# Regional anaesthesia for primary caesarean section in patients with preterm HELLP syndrome: a review of 102 cases

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### **Summary**

Objective: To determine the feasibility and the safety of combined spinal/epidural and spinal anaesthetic techniques for primary caesarean section in case of preterm HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome. *Methods:* A retrospective study was carried out in a tertiary centre including all patients who underwent primary caesarean section for HELLP syndrome. The immediate preoperative and the lowest thrombocyte count, the method of anaesthesia and eventual complications were recorded. Patients were categorised as having antepartum or postpartum HELLP syndrome. *Results:* A total number of 102 charts was reviewed. Mean gestational age was 30.6 weeks (SD 2.7, range 23-36 weeks). There were seven (6.9%) patients with postpartum HELLP and 95 with antepartum HELLP. In case of antepartum HELLP in 37 (36.3%) general anaesthesia was selected; in 53 (52.0%) combined spinal epidural anaesthesia and in 12 (11.8%) single dose spinal anaesthesia. Preoperative thrombocyte count was significantly higher (p < 0.01) in the combined spinal epidural group (113,000/mm³) while there was no difference between general (88,000/mm³) and spinal anaesthesia (95,000/mm³). There were no cases of epidural haematoma. Two patients received a combined spinal epidural although their immediate preoperative thrombocyte count was < 50,000/mm³. *Conclusions:* Our data demonstrate that combined spinal/epidural is feasible and safe in selected cases of HELLP syndrome.

Key words: HELLP; Preeclampsia; Pregnancy; Epidural; Spinal; Combined spinal-epidural; Thrombocytes.

### Introduction

HELLP syndrome is considered a severe form of preeclampsia. The acronym HELLP was first suggested by Weinstein in 1982 and describes hemolysis (H), elevated liver enzymes (EL) and low platelets (LP) [1].

Both regional and general anaesthesia are potentially associated with complications in HELLP syndrome. As low platelet count and liver dysfunction are risk factors for the development of epidural haematoma in case of neuraxial anaesthesia, spinal and epidural anaesthesia have been considered for a long time as a contraindication [2-5]. Although in the early nineties general anaesthesia was recommended as the technique of choice, impaired liver function and an altered metabolism of anaesthetic agents can result in unexpected reactions with general anaesthesia besides the risk of enhanced hepatotoxicity following the use of volatile substances, difficult intubation and hypertensive crisis during induction [2, 5, 6].

In our hospital combined spinal-epidural anaesthesia is the technique of preference for primary caesarean section. Epidural anaesthesia is only selected in case a catheter was already placed during (trial of) labour. Rarely patients with preterm severe preeclampsia or HELLP syndrome are considered for vaginal delivery. With respect to platelet count the following local guidelines have been recommended: any technique is possible with counts above 90,000/mm³, general anaesthesia with counts inferior to 60,000/mm³ while with intermediate

values the technique used is at the discretion of the managing anaesthesiologist with some preference for a less traumatising single-dose spinal.

Studies on spinal and epidural anaesthesia in severe preeclampsia have almost always considered coagulopathy, including HELLP syndrome, a reason for exclusion [7-9]. To our knowledge only three small series have specifically documented regional anaesthesia for HELLP syndrome [10-12] and no report exists on the use of combined spinal epidural anaesthesia (CSE) with a double puncture either at a single or double interspace. We performed this retrospective study to further explore the feasibility and the safety of different regional anaesthetic techniques for primary caesarean section in cases of HELLP syndrome.

### **Material and Methods**

After institutional approval by the local ethics committee we performed a retrospective chart analysis in a tertiary referral centre including all women who underwent primary caesarean section for HELLP syndrome at a gestational age before 37 weeks. The inclusion period was from January 1, 2002 to December 31, 2007. A difference was made between antepartum and postpartum manifestation of HELLP as in case of a first manifestation of HELLP syndrome during the postpartum period this would have had no influence on the choice of anaesthetic technique.

