⁻¹); G = needle gauge; GEN = general surgical population; Helixate FS® = recombinant factor 8 concentrate (CSL Behring); LEA = lumbar epidural anesthesia; LP = lumbar puncture; N = number of patients; N/A = data not indicated in reference; NT = neuraxial technique; OB = obstetric; ORTHO = orthopedic; POD = postoperative day; PCC = prothrombin complex concentrate; Plt = platelets.

before lumbar epidural catheter placement for labor analgesia and no treatment was prescribed.^{36,42,53,54,60} Treatment included DDAVP alone,^{45,59} plasma-derived vWF/FVIII concentrate for Types II and III vWD,⁴¹ or FVIII concentrate alone.³⁴

ITP

Among 14 articles, we identified 325 patients with ITP who underwent a total of 326* neuraxial techniques.^{35,39,40,43,44,46–50,55–57,61} Of 326 neuraxial techniques, 324 were in the obstetric population, 1 thoracic epidural catheter was placed for postoperative analgesia,⁴⁶ and 1 spinal anesthetic was for non-obstetric surgery in an obstetric patient.³⁵ In total, 282 lumbar

epidural anesthetics, 41 spinal anesthetics, 2 paravertebral blocks, and 1 thoracic epidural anesthetic were placed in the setting of ITP. There were no complications reported.

The perioperative management of neuraxial techniques in ITP varied considerably among the 14 source articles (Table 3). The diagnosis of ITP was known before the block in all but three instances in which the low platelet count was revealed on review of the complete blood count after lumbar epidural analgesia had been initiated. Interestingly, three articles (i.e., ITP was undiagnosed before neuraxial technique) reported the lowest platelet counts before needle insertion among all 14 source articles: $2 \times 10^9 \text{ L}^{-1}$,⁴⁰ $18 \times 10^9 \text{ L}^{-1}$,⁵⁶ and $26 \times 10^9 \text{ L}^{-1}$.⁴³

The authors of 10 of the 14 source articles did not seek to treat the thrombocytopenia before needle insertion when the diagnosis of ITP was established

Table 1. Continued

Posttreatment coagulation parameters	Gauge/type	Difficult insertion	Outcome	Authors' recommendations	Remarks
N/A	18G Tuohy	No	No complications	Coagulation studies required in all NT Abnormal values must be investigated	Hemophilia A diagnosed after surgical site wound hematoma on POD 1 DDAVP 0.4 $\mu\text{g kg}^{-1}$, Haemate HS [®] 2000 IU before catheter removal, FVIII = 73%
FVIII >0.5 IU mL ⁻¹ PT/aPTT = 12.5/33.3s	17G Hustead	No	No complications	Suggest midline approach Minimize local anesthetic to monitor motor/sensory function	Infusion continued 48h targeting FVIII >0.5 IU mL ⁻¹
N/A	N/A	N/A	No complications	NT not contraindicated if coagulation screen normal Spinal block regarded as safer than LEA NT used at authors centre if factor levels >50%	Hemophilia subtype not indicated
FVIII/FIX levels normalized	18G Tuohy	N/A	No complications	None	Hemophilia subtype, treatment method, and target factor level not indicated
FVIII/FIX levels normalized	25G Quincke	N/A	No complications	None	Hemophilia subtype, treatment method, and target factor level not indicated
N/A	N/A	N/A	No complications	LP safe in hemophilia if factor replaced to normal levels	7 patients had Plt <100 2 patients had Plt <50 and were transfused 2 cases of AFI developed in patients with inherited hemophilia secondary to chronic factor replacement therapy
N/A	N/A	Yes	Spinal hematoma and permanent paraplegia	None	

preprocedure, four of the authors sought to reduce the severity of the thrombocytopenia. A platelet count of $<50 \times 10^9 \text{ L}^{-1}$ generally prompted treatment consisting of corticosteroids, IV immune globulin, or platelet transfusion before block performance.^{44,46,49,50}

Only one source article made any mention of the platelet count at the time of epidural catheter removal. Frenk et al.⁵⁰ described that, whenever possible, catheter removal was attempted only when the platelet count was in excess of $60 \times 10^9 \text{ L}^{-1}$. Nonetheless, these authors reported that 5 of the 135 catheters studied were still removed (without consequence) when the platelet count was $<50 \times 10^9 \text{ L}^{-1}$, though the reason for this apparent discrepancy was not explained in the article.

