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CASE REPORT

Delivery during extracorporeal membrane oxygenation (ECMO) support of pregnant woman with severe respiratory distress syndrome caused by influenza: a case report and review of the literature

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ABSTRACT

Objective: To report a case of labour induction during extracorporeal membrane oxygenation (ECMO) support in a patient with acute respiratory distress syndrome (ARDS) caused by influenza and review of the literature.

Methods: Case report and the literature search of all English articles on delivery while on ECMO in patients with ARDS caused by influenza.

Results: A 25-year-old pregnant woman was initiated with ECMO due to severe ARDS caused by influenza A (H1N1) virus. When the patient had symptoms of colporrhagia and uterine contractions, the medical team decided to start labour induction while on ECMO. There were in total five case reports identified. Maternal oxygenation was improved after delivery and ECMO was successfully discontinued.

Conclusions: Maternal oxygenation was improved after delivery, which may be beneficial to reduce the duration of ECMO. Caesarean section (CS) may be the most used mode and labour induction could be another option. The procedure should be performed by an experienced ECMO team, cooperating with the obstetrician, anaesthesiologist, and ICU doctors.

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Influenza; extracorporeal membrane oxygenation; acute respiratory distress syndrome; mechanical ventilation; delivery

Introduction

During the past several years, influenza A (H1N1) activity has continued throughout the world. During the 2009 (H1N1) pandemic, many countries such as Mexico, America, and China reported laboratory confirmed cases, including at least 16,000 deaths [1]. Currently, according to World Health Organization (WHO) report, the active circulation of influenza A continues seasonally between October and April every year, especially in temperate regions [2].

Pregnant women are identified as a high-risk group for severe complications of H1N1 influenza, such as acute respiratory distress syndrome (ARDS) and adverse neonatal outcomes [3–5]. While treatment with mechanical ventilation is recommended for patients with ARDS, some severe cases with refractory hypoxaemia need extracorporeal membrane oxygenation (ECMO) [6]. Sometimes pregnancy termination and delivery may be required to save the mother's life, [7,8]. But the lack of information about delivery while on ECMO makes it difficult to assess the safety and efficacy of this procedure in pregnant women. Actually, because of limited published data we have not known whether the delivery can improve the maternal oxygen or not. So, for a pregnant woman undergoing ECMO, it is difficult to decide when and how to perform delivery. In this report, we rescued a patient who underwent labour induction while on ECMO, and for the first time, we describe the effect of labour induction on ECMO. Also, we will summarise the current available data on delivery during ECMO support.

Case presentation

A 25-year-old pregnant woman (G2P1) at 24 weeks of gestation was admitted to the hospital with symptoms of fever, cough, and progressive shortness of breath for 5 days. Infection with influenza A (H1N1) virus was confirmed from a tracheal aspirate sample using polymerase chain reaction assays. A chest x-ray was performed, which revealed radiological changes with extensive bilateral infiltrates. Due to rapid progression from pneumonia to ARDS with PaO_2/FiO_2 ratio of 37, the patient was transferred to the ICU to receive invasive mechanical ventilation.

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Mechanical ventilation

The patient was recommended to receive a protective strategy according to the ARDSnet protocol [9,10]. The mechanical ventilation settings included volume-controlled ventilation with an FiO_2 of 1.0, tidal volume of 5–6 mL/kg (ideal body weight), respiratory rate of 20, and positive end-expiratory pressure (PEEP) of 16–20 cm H_2O. We increased the PEEP and attempted recruitment manoeuvres (RM), however, the plateau pressure (Pplat) was above 35 cm H_2O, and respiratory system compliance was only 17 mL/cm H_2O. The condition of the patient deteriorated again, with PaO_2/FiO_2 ratio of 44. Considering the state of pregnancy, lateral position ventilation instead of prone ventilation was attempted, without significant improvement. Many thick secretions were present in her lungs, and obstetric ultrasonography suggested that the foetus was hypoxic, with a heart rate as low as 90–100 beats/min. Thus, to immediately improve maternal oxygenation and preserve the life of the foetus, the medical team chose initiate ECMO instead of HFOV after consultation with respiratory, ICU, and obstetrics experts.