In our centre HELLP syndrome is classified according to the Mississippi three class system [13], based on the lowest measured maternal platelet count, either before or after delivery. In all cases haemolysis and hepatic dysfunction had to be present, demonstrated by an increase of lactic dehydrogenase (LDH) level  $\geq$  600 IU/l and aspartate transaminase (AST) and or

alanine transaminase (ALT) ≥ 40 IU/l. Women with class 1 HELLP syndrome have a maternal platelet nadir of ≤ 50,000/mm³; patients with class 2 HELLP syndrome a platelet nadir of > 50,000 but ≤ 100,000/mm³ and those with class 3 disease a platelet count of > 100,000 but < 150,000/mm³. Daily laboratory evaluation included liver function tests, complete blood count, fibrinogen and fibrin degradation products and renal function tests. Maternal hypertension was treated if systolic blood pressure was ≥ 160 mmHg and/or the diastolic value ≥100 mmHg. Treatment consisted of oral felodipine (5 to 20 mg daily) followed by urapidyl intravenously if blood pressure rose to ≥ 180 mmHg systolic or ≥ 110 mmHg diastolic values. If gestational age was < 35 weeks, betamethasone (2 x 12 mg) was given intramuscularly (if maternal thrombocyte count was > 50,000/mm³) or intravenously in case of a lower count.

All patients received intravenous MgSO4 (loading dose 5 g, followed by 1 g/hour IV) continued for 48 hours after the delivery. Thrombocyte transfusion was not systematically performed and the decision to give thrombocytes was left to the discretion of the obstetrician and anaesthesiologist.

When regional anaesthesia was selected patients were positioned either in the sitting or right lateral decubitus position. Before initiation of the spinal block, each patient received 500 ml of hetastarch 6% (Voluven®, Fresenius, France).

A skin wheal was raised with 1% lidocaine at the L3-4 or L4-5 intervertebral space. For the CSE technique an Adjustable Durasafe® BD needle combination was used. The epidural space was identified with a 17-gauge Tuohy needle to which a glass syringe filled with 4 ml of air was connected. Subsequently if gestational age was < 35 weeks a lockable 27-gauge spinal Whitacre needle was introduced. After appearance of cerebrospinal fluid, 6.66 mg of hyperbaric bupivacaine and 3.33 μg of sufentanil were slowly injected with the orifice of the spinal needle directed cephalad. This combination is 2 ml out of a 3 ml mixture containing 10 mg hyperbaric bupivacaine 0.5% and 5 μg sufentanil.

In the case of insufficient initial cephalad spread, or when pain sensations reappeared intraoperatively, incremental epidural supplements consisting 0.75% of ropivacaine were injected, starting with 4 ml. When necessary, additional 2-ml boluses were given no earlier than 5 min after the preceding top-up.

For single-dose spinal anaesthesia a 27-gauge spinal Whitacre needle was introduced at the L3-4 or L4-L5 intervertebral space. Hyperbaric bupivacaine (8.3 mg) and 4.15  $\mu$ g of sufentanil (i.e., 2.5 ml of above-mentioned mixture) were slowly injected.

Intraoperative haemodynamics were registered every two minutes. Ephedrine increments of 5 mg were given IV to treat hypotension, defined as a decrease in systolic blood pressure of 20% below baseline values or to less than 100 mm Hg.

General anaesthesia was induced after preoxygenation (100% oxygen for 5 min) with 3-5 mg/kg thiopenthal (Pentothal®) and 1.5 mg/kg succinylcholine (Lysthenon®) administered intravenously. Tracheal intubation was performed under cricoid pressure. Sevoflurane at 0.5 MAC with an oxygen:air mixture aimed at obtaining a FiO2 of 0.5 was given until delivery after which fentanyl and atracurium were given as required.

After delivery, all patients received a single dose of 2 g of cefazoline IV, 10 IE of oxytocine IV slowly over five minutes, and 10 IE IV over six hours. Starting on the first postoperative day all patients received low molecular weight heparin subcutaneously (nadroparine 2850 IE anti-Xa) daily for ten days. In case of combined spinal epidural anaesthesia the epidural catheter was left in place for at least 48 hours for patient-con-

trolled analgesia delivering 4 ml levobupivacaine 0.1% with sufentanil 1 µg/ml per demand at a lock out time of 15 minutes.