DISCUSSION

Spinal hematoma after neuraxial techniques in modern anesthetic practice is rare. The frequency of

spinal hematoma in the large (>1000 subjects) contemporary studies (1995–present) ranges from 0 to 3.70:10,000^{62–73} and varies considerably depending on the surgical indication, particularly with respect to the obstetric (0–0.20:10,000) versus the non-obstetric population (0–3.7:10,000). It, nonetheless, remains one of the most feared complications, mostly because of its potential for irreversible injury and partly because it may be minimized with close attention to modifiable risk factors, namely thromboprophylaxis, traumatic needle insertion, and known coagulopathies.⁷⁴ However, there is a paucity of data in the literature regarding the provision of neuraxial techniques in patients with the most common bleeding diatheses. Among the 507 neuraxial techniques identified from 30 published articles of neuraxial techniques in the setting of hemophilia, vWD, or ITP, there was only one reported complication in which the bleeding diathesis was undiagnosed before needle

Table 2. Data Summary of Neuraxial Techniques in the Setting of von Willebrand's Disease (vWD)

Author/reference	Type/N	Surgical population	No. of blocks	Pretreatment coagulation parameters	Treatment
<i>Lumbar epidural</i>					
Varughese and Cohen ⁶⁰	I N = 14 IIA N = 1	OB	17	Median % normal: FVIII = 65; vWF = 46; vWRCo = 50	None
Marrache et al. ⁵⁴	I N = 9	OB	9	Mean (IU mL ⁻¹): FVIII = 1.42 ± 0.42; vWF = 1.42 ± 0.62; vWRCo = 1.42 ± 0.79	None
Perez-Barrero et al. ⁴⁵	I N = 1	OB	1	% normal: FVIII = 38; vWF = 25; vWRCo = 65	DDAVP 0.3μg kg ⁻¹
Suddeth et al. ⁵⁹	N/A N = 34	OB	34	N/A	DDAVP to 5 patients (dose N/A)
Kadir et al. ⁵³	I IIA IIB III N = 8	OB	8	Median (IU mL ⁻¹): FVIII = 0.53; vWF = 0.43; vWRCo = 0.40	N/A
Caliezi et al. ³⁴	III N = 1	OB	1	IU mL ⁻¹ : FVIII = 0.08; vWF = 0.125	FVIII concentrate 3500 IU; Haemate HS [®] 1000 IU
Milaskiewicz et al. ⁴²	I N = 1	OB	1	% normal: FVIII = 108; vWF = N/A; vWRCo = 10	None
Cohen et al. ³⁶	I N = 1	OB	1	% normal: FVIII = 200; vWF = N/A; vWRCo = N/A	None
<i>Combined spinal epidural</i>					
Butwick and Carvalho ³³	I N = 1	OB	1	% normal: FVIII = 189; vWF = >200; vWRCo = 247	DDAVP 0.3μg kg ⁻¹
Jones et al. ⁴¹	I N = 1	OB	1	% normal: FVIII = 72; vWF = 89; vWRCo <25	Humate P [®] 30 U kg ⁻¹ continued for 6 d

CSE = combined spinal epidural analgesia; DDAVP = 1-deamino-8-D-arginine vasopressin; FVIII = factor 8 (normal = 0.5–1.5 IU mL⁻¹); G = needle gauge; GM = gertie-max needle; Haemate HS[®] = intermediate purity plasma derived FVIII/vWF concentrate (Aventis Behring); Humate P[®] = high purity plasma derived FVIII/vWF concentrate (CSL Behring); LEA = lumbar epidural analgesia; N = number of patients; OB = obstetric; N/A = data not indicated in reference; vWD = von Willebrand's disease; vWF = von Willebrand factor (normal = 0.5–2.0 IU mL⁻¹); vWRCo = Ristocetin Co-factor activity (normal = 0.5–2.0 IU mL⁻¹).

insertion. There was a single case of spinal hematoma after diagnostic lumbar puncture in an undiagnosed hemophilic infant resulting in permanent paraplegia.³⁸ We found no other reports of catastrophic or noncatastrophic hemorrhagic complications in the setting of hemophilia, vWD, or ITP. Nonetheless, the data presented herein must be interpreted with caution.

