Psychiatria Danubina, 2019; Vol. 31, Suppl. 1, pp S60-S62
Medicina Academica Mostariensia, 2018; Vol. 6, No. 1-2, pp 60-62 *Brief review*

ANAPHYLAXIS DURING PREGNANCY

Krešimir Reiner[1], Tajana Zah Bogović[2], Marko Ćaćić[3], Slobodan Mihaljević[2] & Branko Krišto[4]

[1]*University of Zagreb, School of Medicine, Department of Obstetrics and Gynecology, University Hospital Zagreb, Zagreb, Croatia*
[2]*University of Zagreb, School of Medicine, Department of Anesthesiology, Reanimatology and Intensive Care Medicine, University Hospital Zagreb, Zagreb, Croatia*
[3]*Department of Cardiology, St. Antonius Hospital Kleve, Kleve, Germany*
[4]*Department of Internal Medicine, University Hospital Mostar, Mostar, Bosnia and Herzegovina*

received: 10.1.2018; revised: 18.4.2018; accepted: 14.6.2018

SUMMARY

Anaphylaxis occuring during pregnancy has a potential to cause devastating damage to the unborn baby and the mother. However, majority of adverse outcomes of anaphylaxis during pregnancy frequently affect the neonates rather than the mothers. The negative neurologic outcomes of the fetus are mostly due to delayed caesarean delivery or inadequate doses of adrenaline during anaphylaxis. Most of the current knowledge on this clinical scenario is based on case reports and very few review articles. This is a mini review of the causes, diagnosis and management of anaphylaxis occuring during pregnancy.

Key words: *anaphylaxis – pregnancy - caesarean section*

* * * * *

INTRODUCTION

Anaphylaxis occuring during pregnancy is usually underestimated and underreported, probably because of the lack of confirmation of diagnosis and timely reporting. However, this complication has a potential to cause devastating damage to the unborn baby and the mother. It is important to highlight that the majority of adverse outcomes of anaphylaxis occuring during pregnancy, frequently affects the neonates rather than the mothers. Most of the current knowledge on this clinical scenario is based on case reports and very few review articles. This is a mini review of the causes, diagnosis and management of anaphylaxis occuring during pregnancy.

PATHOPHYSIOLOGY OF ANAPHYLAXIS DURING PREGNANCY

The prevalence of anaphylaxis during pregnancy is approximately 3 per 100 000 delieveries (Chaudhuri 2015, Hepner et al. 2013). It is thought that the pregnant patients are predisposed to anaphylaxis because of the alteration in cellular immunity which is a consequence of increased levels of progesterone during pregnancy. Maternal T cells at the fetomaternal interface produce Th2 type cytokine which initiates the immediate hypersensitivity reaction and at the same time, there is an inhibition of cytokine production form the Th1 cells which normally play an important role in allograft rejection (Chaudhuri 2015). Table 1 shows the most common causes of anaphylaxis during pregnancy. For clinically practical reasons, the most common causes of anaphylaxis during pregnancy are divided into two groups: the most common causes of anaphylaxis during pregnancy and the most common causes of anaphylaxis during anaesthetic procedures during pregnancy (i.e. caesarean section, epidural analgesia for vaginal delivery) (Chaudhuri 2015, Hepner et al. 2013, Draisci et al. 2007). As with every anaphylaxis, symptoms of anaphylaxis during pregnancy can be divided into four grades, according to the Ring and Messmer grading scale. Grade 1 is characterised by the involvement of the skin and mucosa only (generalised erythema, urticarial, angioedema). Grade 2 is characterised by the moderate multiorgan system involvement (cardiovascular: hypotension, tachycardia; respiratory: bronchospasm and/or difficulty to ventilate; gastrointestinal: nausea and/or vomiting). Grade 3 anaphylaxis regards to severe life-threatening symptoms (cardiac collapse, bradycardia, dysrhytmia, bronchospasm). Grade 4 anaphylaxis regards to the cardiac arrest and requires measures of cardiopulmonary resuscitation (Chaudhuri 2015, Hepner et al. 2013, Glibo Bevanda et al. 2017). If the anaphylaxis occurs after the 20th gestational week, hypotension from peripheral vasodilation and capillary leakage is compounded by the decreased venous return as the result of aortocaval compression from the gravid uterus. Because the fetal perfusion is directly proportional to uterine blood flow, the magnitude and duration of hypotension are probably the most important factors that determine the potential ishemic damage to the central nervous system of the baby infant (Chaudhuri 2015). The fetus is protected from asphyxia by the three main mechanisms. First, the fetal hemoglobin carries up to 50% more oxygen