On the second postoperative day the epidural catheter was removed if the maternal platelet count was  $\geq 100,000/\text{mm}^3$ , otherwise a repeat IV dose of 12 mg of betamethasone was given and the platelet count repeated one day later with the catheter staying in place.

For every patient the gestational age at the time of the caesarean section was documented as were the immediate preoperative thrombocyte counts, the lowest thrombocyte count reached and the method of anaesthesia. The preoperative thrombocyte counts in the different anaesthetic groups were compared using analysis of variance (one-way ANOVA on SPSS 15.0) with posthoc analysis using the Bonferroni test for eventual differences.

### Results

During the period studied 102 patients fulfilling the criteria for HELLP syndrome had a primary caesarean section at less than 37 weeks gestational age. Mean gestational age at the time of caesarean section was 30.4 weeks (standard deviation 2.8; range 23-36 weeks). In seven (6.9%) patients HELLP syndrome first manifested after delivery – all of these had caesarean section for severe preeclampsia with a rapidly deteriorating maternal condition but without the laboratory changes necessary for diagnosing HELLP syndrome preoperatively; four received general anaesthesia and three had combined spinal epidural anaesthesia. Obviously these patients were excluded from further analysis as the postpartum diagnosis of HELLP syndrome can not influence the choice of anaesthetic method used.

Of the remaining 95 patients, there were 21 (20.6%) Mississipi class 1; 58 (56.9%) class 2 and 16 (15.7%) class 3 patients, based on the lowest thrombocyte count reached either pre- or postoperatively.

In 33 (36.3%) general anaesthesia was used, whereas in 50 (51.9%) combined spinal epidural anaesthesia was chosen and 12 (11.8%) received single-dose spinal anaesthesia. None of the patients received plain epidural anaesthesia alone. Table 1 gives the types of anaesthesia for the three classes in antepartum HELLP cases.

Table 1. — Mississippi class and type of anaesthesia.

	Class 1 HELLP	Class 2 HELLP	Class 3 HELLP	Total no.
Combined spinal epidural	11 (1)	29 (2)	10	50
Spinal single shot	1	8	3	12
General anaesthesia	9	21	3	33
Overall	21	58	16	95

Table 2 describes preoperative thrombocyte count and the type of anaesthesia used. All patients had a preoperative count of  $< 150,000/\text{mm}^3$ , but some had a preoperative count of  $> 100,000/\text{mm}^3$ , which postoperatively went down to < 100,000 or  $< 50,000/\text{mm}^3$ . This explains the different numbers of patients in Tables 1 and 2.

We also looked for patients with a preoperative platelet count below 80,000/mm<sup>3</sup>. There were 27 women in this group, seven (25.9%) received CSE, three (11.1%) a single spinal shot and 17 (62.9%) general anaesthesia.

Table 2.— Type of anaesthesia and immediate preoperative thrombocyte count (.10³/mm³).

Anaesthesia	Mean (SD)	Range	≤ 50 no.		< 50 ≤ 100 (no.)		< 100 ≤ 150 (no.)	Total no.
				T		T		
CSE	112.6 (27.7)	46-149	2	1	18	8	30	50
Spinal	95.7 ( 27.4)	55-146	0	0	8	1	4	12
General								
anaesthesia	76.8 (28.7)	27-140	8	2	20	0	5	33
Overall	98.7 (32.1)	27-149	10	3	46	9	39	95

CSE: Combined spinal epidural anaesthesia; SD: Standard deviation; T: preoperative thrombocyte transfusion.

Despite local guidelines, two patients with a preoperative platelet count lower than 50,000/mm received a combined spinal epidural. In one patient with a count of 46,000/mm³, a thrombocyte transfusion was given and a combined spinal epidural was placed immediately thereafter without awaiting further results. The other patient had a combined spinal epidural placed based on blood results from four hours earlier (thrombocyte count 80,000/mm³); a sample taken immediately before the patient went to the operating theatre later showed to be 46,000/mm³.

