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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Cesarean delivery under neuraxial anesthesia in a patient with a liver transplant

Slavica Krušić[1], Nada Pejčić[2], Mirjana Stojanović-Tasić[3], Dijana Damnjanović[4], Gillian Abir[5]

[1]Narodni Front Clinic for Gynecology and Obstetrics Belgrade, Serbia;
[2]Leskovac General Hospital, Leskovac, Serbia;
[3]Dr. Laza Lazarević Clinic for Mental Disorders, Belgrade, Serbia;
[4]Jevremova Special Gynecology Hospital with Maternity Ward, Belgrade, Serbia;
[5]Stanford University, School of Medicine, Palo Alto, California, United States

SUMMARY

Introduction Improved outcomes after liver transplantation contribute to a successful pregnancy and delivery in transplant recipients. Anesthesiology teams face challenges when providing perioperative care to patients who have a liver transplant and undergo cesarean delivery, which include: an increased rate of cesarean delivery, a high risk of infection, and a high risk of interaction between immunosuppressant and anesthetic drugs.

Case outline We report the case of a 28-year-old patient with a liver transplant (from a live donor) who underwent elective cesarean delivery under neuraxial anesthesia. Appropriate anesthetic management is critical to ensure optimal perioperative maternal and fetal outcomes. Cardiovascular stability after neuraxial anesthesia was maintained with adequate perioperative intravenous fluid management and early vasopressor(s) administration to preserve hepatic perfusion. Multimodal postoperative analgesia was administered; however, caution is required when prescribing drugs that have the potential for hepatic and renal side effects.

Conclusion Multidisciplinary team evaluation, planning, and preparation are vital for optimizing safe care and delivery of pregnant patients with transplanted organs.

Keywords: anesthesia; cesarean delivery; liver transplant

INTRODUCTION

In 1967, the first successful liver transplant was performed at the University of Colorado in the United States, and the first successful pregnancy in a patient with a liver transplant was reported in 1978 [1]. The inaugural liver transplant in Serbia was performed in 1995 [2]. The liver is the second most commonly transplanted organ, with a one-year survival rate greater than 90% and a three-year graft survival rate of 80% [1]. Out of all liver transplant recipients, female patients of reproductive age represent 8%, and female children represent 5%, the majority of whom will reach reproductive age [3]. There are a few publications that describe the anesthetic management of cesarean delivery (CD) and labor analgesia management in patients who have undergone a liver transplant. This case report describes the first successful pregnancy and CD performed in a patient with a liver transplant in Serbia.

CASE REPORT

In 2015, a multidisciplinary team that included an anesthesiologist, obstetrician, hepatologist, and cardiologist provided care to a 28-year-old patient (G1P0) at 38 weeks gestation who underwent an elective CD under neuraxial anesthesia at Narodni Front Clinic for Gynecology and Obstetrics, Belgrade. The patient's past medical history included a living-donor liver transplant (donated by the patient's father) due to fulminant hepatic failure secondary to Wilson's disease nine years earlier. Nine months post-transplant, hepatitis B infection was diagnosed, and the patient received treatment with lamivudine (antiviral drug) which was replaced with tenofovir after several years due to seroconversion. The patient also received immunosuppressive therapy with tacrolimus and had stable serum levels and liver function tests (within normal limits) prior to and during pregnancy. The patient was American Society of Anesthesiologists classification 3 and had a body mass index of 22.1 (height 1.78 m, weight 70 kg).

Preoperative liver and kidney function tests were within normal limits, and the platelet count was 127 × 10^9/L (reference range 140–450 × 10^9/L). Two large-bore peripheral intravenous (IV) cannulas (16 G) were placed, and preoperative prophylactic drugs were administered, including ranitidine 50 mg IV, metoclopramide 10 mg IV, dexamethasone 4 mg IV and ceftriaxone 2 g IV. Preoperative vital signs were stable (blood pressure 149/89 mm Hg; heart rate 104 beats per min; oxygen saturation 98% (room air)), and a combined spinal-epidural anesthetic technique using the

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Correspondence to:
Slavica KRUŠIĆ
Narodni Front Clinic for Gynecology and Obstetrics
Kraljice Natalije 62
11000 Belgrade
Serbia
vicesla@gmail.com

loss of resistance to saline was performed in the sitting position at the L3/4 interspace (Perican® 18G Tuohy needle, Pencan® 27G spinal needle, Perifix® 20G nylon epidural catheter, Espocan® docking system; B. Braun Medical Inc., Melsungen, Germany). Isobaric bupivacaine 12 mg, morphine hydrochloride trihydrate 200 mcg, and fentanyl 15 mcg were administered intrathecally using a needle-through-needle technique to produce a bilateral T4 dermatome sensory block to cold and sharp sensation. Vital signs remained stable post-neuraxial anesthesia, requiring only four doses of phenylephrine 50 mcg IV throughout the 22-minute surgery. A healthy male infant was delivered weighing 3150 g, with Apgar scores of 8 and 9 (at minutes one and five, respectively). Post-delivery, an oxytocin IV infusion was administered at 5 IU/h. The total fluid volume was 1500 mL of Ringer's lactate solution with an estimated blood loss of 500 mL.