ECMO

ECMO system including Bio-Console 560 Speed Controller System and 540T External Drive Unit (Medtronic, Inc., Minneapolis, MN) was initiated using venovenous bypass (right femoral-jugular). The custom tubing pack including gas exchange device was also provided by Medtronic. Ultrasound and x-rays were used to confirm the cannula position. The actual body weight of the patient was approximately 64 kg. The ECMO system was set to 3200–3400 rpm with a blood flow of 3.5–4.0 L/min and a sweep flow rate of 3.0 L/min, which was adjusted according to the $PaCO_2$ obtained by blood gas analysis. We decreased the ventilator parameters to a frequency of 10/min, tidal volume of 300 mL, PEEP of 8 cmH_2O, and FiO_2 of 0.4. A strict protocol for anticoagulation with heparin was adopted to maintain the ACT between 160 and 180 seconds. With the support of ECMO, the maternal oxygenation improved immediately, with the PaO_2/FiO_2 ratio rising to 240 and the respiratory system compliance reaching 55 mL/cm H_2O. Otherwise, lactic acid decreased from 3.3 to 1.7 mmol/L.

Induced delivery

Unfortunately, although the maternal condition improved, on day 2 of ECMO support, the foetal heartbeat disappeared, and foetal death was confirmed by ultrasound. After weighing the risks, the gynaecologist did not initially recommend the delivery. However, on day 3 of ECMO support, the patient had symptoms of obvious colporrhagia and slight uterine contractions, which led to intermittent low blood flow in the ECMO system. Accordingly, the medical team, including the obstetric expert, chose to induce delivery of the foetus. The patient received misoprostol (50 μg) once and mifepristone (100 mg/day) orally for 2 days. Concurrently, we reduced the dose of sedative drugs (midazolam). On day 5 of ECMO support, uterine contractions increased. The gynaecologist placed misoprostol (100 μg) in the posterior vagina fornix. Three hours later, the dead foetus was completely delivered. The ultrasound confirmed that the placenta was not retained. Oxytocin (20 U) was given twice (intramuscularly and intravenously) to promote uterine contraction. Carboprost tromethamine (Hemabate, intramuscular injection, 250 μg) was given to prevent bleeding. During labour induction, heparin was infused at a relatively low dose to maintain an activated clotting time between 120 and 140 seconds. The volume of bleeding was only approximately 300 mL.

Effects and side-effects of induced delivery on ECMO

After the delivery, the lung compliance and oxygenation improved, and ECMO use was reduced. On the day after delivery, ECMO was successfully terminated. An x-ray of the chest was performed, which confirmed reduction of the bilateral infiltrates (Figure 1(A,B)). After seven more days, the patient was weaned from mechanical ventilation.

However, the side-effects of induced delivery on ECMO were apparent. The blood flow of ECMO was unstable and decreased as uterine contractions strengthened. Therefore, to keep the ECMO system working continuously the rpm rate was reduced to 1000–1200 rpm. Due to the lower rpm rate and blood flow, maternal oxygenation decreased slightly. The ventilator parameters were adjusted to a frequency of 15/min and FiO_2 of 0.8 to maintain oxygenation.

Discussion

Acute respiratory distress syndrome is frequently found in critically ill obstetric patients with H1N1 influenza and is associated with a high risk of emergent caesarean delivery. To those patients with severe ARDS, ECMO can guarantee oxygenation of the parturient when the conventional treatments fail [11]. However, it may be an ethical and clinical challenge to