Mean preoperative thrombocyte count was significantly different between groups, as demonstrated in Table 2 (F = 3.4; p < 0.05 in ANOVA). Posthoc analysis with the Bonferroni test demonstrated a significantly lower preoperative thrombocyte count for general anaesthesia versus combined spinal epidural anaesthesia (p < 0.05) but no significant differences between combined spinal epidural anaesthesia and spinal anaesthesia nor between spinal and general anaesthesia.

Thirteen patients received thrombocyte transfusions, 12 of these during the preoperative period (Table 2).

There were no cases of epidural haematoma. The only recorded anaesthetic complication was a bloody tap in a planned spinal anaesthesia, necessitating conversion to general anaesthesia. No major preoperative bleeding occurred, but one patient needed to be re-operated within 24 hours due to severe intraabdominal bleeding.

One patient scheduled for spinal anaesthesia developed an anaphylactic reaction upon the hetastarch with hypotension, dyspnoea and generalised oedema. She was transferred to the ICU where she received corticosteriods and supportive therapy until the next morning when platelet counts and liver tests had much improved upon which she underwent uneventful surgery under spinal anaesthesia (this patient has been reported on before) [14].

## Discussion

Our study describes a well-defined group of high-risk obstetric patients undergoing primary caesarean section in case of HELLP syndrome. No direct anaesthesia-related complications were found. The number of platelets was indeed higher for patients receiving a catheter technique whereas no difference in platelet count was found between general and single-dose spinal.

Based on case reports and assumptions HELLP syndrome is often considered a contra-indication for regional anaesthesia [4, 5, 15]. This is mainly due to fear of the development of an epidural haematoma, but other complications have been described such as intracranial subdural haematoma [16]. On the other hand, it is well known that general anaesthesia is a risk factor for maternal mortality, mainly due to problems of airway management or haemodynamic perturbations [17, 18]. Slow metabolic degradation of choline-ester drugs can occur in HELLP syndrome, probably due to decreased pseudocholinesterase activity [14]. The minimum platelet count above which it is safe to perform spinal or epidural anaesthesia is still unknown, but several studies suggest that this may be safely done at thrombocyte counts less than 100,000/mm<sup>3</sup> [17, 19-24]. None of these studies contains data specific for patients with HELLP syndrome nor is the use of combined spinal epidural mentioned.

Not many studies have reported on anaesthetic techniques in patients with HELLP syndrome. In the majority of reports the number of patients varies from 20 to 40 collected during four to six-year periods [2-5, 24] while some have mainly described and recommended intensive care treatment for these patients while strongly dissuading regional anaesthesia without strong supportive evidence [4, 5].

In a landmark study by Sibai *et al*. [11] 16 of 112 patients with HELLP syndrome received epidural anaesthesia. The mean platelet count in this group was  $83 \pm 8.10^3$ /mm³. There was one maternal bleeding in the epidural space in a patient with a platelet count of 93,000/mm³. The catheter was kept in place for 24 hours and the bleeding stopped spontaneously. In their discussion they wrote that "the use of epidural anaesthesia in such patients is potentially dangerous".

Crosby *et al.* [2] reported on 33 patients with HELLP syndrome of whom 32 received general anaesthesia and eight patients had uneventful epidural anaesthesia, but at the time of catheter insertion the diagnosis of HELLP syndrome had not been made in six of these eight patients. They had much evidence of abnormal haemostasis while 36% of patients received blood transfusions.

Miyamoto *et al.* [10] reported on 11 caesarean sections for HELLP syndrome, six under general anaesthesia, one epidural and four spinal blocks. No complications were noted.

In a report by Osmanagaoglu *et al.* [25] 27 caesarean sections in a group of 37 HELLP syndrome patients were performed. General anaesthesia was used in 12 and single-dose spinal anaesthesia in 25 patients. In this study no distinction could be made for the anaesthetic used in the vaginal delivery or the caesarean section group. There were no complications of regional anaesthesia but these were also not explicitly looked for. In this study maternal mortality was as high as 30% but it is unclear whether the risk was higher for vaginal than for abdominal delivery. In our hospital vaginal delivery was performed in only one non-included case during the study period evaluated.