The source articles included in this review are limited to case reports and case series with relatively few total subjects. In addition, the effects of negative reporting and publication bias cannot be discounted. Accordingly, it must be recognized that the absence of evidence does not imply evidence of absence. That is, just because the literature does not contain

Table 2. Continued

Posttreatment coagulation parameters	Gauge/type	Difficult insertion	Outcome	Authors' recommendations	Remarks
N/A	N/A	N/A	No complications	LEA safe in mild Type I vWD when defects normalized	2 patients with Type I vWD received 2 NTs for different pregnancies
N/A	N/A	No	No complications	None	vWD indices spontaneously normalized at term before NT
N/A	18-G Tuohy	No	No complications	None	
N/A	N/A	N/A	No complications	None	vWD subtypes not indicated
Median (IU mL ⁻¹): FVIII >0.5; vWF >0.5; vWRCo >0.5	N/A	N/A	No complications	NT not performed unless factor levels >0.5 IU mL ⁻¹	Selection criteria for DDVAP not indicated vWD subtypes not indicated among 8 patients who received LEA 1 patient with moderate Type I treated, method not indicated 7 patients spontaneously normalized at term
IU mL ⁻¹ : FVIII = 1.4; vWF = 1.34	N/A	N/A	No complications	None	
% normal: FVIII = 108; vWF = N/A; vWRCo = 10	16-G Tuohy	No	No complications	None	
% normal: FVIII = 200; vWF = N/A; vWRCo = N/A	17-G Tuohy	No	No complications	Decision must be made on case-by-case basis Careful surveillance for neurological symptoms LEA safe in mild Type I when defects normalized	
N/A	17-G Tuohy; 26-G GM; 19-G Catheter	No	No complications	None	DDAVP administered despite supra-normal factor levels
% normal: FVIII = 115; vWF = 122; vWRCo = 112	N/A	No	No complications	None	vWRCo >68% throughout hospitalization

sufficient data regarding the frequency of hemorrhagic complications after neuraxial techniques in patients with bleeding diatheses does not mean that hemorrhagic complications do not occur often. Vastly (and prohibitively) larger numbers of patients are required to determine the true incidence

of epidural hematoma, as well as support or refute the safety of neuraxial techniques, in patients with hemophilia, vWD, or ITP.

Moreover, the gross disproportions between surgical indication (e.g., obstetrics vs orthopedics) and neuraxial technique type (e.g., lumbar epidural vs

Table 3. Data Summary of Neuraxial Techniques in the Setting of Idiopathic Thrombocytopenic Purpura (ITP)