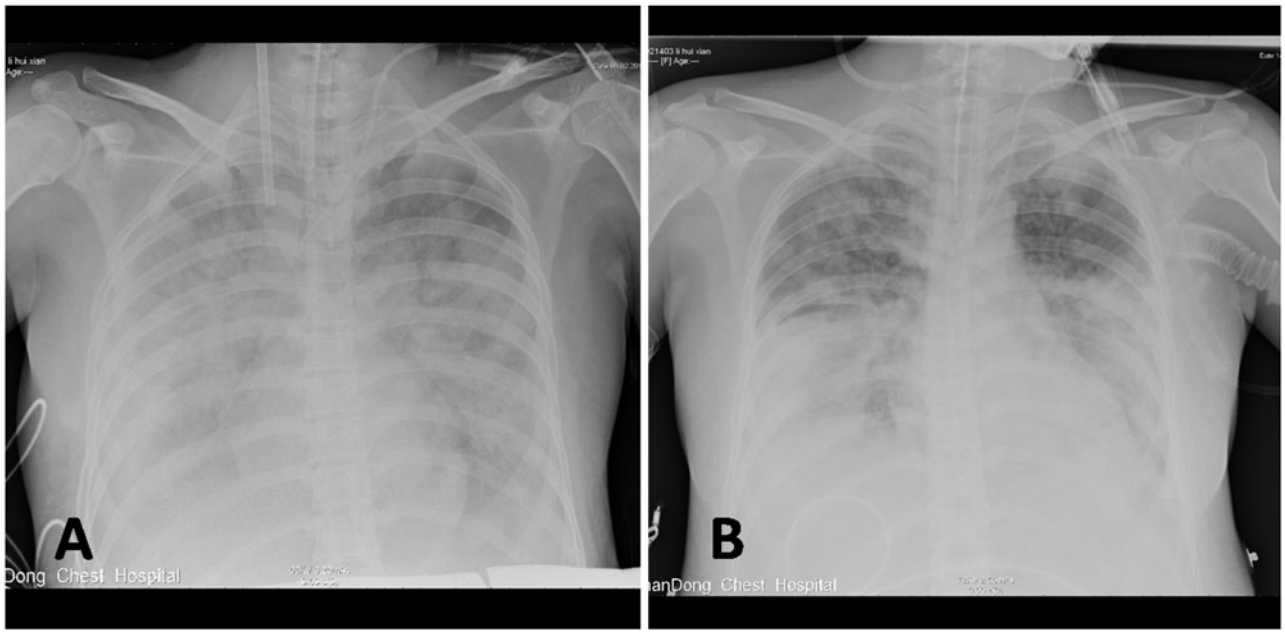

Figure 1. Chest X-ray was performed before labour induction with ECMO (A) and after labour induction weaned from ECMO (B), respectively. In figure (A), the outflow cannula was visible in the right jugular vein. Extensive bilateral infiltrates were severe in figure (A) and absorbed in both upper lobes in figure (B).

terminate the pregnancy while on ECMO. Physician experience in the management of delivery during ECMO is scarce. To date five cases of delivery during ECMO support have been reported in the literature. The data from all currently available case reports are summarised in Table 1.

Snyder et al. reported that 71% of viable pregnancies required emergent caesarean delivery and 50% of these patients were second to maternal worsening respiratory function or non-reassuring foetal status [12]. While on ECMO, the cause to initiate delivery is more complicated. Commonly, while on ECMO, maternal care will take precedence. Panarello [13] reported caesarean section while on ECMO to improve the mother's lung ventilation and facilitate ECMO weaning. Other case carried out caesarean section due to the increasing threat to the life of the foetus when the foetal heart rate increased to 190 bpm [14]. Another case required emergent caesarean after connection to ECMO because of the low flow rate [15]. As Kunstyr and Crawford reported [16,17], the patient was recommend to delivery because of obvious colporrhagia or uterine contractions. In other word, emergency delivery was considered to improve maternal oxygenation or to keep ECMO working, and then to preserve the life of the foetus. So, it was some different between a viable baby and a dead baby. If the foetus was confirmed to dead *in utero*, induction must be performed as early as possible. If the baby was in good condition, the medical team may postpone delivery unless the maternal respiratory function deteriorated or the blood flow of ECMO was decreased due to uterine contractions. The termination of pregnancy was also depended on the period of the foetus. During the late period of pregnancy, the medical team would prefer to terminate the pregnancy to preserve both the baby and mother.