The largest published series to date reported on 85 cae-

sarean sections [12], of whom 14 had a post caesarean and 71 a preoperative diagnosis of HELLP syndrome. In this series 58 (81.7%) had epidural anaesthesia, nine (12.7%) had general anaesthesia and four (5.6%) had spinal anaesthesia. Neurological complications or epidural haematoma were not diagnosed.

To our knowledge there is a lack of reports using combined spinal-epidural anaesthesia for caesarean section in HELLP syndrome. Although simply a combination of spinal and epidural anaesthesia it signifies a double risk of perispinal bleeding as two needles are introduced in two vascularised spaces. Theoretically this risk may be even greater when a double-interspace technique is used. Contrary to earlier publications on plain epidural we chose to use the catheter for patient controlled anaesthesia and leave it in place until the platelet count had risen over 100,000/mm³, also because meanwhile LMWH had been started.

Our results, as those from Vigil-De Gracia *et al.* [12], question the often cited advice that a platelet count below an arbitrary limit (be it 100,000 or 80,000/mm³) precludes the placement of an epidural catheter in cases of HELLP syndrome. In patients with a platelet count below 80,000/mm³ the anaesthesiologists in our centre prefer general or spinal anaesthesia three times more frequently than CSE anaesthesia.

From the point of view of maternal safety no data on anaesthesia-related maternal death in HELLP syndrome are available, but control of blood pressure is more difficult with general anaesthesia .

In a survey of severe neurological complications after a central neuraxial blockade [26] it was found that 33 spinal haematomas out of a total of 127 complications were present, two of which were in patients with HELLP syndrome, one with a spinal block and one with an epidural catheter being removed with apparent signs of coagulopathy. In this study the highest risk for developing spinal haematoma was in female orthopaedic patients subject to knee arthroplasty, and clearly not in obstetric patients.

Other studies on thrombocytopenic parturients have failed to demonstrate the feared complication of spinal haematoma [19, 23, 27, 28].

In a recent letter to the editor Frenk *et al.* [10, 29] reported their experience with regional anaesthesia in parturients with thrombocytopenia. No neurological complications nor spinal haematomas were reported, but this series did not include patients with HELLP syndrome, and neither did the series reported by Bernstein *et al.* [27].

It is evident that there is more than just the platelet count alone as altered platelet function has long since and repeatedly been suggested but has not yet been clearly demonstrated in HELLP syndrome [30].

Thrombocyte function is difficult to evaluate. Studies on the use of thromboelastography in HELLP syndrome found that in cases with preeclampsia women with a platelet count less than 100,000/mm<sup>3</sup> are significantly hypocoagulable when compared to preeclamptic women

with platelet counts  $\geq 100,000/\text{mm}^3$ , but the level of thromboelastographic parameters that would allow safe epidural anaesthesia to be performed in these women is not known [31].

Thromboelastography has been reported in a case report to reveal accompanying fibrinolysis in cases of HELLP syndrome [32]. No reports are available on the use of platelet function analysis (PFA-100) in HELLP syndrome, but in patients with preeclampsia false positives (suggesting disturbed clothing in normal patients) have been described [33]. On the other hand it was demonstrated that in patients with pregnancy induced thrombocytopenia, platelet function is not disturbed with counts as low as 60,000/µl. Conflicting results have been obtained demonstrating impairment of haemostatic function in severe preeclampsia with PFA-100 even with a normal thrombocyte count, but not when testing with thromboelastography [34].

### Conclusion

Based on a small series, our study demonstrates that regional anaesthesia, including combined spinal/epidural anaesthesia for primary caesarean section in HELLP syndrome probably is feasible and safe, but until now no larger studies are available. Despite local guidelines regional techniques have been used more frequently, which may indicate that there is more than platelet count alone in the decision making of an anaesthetic technique such as the speed of platelet loss, technical aspects, emergency, anticipated intubation difficulty and personal preferences [35].

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