Author/reference	Population/N	No. of blocks	Preblock platelet count ($\times 10^9 \text{ L}^{-1}$)	Treatment	Gauge/type	Difficult insertion	Outcome	Authors' recommendations	Remarks
Lumbar epidural									
Deruddre et al. ⁴⁹	OB N = 19	19	Plt <100 (N = 6) Plt = 100–150 (N = 13)	Steroids (N = 12) IVIg (N = 2) Both (N = 5) None (N = 13)	N/A	N/A	No complications	Plt <100 not contraindication to NT	
Frenk et al. ⁵⁰	OB N = 135 ^a	135	Plt <50 (N = 2) Plt = 51–60 (N = 2) Plt = 61–100 (N = 131)	Transfused to Plt > 50	N/A	N/A	No complications	Decision must be made on case-by-case basis	Patients included ITP, GT, preeclampsia Epidural catheter removed if Plt >60
Ramos et al. ⁵⁵	OB N = 10	10	Plt >101 (N = 5) Plt = 70–100 (N = 5)	None	N/A	N/A	No complications	None	
Moeller-Bertram et al. ⁴³	OB N = 1	1	Plt = 26	None	18-G Tuohy 20-G Catheter	No	No complications	None	ITP undiagnosed before block Platelet count determined after placement of epidural catheter Exclusion criteria for epidural not indicated
Webert et al. ⁶¹	OB N = 42	42	Plt >150 (N = 8) Plt = 101–150 (N = 8) Plt = 76–100 (N = 19) Plt = 51–75 (N = 6) Plt <50 (N = 1)	N/A	N/A	N/A	No complications	None	
Frolich et al. ³⁹	OB N = 1	1	Plt = 61	None	N/A	No	No complications	None	TEG analysis normal
Beilin et al. ⁴⁸	OB N = 1	3	Plt = 93–96	None	18-G Hustead 20-G Catheter	N/A	No complications	Plt <100 not contraindication to NT	
Steer ⁴⁷	OB N = 1	1	Plt = 73	None	N/A	No	No complications	None	TEG analysis normal
Hew-Wing et al. ⁴⁰	OB N = 1	1	Plt = 2	None	N/A	No	No complications	Plt <100 not contraindication to NT	
Rasmus et al. ⁵⁶	OB N = 6	6	Plt = 18–82 (Plt <50 = 2)	None	17-G Tuohy 19-G Catheter	N/A	No complications	Plt <100 not absolute contraindication to NT	
Rolbin et al. ⁵⁷	OB N = 61	61	Plt = 50–75 (N = 2) Plt = 76–100 (N = 1) Plt = 101–125 (N = 17) Plt = 126–149 (N = 41)	None	N/A	N/A	No complications	LEA safe if Plt >100	
Thoracic epidural									
Roulet et al. ⁴⁶	Pediatric N = 1	1	Plt = 83	Transfused to Plt = 83 from 50	20-G Tuohy 24-G Catheter	No	No complications	None	
Spinal									
Frenk et al. ⁵⁰	OB N = 35 ^a	35	Plt <50 (N = 2) Plt = 50–60 (N = 4) Plt = 61–100 (N = 29)	Transfused to Plt >50	N/A	N/A	No complications	Decision must be made on case-by-case basis	Patients included ITP, GT, preeclampsia
Ramos et al. ⁵⁵	OB N = 7	7	Plt >101 (N = 2) Plt = 70–100 (N = 5)	None	27G or 29G Whitacre or Yale	N/A	No complications	None	
Chang et al. ³⁵	GYN N = 1	1	Plt = 46–64	None	25G Type N/A	N/A	No complications	Plt \geq 50 safe for spinal block	
Paravertebral									
Okutomi et al. ⁴⁴	OB N = 1	2	Plt = 69	Steroids, IVIg	17G Type N/A	No	No complications		

Numeric values presented as $\times 10^9 \text{ L}^{-1}$.

OB = obstetric; G = needle gauge; GT = gestational thrombocytopenia; GYN = gynecologic; IVIg = intravenous immune globulin; ITP = idiopathic thrombocytopenic purpura; LEA = lumbar epidural anesthesia; N = number of patients; N/A = data not indicated in reference; NT = neuraxial technique; Plt = platelets; TEG[®] = thromboelastography.

^aIn the largest case series by Frenk et al., there were 170 patients (135 LEA, 35 spinal blocks) with ITP, GT, and Preeclampsia. The authors did not enumerate each entity.

spinal) undermine the validity of any general management recommendations that can be drawn from the present review for at least two important reasons. First, it has been shown that the prevalence of spinal hematoma after neuraxial techniques is considerably less in the obstetric population.^{70,71} Second, among the 406 neuraxial techniques placed in obstetric patients with hemostatic defects, 96% had Type I vWD (69 of 72 patients) or ITP (325 patients),

leaving only 2 patients with Type IIA vWD and 1 with Type III vWD which are arguably more severe than either Type I vWD or ITP in pregnancy. In particular, deficiencies in factor levels almost universally improve near term in Type I vWD. These limitations certainly serve to underestimate the rate of hemorrhagic complications in patients with bleeding diatheses and underscore the need for large-scale, multi-center international investigation to

Table 4. Guidelines for Neuraxial Techniques in Hemophilia, von Willebrand's Disease, and Thrombocytopenia