Table 1. The most common causes of anaphylaxis during pregnancy and during anaesthetic procedures during pregnancy

The most common causes of anaphylaxis during pregnancy	The most common causes of anaphylaxis during anaesthetic procedures during pregnancy (i.e. caesarean section, epidural analgesia for vaginal dlivery)
Ampicillin	Succinylcholine
Penicillin	Rocuronium
Cephalosporins	Latex and chlorhexidine
Bee sting	Antibiotics (penicillins and cephalosporins)
Snake bite	Intravenous anaesthetic agents
Iron supplement medications	Colloids
	Ranitidine
	Local anaesthetics
	Synthetic oxytocin

than maternal hemoglobin which leads to a leftward shift of the fetal oxyhemoglobin dissociation curve. Second, fetal acidosis relative to the mothers enhances oxygen uptake by the fetal blood. Third, fetal circulation during hypoxia causes increased blood flow to the fetal brain and heart. Because all of the reasons mentioned above, fetus can theoretically survive hypoxia for greater than 10 minutes (McCown & McKay 2015). However, it is important to know that the reports of intact fetal neurologic status after more than 10 minutes of maternal cardiac arrest are rare (McCown & McKay 2015, Nellisen et al. 2009). Conclusively, to prevent the fetal brain damage, it is crucial to maintain the maternal blood pressure and to make a fast decision of immediate caesarean section in the cases of severe anaphylaxis (grades 3 or 4). From the case reports of anaphylaxis during pregnancy, negative neurologic outcomes were observed in around 46% of cases of anaphylaxis occuring during labour. In most of the mentioned cases, the parturients experiencing anaphylaxis had a delayed caesarean delivery or did not receive adequate doses of adrenaline despite undetectable arterial blood pressure. Fetal neurologic outcome was much better in the cases of anaphylaxis occuring during the caesarean delivery which can obviously be attributed to the short time period of the fetal brain ishemia (Hepner et al. 2013).

TREATMENT OF ANAPHYLAXIS DURING PREGNANCY

Primary management of anaphylaxis during pregnancy includes the following measures: maintaining the airway with 100% oxygen, left uterine displacement, aggresive fluid resuscitation (rapid infusion of 1 to 2 L of crystalloid solution), informing the obstetrician and considering immediate caesarean section and administering intravenous adrenaline which is the cornerstone of anaphylaxis management (Chaudhuri 2015). Even though adrenaline increases uterine vascular resistance, an appropriate dose of adrenaline titrated to the desirable effect, will increase cardiac output and systemic vascular resistance which will lead to improved uteroplacental perfusion (Hepner et al. 2013). Administration of adrenaline is unnecessary in grade 1 anaphylaxis. In cases with grade 2 anaphylaxis, adrenaline should be administered in bolus doses of 10 to 20 mcg which can be increased if necessary. In grade 3 anaphylaxis, the initial dose of adrenaline should be 100 to 200 mcg and it can be repeated every 1 to 2 minutes if necessary. Also, if there is a need for repeated dosing, an intravenous infusion of adrenaline (1-4 mcg/min) can be considered. Grade 4 anaphylaxis implies cardiopulmonal resuscitation. For that reason, adrenaline shoud be given in a dose of 1 to 3 mg for the first three minutes and than in a dose of 3 to 5 mg for the next three minutes. After the first six minutes, an adrenaline infusion (4 to 10 mcg/min) can be innitiated. In patients resistant to adrenaline, administration of vasopresin (2-10 IU intravenously) or noradrenaline (0.05-1 mcg/kg/min) can be considered. Secondary management of anaphylaxis includes administration of antihistamines (25-50 mg of diphenhydramine intravenously) and corticosteroids (250 mg of hydrocortisone intravenously or 80 mg of methylprednisolone intravenously). It is important to highlight that the role of antihistamines and corticosteroids in acute anaphylaxis has not been proven. However, in a biphasic anaphylactic reaction, corticosteroids may help prevent the second phase of hypersensitivity reaction which can occur 4 to 6 hours after the acute reaction. After the innitial care and stabilisation, every patient who suffered anaphylactic reaction of grade 2 or higher should be transfered to the critical care unit for further observation and monitoring. If available, collection of blood samples to diagnose anaphylaxis should be performed. Laboratory investigations for diagnosing anaphylaxis include serum histamine levels, serum tryptase levels and specific immunoglobulin E assays of common offenders. Appropriate skin testing with suspected agents should be performed approximately 4 to 6 weeks after the incident (Chaudhuri 2015).