Postoperative multimodal analgesia included acetaminophen 1 g IV (eight-hourly) and two 5 mL boluses of 0.25% bupivacaine with fentanyl 5 mcg/mL via the epidural catheter in the first 24 hours, which produced a visual analog scale score < 4/10.

Breastfeeding did not occur since there were no definitive recommendations regarding immunosuppressive therapy. Liver, renal, and platelet count results remained stable with no postoperative complications. The patient met discharge criteria on the second postoperative day (the minimum standard at Narodni Front Clinic), but discharge was delayed until the fifth postoperative day due to neonatal hyperbilirubinemia.

DISCUSSION

Liver transplantation can be a lifesaving treatment for patients with acute and chronic hepatic disorders, including end-stage liver disease, decompensated cirrhosis, acute liver failure due to Wilson's disease, or benign or malignant liver tumors [4, 5, 6].

Metabolic, endocrine, nutritional disorders, and sexual dysfunction associated with some hepatic disorders can contribute to infertility [7]. Increased estradiol and testosterone levels suppress the hypothalamic-pituitary axis, which leads to anovulation and amenorrhea [7]. In 90% of premenopausal patients, libido, menstruation, and fertility return by 6–10 months following successful liver transplantation [8, 9, 10]. However, persistent sexual dysfunction and *de novo* sexual dysfunction after transplantation are reported in men and women [8]. The American Association for the Study of Liver Diseases and the American Society of Transplantation recommend that pregnancy be delayed for at least one year following liver transplantation to ensure graft stability and function and to achieve immunosuppression at low maintenance levels [8, 11]. Therefore, liver transplant recipients should receive appropriate counseling for contraception and pregnancy planning [8, 11, 12].

Commonly administered immunosuppressive drugs include tacrolimus and cyclosporine (calcineurin inhibitors) with or without steroids [9]. While fetal/infant risk cannot be ruled out, the reported incidence of fetal malformations in liver transplant recipients is the same as in the general population, so these calcineurin inhibitors can be administered during pregnancy [9]. Due to the increased volume of distribution during pregnancy, an increased dose of immunosuppressant drug(s) is required (with regular monitoring) to avoid acute graft rejection [8, 13]. If the transplanted liver function is stable prior to conception, pregnancy itself should not cause graft dysfunction [7, 12, 14]. Graft loss within two years after delivery occurred among 1.4–1.9% of patients. There was no difference in short-term graft loss based on the mode of delivery [15].

Immunosuppression makes patients prone to infection, so close surveillance during pregnancy and the perioperative/peripartum period is prudent [8, 13, 16]. There are no recommendations regarding specific antibiotic prophylaxis [16]. It is unclear if antibiotics in the immunosuppressed transplant population would decrease the risk of infection [15]. In the case of hemorrhage requiring blood transfusion, leukocyte-reduced, and irradiated blood products are necessary to avoid leukocyte-related reactions, such as graft-versus-host disease [12, 16]. Blood product transfusion and sepsis were the most common factors associated with severe maternal morbidity in liver transplant parturients [15].

Published data suggest pregnancy is well tolerated, and favorable neonatal outcomes can be expected if graft function is stable prior to conception [7, 12]. However, pregnancy post-liver transplant is considered a high-risk pregnancy with increased maternal and fetal complications, including gestational hypertension, preeclampsia, premature labor, low birth weight, and fetal mortality [8, 9, 13, 17–21].

The rate of successful delivery among liver transplant women who attempted vaginal delivery was approximately 70%. There was no difference in maternal morbidity by mode of delivery, and of importance, the risk of graft loss within two years after childbirth was not associated with mode of delivery [15, 20]. In liver transplant recipients, successful vaginal delivery was associated with a lower composite neonatal morbidity rate [15, 20]. These findings are consistent with data from general population-based studies demonstrating an association of CD with increased rates of neonatal morbidity, primarily respiratory morbidity [20]. However, there is an increased incidence of CD in patients with a liver transplant versus non-transplant patients (45–68% *vs.* 24–32%, respectively, due to temporal changes in illness severity and/or patient and physician attitudes towards the mode of delivery [9, 15, 18, 22, 23]. Anesthesiologists must optimize labor analgesia and surgical anesthesia techniques when managing a patient with a liver transplant to preserve function [16].