Author/ reference	Society	Title	Bleeding diathesis	Level of evidence	Recommendations	Remarks
Demers et al. ⁷⁹	SOGC	Gynaecological and obstetric management of women with inherited bleeding disorders	Hemophilia	V	Neuraxial techniques safe when coagulation factors normal	'Normal' levels not defined No case series referenced
			vWD	V	Neuraxial techniques safe when coagulation factors normal	'Normal' levels not defined No distinction made between vWD subtypes vWD recommendation based on single case report and single case series reviewed herein ^{37,43}
Lee et al. ⁸⁰	UKHCDO	The obstetric and gynaecological management of women with inherited bleeding disorders	Hemophilia	V	Neuraxial techniques safe when coagulation factors >0.5 IU mL ⁻¹ Use midline technique with minimum local anesthetic concentration	Hemophilia recommendation based on single case series and case report ^{38,53}
			vWD Type I	V	Neuraxial techniques safe when coagulation factors >0.5 IU mL ⁻¹ Use midline technique with minimum local anesthetic concentration	vWD recommendations based on 5 of 10 case series reviewed herein ^{34,37,42,43,54} Rationale for avoidance in vWD Types II and III not explained
Pasi et al. ⁸¹	UKHCDO	Management of von Willebrand disease	vWD	V	Neuraxial techniques safe when coagulation factors >0.5 IU mL ⁻¹ Avoid neuraxial techniques in patients with vWD Types II and III	Rationale for avoidance in vWD Types II and III not explained No case series referenced
77	BCSH	Guidelines for the management of idiopathic thrombocytopenic purpura in adults, children, and in pregnancy	ITP	V	Platelet count >80 × 10 ⁹ L ⁻¹ recommended for neuraxial techniques	No case series referenced Conflicts with 2003 recommendations also published by BCSH in 2003 regarding platelet transfusion ⁷⁸
78	BCSH	Guidelines for the use of platelet transfusion	Thrombocytopenia	V	Platelet count >50 × 10 ⁹ L ⁻¹ recommended for neuraxial techniques and major surgical procedures	Based on single case series and 2 consensus statements ^{83,84,87} Conflicts with 2003 recommendations also published by BCSH regarding management of ITP in pregnancy ⁷⁷
Schiffer et al. ⁸²	ASCO	Platelet transfusions for patients with cancer: clinical practice guidelines of ASCO	Thrombocytopenia	V	Platelet count >40–50 × 10 ⁹ L ⁻¹ recommended for neuraxial techniques and major surgical procedures	Based on 2 case series reviewed herein ^{85,86}

ASCO = American Society for Clinical Oncology; BCSH = British Committee for Standards in Haematology; SOGC = Society of Obstetrics and Gynaecology of Canada; UKHCDO = United Kingdom Haemophilia Doctors Organization.

validate the results presented in this review article and generate meaningful management strategies for neuraxial techniques.

Relevant professional societies provide minimal, if any, evidence-based guidelines to assist anesthesiologists considering neuraxial techniques in patients with hemophilia, vWD, or ITP. Drawn from expert opinion, retrospective data and case reports, the widely cited consensus statements published by ASRA and the German Society of Anesthesiology and Intensive Care pertain exclusively to patients undergoing neuraxial techniques in the setting of hemostasis altering medications. Neither ASRA, European Society of Regional Anesthesia, the American Society of Anesthesiologists,

the Canadian Anesthesiologists Society,[†] nor the American College of Obstetrics and Gynecology offers any guidelines for the practice of neuraxial techniques in patients with inherited coagulopathies or ITP.^{16,17,75,76}

Table 4 summarizes available recommendations from professional societies and government agencies regarding the provision of neuraxial techniques in the setting of hemophilia, vWD, or thrombocytopenia.^{77–82} Importantly, each of these guidelines is based

Table 5. Data Summary of Lumbar Puncture or Caudal Injection in Nonimmunologic Thrombocytopenia