CONCLUSIONS

Anaphylaxis occuring during pregnancy has a potential to cause devastating damage to the unborn baby and the mother. Majority of adverse outcomes after anaphylaxis occuring during pregnancy frequently affect the neonates rather than the mothers. Based on the case reports and few review articles, it can be concluded that the negative neurologic outcomes of the fetus are mostly due to delayed caesarean delivery or inadequate doses of adrenaline during anaphylaxis. Adequate knowledge on the recognition of anaphylaxis during pregnancy, adrenaline dosing depending on the grade of anaphylaxis and making a fast decision on performing immediate caesarean section are crucial to prevent severe morbidity and mortality, both of the fetus and the mother, during anaphylaxis occuring during pregnancy.

Contribution of individual authors:

Krešimir Reiner: concept and design of the article; writing the manuscript.

Tajana Zah Bogović: concept and design of the article; writing the manuscript.

Marko Ćaćić: revision the manuscript; approval of the final version.

Slobodan Mihaljević & Branko Krišto: literature searches; comments on the draft paper.

Acknowledgements: None.

Conflict of interest : None to declare.

References

1. *Chaudhuri K. Anaphylaxis during pregnancy. In: Santos AC, Epstein JN, Chaudhuri K, editors. Obstetric Anesthesia. New York, Chicago, San Francisco, Athens, London, Madrid, Mexico City, Milan, New Delhi, Singapore, Sydney, Toronto: Mc Graw Hill; 2015. pp. 221-231*
2. *Draisci G, Nucera E, Pollastrini E, Forte E, Zanfini B, Pinto R, Patriarca G, Schiavino D, Pietrini D. Anaphylactic reactions during cesarean section. Int J Obstet Anesth 2007; 16:63-7*
3. *Glibo Bevanda D, Cacic M, Mihaljevic S, Bevanda M, Bogut A, Karin M. Allergic reactions and anesthesia. Psychiatr Danub 2017; 29:778-786*
4. *Hepner DL, Castells M, Mouton-Faivre C, Dewachter P. Anaphylaxis in the clinical setting of obstetric anesthesia: a literature review. Anesth Analg 2013; 117:1357-67*
5. *McCown A, McKay RSF. Cardiopulmonary resuscitation in pregnancy. In: Santos AC, Epstein JN, Chaudhuri K, editors. Obstetric Anesthesia. New York, Chicago, San Francisco, Athens, London, Madrid, Mexico City, Milan, New Delhi, Singapore, Sydney, Toronto: Mc Graw Hill; 2015. pp. 459-467*
6. *Nellisen EC, de Zwaan C, Marcus MA, et al. Maternal cardiac arrest in early pregnancy. Int J Obstet Anesth 2009; 18:60-63*

Correspondence:
Krešimir Reiner, MD
University of Zagreb, School of Medicine,
Department of Obstetrics and Gynecology, University Hospital Zagreb
Kišpatićeva 12, 10 000 Zagreb, Croatia
E-mail: kreso.reiner@gmail.com