Renal dysfunction after liver transplantation (prevalence 30–50%) is multifactorial and includes chronic exposure to calcineurin inhibitors, hypertension, diabetes mellitus, obesity, atherosclerosis, hyperlipidemia, chronic hepatitis C infection, pre-transplant renal dysfunction, and perioperative acute kidney injury [8].

Some liver dysfunction may remain post-transplant, so renal and hepatic drug metabolism and excretion should be considered [16]. Liver dysfunction may cause hepatopulmonary syndrome, characterized by portal hypertension, hypoxemia, and intrapulmonary shunting, so anesthesia could be life-threatening due to cardiovascular and/or respiratory instability [24].

Thrombocytopenia can persist in many patients for several years post-liver transplant due to the late resolution of splenomegaly despite improvement in portal blood flow [12]. With a normal coagulation profile, there are no contraindications to neuraxial labor analgesia or neuraxial anesthesia for CD, and epidural catheter removal should follow standard practice [13].

Standard prophylactic procedures to avoid post-neuraxial anesthesia hypotension, such as IV fluid pre- or co-loading and early administration of vasopressor(s), should be instituted, particularly due to the potential of an atypical response of the denervated liver allograft to stress [25]. The vasopressor of choice in patients with liver dysfunction is norepinephrine because it affects circulation through the splanchnic organs the least compared to vasopressin and epinephrine [26]. The normal compensatory mechanism of splanchnic blood volume being redistributed to the central circulation as a response to hypovolemia or blood loss is lost in liver transplant recipients. Furthermore, the hepatic blood flow autoregulation is also decreased, making the liver allograft more susceptible to hypoperfusion and hypovolemia [12, 27]. Transthoracic echocardiography is a good modality to monitor cardiac function and volume status (or transesophageal echocardiography during general anesthesia) [16].

With normal hepatic and renal function, there are no contraindications to standard anesthetic and analgesic drugs (including acetaminophen and nonsteroidal anti-inflammatory drugs); however, titration is advised because drug effects can be unpredictable [26]. Anesthetic and analgesic drugs with non-organ-dependent elimination (e.g., remifentanil, atracurium, or cisatracurium) are advised, and caution is recommended with depolarizing muscle relaxants (e.g., succinylcholine) in patients receiving calcineurin inhibitors or with renal dysfunction due to risk of hyperkalemia [12].

There are no published recommendations regarding breastfeeding in patients with liver transplants [8, 12, 10].

Multidisciplinary team management is recommended to optimize safe delivery planning for pregnant patients with transplanted organs. Neuraxial and general anesthesia techniques are safe in this patient population and should be individualized based on co-existing comorbidities, immunosuppression, and liver and renal function tests.

Conflict of interest: None declared.

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Царски рез у неураксијалној анестезији код трудница са трансплантираном јетром

Славица Крушић[1], Нада Пејчић[2], Мирјана Стојановић-Тасић[3], Дијана Дамњановић[4], Џилијен Абир[5]

[1]Гинеколошко-акушерска клиника „Народни фронт", Београд, Србија;
[2]Општа болница „Лесковац", Лесковац, Србија;
[3]Клиника за психијатријске болести „Др Лаза Лазаревић", Београд, Србија;
[4]Специјална гинеколошка болница са породилиштем „Јевремова", Београд, Србија;
[5]Универзитет „Станфорд", Медицински факултет, Станфорд, Калифорнија, Сједињене Америчке Државе

САЖЕТАК

Увод Напредак у лечењу трансплантираних болесника омогућио је да све већи број болесница са трансплантираним органом успешно изнесе трудноћу. Анестезиолошки тимови се сусрећу са многим изазовима у збрињавању породиља које имају трансплантирану јетру, као што су: повишена стопа царског реза, висок ризик за развој инфекције и развој интеракција између имуносупресива и анестезиолошких лекова.

Приказ болесника Приказујемо извођење неураксијалне анестезије за елективни царски рез код 28-годишње труднице са трансплантираном јетром (од живог донора). Адекватан анестезиолошки приступ је пресудан како би се обезбедио оптимални периоперативни матернални и фетални исход. Одржавање кардиоваскуларне стабилности благовременом надокнадом течности и раном применом вазопресора је важно за очување адекватне перфузије јетре. Препоручује се мултимодални приступ у терапији постоперативног бола уз опрез приликом примене лекова са могућом хепатореналном токсичношћу.

Закључак Мултидисциплинарна евалуација, планирање и припрема су кључни за безбедни ток порођаја код трудница са трансплантираним органима.

Кључне речи: анестезија; царски рез; трансплантација јетре