Author/reference	Population/N	No. of punctures	Preblock platelet count ($\times 10^9 L^{-1}$)	Treatment	Gauge/type	Difficult insertion	Outcome	Authors' recommendations	Remarks
Lumbar puncture Lee et al. ¹⁰⁴	ONC N = 4	4	Patient A— Plt = 46 Patient B— Plt = 159 Patient C— Plt = 8 Patient D— Plt = 250	A—Plt = 46 post transfusion B—None C—None D—None	N/A	A, D—traumatic	A, B—Epidural hematoma C, D—Subdural hematoma	None	All 4 cases resolved with conservative management and no neurologic compromise All 4 cases occurred in the setting of injection of chemotherapeutic agents
Ayerbe et al. ¹⁰²	ONC N = 1	1	Plt = 26	None	N/A	N/A	Subarachnoid hematoma, no permanent neurologic deficit	Authors speculate that Plt = 25 too low for LP	Immediate surgical decompression
Vavricka et al. ¹⁰⁵	ONC N = 66	195	Plt = 101–150 (NT = 77) Plt = 50–100 (NT = 43) Plt = 20–50 (NT = 75)	Plt transfusion to >20	N/A	N/A	No complications	LP safe without transfusion if Plt >20	
Howard et al. ⁸⁶	ONC N = 952	5,223	Plt = 101–150 (NT = 3,424) Plt = 51–100 (NT = 858) Plt = 21–50 (NT = 742) Plt = 11–20 (NT = 170) Plt <10 (NT = 29)	None	N/A	N/A	No complications	LP safe without transfusion if Plt >10	
Wirtz et al. ¹⁰⁷	ONC N = 1	1	Plt = 42	Plt transfusion, but no repeat Plt count	N/A	No	Subdural hematoma with nonpermanent paraparesis	LP safe without transfusion if Plt >50 Plt should be rechecked posttransfusion	
Blade et al. ¹⁰³	ONC N = 1	1	Plt = 10	None	19G	No	Subarachnoid hematoma Mild residual paraparesis	None	Initial treatment for 48 h after symptoms developed was repeated transfusion, target Plt >50 Surgical decompression 48 h after symptoms developed
Caudal injection Waldman et al. ¹⁰⁶	ONC N = 19	19 ^a	Plt <50 (N = 19)	None	25G	No	No complications	Caudal block safe with 25-G needle in severely thrombocytopenic patients	Authors indicate they have expanded use of technique to inject local anesthetic and methylprednisolone
Thoracic epidural Wulf et al. ¹⁰⁸	ONC N = 1	1	Plt = 48	None	21-G needle 26-G catheter	No	Asymptomatic epidural hematoma	Plt count should be known before NT	Epidural hematoma discovered on autopsy after unrelated death

Numeric values presented as $\times 10^9 L^{-1}$.

LP = lumbar puncture; N = number of patients; NT = number of LPs performed; ONC = oncologic patients thrombocytopenic from malignancy, chemotherapy, or radiation; Plt = Platelets.

^a Thirty-seven anticoagulated patients and 19 patients with nonimmunologic thrombocytopenia underwent 336 caudal blocks. Each patient with thrombocytopenia underwent more than one caudal block but authors did not indicate specific numbers.

on expert opinion and/or case series with fewer patients than are presented in this review.^{52,83–87}

An in-depth review of hemophilia, vWD, and ITP is not provided as the implications for anesthesia in general have been presented elsewhere.⁸⁸ In brief, hemophilia is an inherited bleeding disorder resulting

from deficiencies in specific coagulation factors and is diagnosed by direct factor assay. Hemophilia A (80% of hemophiliacs) occurs when there is a deficiency in Factor VIII, and B (20% of hemophiliacs) occurs when Factor IX is deficient. The prevalence of hemophilia A is approximately 1 in 5000, whereas that of hemophilia

B is approximately 1 in 25,000.⁸⁹ Traditional surgical recommendations for hemophiliacs suggest that major surgery can be safely performed when Factor VIII/IX levels are normalized ($>0.5 \text{ IU mL}^{-1}$).⁹⁰⁻⁹²

vWD is the most common inherited coagulopathy and is estimated to affect approximately 1%–2% of the general population. It results from either a quantitative or qualitative defect of von Willebrand Factor and is classified into four major subtypes.⁹³⁻⁹⁵ Laboratory values helpful in diagnosing or assessing the severity of vWD are Factor VIII levels, von Willebrand Factor levels, and Ristocetin Co-factor Activity that assesses von Willebrand Factor binding to platelet glycoproteins. Normal values for each of these laboratory assays are 0.5–1.5 IU mL^{-1} .^{96,97} Treatment in the perioperative period ranges from 1-deamino-8-D-arginine vasopressin for mild Type I disease, but can progress to cryoprecipitate and high concentration factor replacement as necessary. Specific treatment strategies may be determined in consultation with a hematologist.⁹⁰