It remained uncertain whether delivery can improve the respiratory status of pregnant women [18]. Tomilson et al. [19] performed a retrospective analysis of oxygen requirements during labour and at 24 hours after delivery in 10 patients that showed that inspired oxygen requirements were reduced after delivery. Some other reports have suggested that before 30–32 weeks, the size of the uterus should not significantly affect mechanical ventilation. However, for pregnant women treated with ECMO, delivery may play a positive role in improving maternal oxygenation. As documented by our experience, the effects on ECMO may have been gestation related. Firstly, the size of uterus would increase difficulty to place the cannula. Secondly, the bigger uterus may influence blood flow of ECMO by oppressing the vein [15]. In addition, the flow rate could be unstable and decreased as uterine contractions strengthened. In the case reported by Kunstyr [16], after delivery, the maternal PaO_2/FiO_2 improved from 116 to 144. Especially when encountered the difficult to wean from ECMO, termination of pregnancy could improve mother's lung ventilation and facilitate ECMO weaning [13]. The same things

Table 1. Summary of data from prior published reports of the delivery while on ECMO.

Case	Age/ years	Gestation/ weeks	Type of delivery	Timing of delivery while on ECMO	Why to deliver	ECMO duration after delivery	ECMO flow rate		Maternal PaO_2/FiO_2		Outcome			
							Pre delivery	Pro delivery	Pre delivery	Pro delivery	Mother	Neonatal	Heparin discontinuation	Bleeding or thrombo-embolic
Panarello [13] Influenza H1N1	38	25	CS	28th day	To facilitate ECMO weaning	7 days	Not given	Not given	Not given	Improved	Weaned off ECMO and survived	Male (1200 g) with Apgar score of 2[a]	4 hours	Brain haemorrhage with neonate
Łysenko [14] Influenza H1N1	24	29.4	CS	7th day	The foetal heart rate was 190 bpm	10 days	Not given	Not given	Not given	Not given	Survived	Female neonate with Apgar score of 2[a]	19 hours	No
Parkins [15] Influenza H1N1	16	32	CS	Just after initiation	Flow rate was low	13 days	Low	Normal	Not given	Not given	Survived	Survived	Not mentioned	No
Kunstyr [16] Influenza H1N1	26	22	Spontaneous delivery	30th hour	Spontaneous	14 days	Not given	Not given	116	144	Survived	female neonate (630 g)	3 hours	Thrombosis of the right cephalic vein
Crawford [17] Influenza A	37	21	CS	10th days	Preeclampsia	3 days	Not given	Not given	Not given	Not given	Survived	Survived	Not mentioned	No

[a]Apgar score of 1 minute after delivery.

occurred in the case we reported. After the induction of labour, the maternal condition improved and ECMO was successfully terminated. Accordingly, from the limited reports, delivery may be beneficial to the maternal oxygenation. So we believe that delivery may be worth considering as a therapeutic option for those patients with respiratory function deteriorated or the ECMO could not continue. Although there need more clinical research to evaluate this strategy.

Regarding the mode of delivery, caesarean section (CS) has been performed in a few cases with ECMO support [13–15,17]. But the decision to perform a CS while on ECMO was not easy due to the increased risk of thrombosis from the required duration of heparin discontinuation. In four cases, heparin discontinuation was 3–19 hours. Spontaneous delivery may be associated with the shorter discontinuation than CS [16]. In our case during labour induction, heparin was infused at a relatively low dose to maintain an activated clotting time between 120 and 140 seconds. The volume of bleeding was little. Compared to CS, another interesting point of labour induction was that the patient did not have to be treated in the operating room, which decreased the risks compared to transfer with ECMO. Every coin has two sides. Another key point needed to be mentioned is that during the induction of labour, the blood flow was unstable and decreased when uterine contractions strengthened. Furthermore, several days may elapse between the start of uterine contractions and the completion of delivery. The long duration will increase the risk to the foetus. Therefore, labour induction may not be suitable for a viable foetus.

In conclusion, delivery while on ECMO may be beneficial for pregnant women. Caesarean section (CS) may be the most used mode. Labour induction could be another option when CS could not be performed or the foetus has died *in utero*. We recommend the procedure should be performed by an experienced ECMO team, cooperating with the obstetrician, anaesthesiologist, and ICU doctors. More study is needed to evaluate the efficacy and safety of delivery including labour induction on pregnant women while on ECMO.

Disclosure statement

No potential conflict of interest was reported by the authors.

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