ITP is characterized by thrombocytopenia without identifiable cause. Its estimated incidence ranges from 1.6 to 6.6 in 100,000 adults per year.^{98,99} Diagnosis is made by history, physical, complete blood count, and peripheral blood smear that have excluded all other etiologies of thrombocytopenia.⁹⁸ It is important to note that the platelets that do circulate, and thus are reflected in the platelet count, are fully functional. First-line therapy for ITP, should it be necessary, is the administration of corticosteroids. Second-line therapies include chemotherapeutic drugs, such as azathioprine and vinca alkaloids. For urgent or emergent surgery, transfusion of single donor platelets or IV immune globulin can be most effective. Unfortunate refractory cases of ITP usually undergo splenectomy which offers a 50% chance of cure.⁸⁸ The minimum acceptable platelet count that is widely cited for most surgical procedures is $50 \times 10^9 \text{ L}^{-1}$ to maintain adequate primary hemostasis.^{78,82,100,101} However, the minimum platelet count at which the risk of hemorrhagic complications from neuraxial techniques becomes prohibitively high remains undefined.

It is noteworthy that lumbar puncture is frequently performed for diagnostic or therapeutic purposes in severely thrombocytopenic patients. Our literature search identified 5445 patients among eight published reports describing the use of neuraxial techniques in the setting of nonimmunologic thrombocytopenia (oncologic primary, chemotherapy, or radiation induced) (Table 5).^{86,102-108} These patients did not meet our inclusion criteria and are arguably at higher risk for spinal hematoma because lumbar punctures are often performed by individuals with less experience, using larger gauge needles, in more severely thrombocytopenic patients, particularly in cases of leukemia, than

neuraxial techniques performed by anesthesiologists. Eight cases of spinal hematomas were reported in patients with platelet counts ranging from 8 to $250 \times 10^9 \text{ L}^{-1}$ and 2 needle insertions described as traumatic.^{102-104,108} It seems plausible that, given identically low platelet counts, neuraxial techniques in the setting of leukemic thrombocytopenia may be more dangerous than in ITP in pregnancy, but this is wholly speculative.

In summary, there is a paucity of published data regarding the provision and safety of neuraxial techniques in patients with common bleeding diatheses. Based on reports of only 507 neuraxial techniques, of which 406 were in the obstetric population, hemorrhagic complications after neuraxial techniques in patients with known hemophilia, vWD, or ITP appear infrequent when factor levels are more than 0.5 IU mL^{-1} for Factor VIII levels, von Willebrand Factor levels, and Ristocetin Co-factor Activity levels, or when the platelet count is more than $50 \times 10^9 \text{ L}^{-1}$ before block performance. The minimum “safe” factor levels and platelet count for neuraxial blockade remain undefined in both the obstetric and general populations and evidence-based recommendations for neuraxial techniques in the setting of hemophilia, vWD, or ITP cannot be offered.

ACKNOWLEDGMENTS

The authors thank Dr. Erik Yeo, MD, FRCPC, Director of Hemostasis and Thrombosis, Department of Hematology, Toronto General Hospital, University Health Network and Toronto Medical Laboratories, Toronto, Ontario, and Dr. Hossam El-Beheiry, MBBCh, PhD, FRCPC, Department of Anesthesia, Trillium Health Centre, Mississauga, Ontario for their guidance during the preparation of this manuscript.

APPENDIX^{30,31}

Level of evidence	Description
Level I	Randomized controlled trial Systematic review of Level I randomized controlled trials (homogeneous studies)
Level II	Prospective cohort study Poor-quality randomized controlled trial (e.g. <80% follow-up) Systematic review Level II studies Nonhomogeneous Level I studies
Level III	Case control study Retrospective cohort study Systematic review of Level III studies
Level IV	Case series (no, or historical, control group)
Level V	Expert opinion

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