

Outcomes of Oseltamivir Treatment for H1N1 Infection During Pregnancy: A Retrospective Study

Nermin AKDEMİR¹, Osman ÖZDEMİR², Filiz KOÇ³

Ankara, Turkey

OBJECTIVES: Oseltamivir is an antiviral agent which can be used for treatment and chemoprophylaxis against H1N1 influenza for people at high risk of complications, including pregnant women. In this study, we aimed to present our single center experience about the usage of oseltamivir for H1N1 infection during pregnancy on maternal and fetal outcomes.

STUDY DESIGN: Between September 2009 and June 2010, total ten patients who were treated by the diagnosis of swine flu included the study. Oseltamivir was started in all patients as 75 mg twice daily for five days. Because of adverse effects and complications due to H1N1 and oseltamivir, all patients were hospitalized for 5-7 days. All the data concerning about maternal and newborns were analyzed retrospectively. Post partum echocardiography was performed in all newborns and patients.

RESULTS: Data of ten patients were analyzed retrospectively. There was not any maternal or fetal death due to H1N1 and oceltamivir therapy. There was not any premature membrane rupture. Peripartum cardiomyopathy was detected and treated successfully in one patient in whose the disease has not been attributed to H1N1. Combined atrial septal and ventricular septal defect were detected in one newborn and Patent Foramen Ovale was detected in 2 newborns as fetal outcome.

CONCLUSION: In this retrospective, study, we found that, H1N1 infection during pregnancy has a good prognosis and without complication for maternal health. Although oseltamivir therapy is safe in pregnant women, it can be associated with cardiac structural cardiac malformations in H1N1 infected pregnancy newborns

Key Words: Swine flu, H1N1, Oseltamivir, Fetal malformation, Echocardiography

Gynecol Obstet Reprod Med 2011;17:4-6

Introduction

H1N1 is a strain of Influenza virus that originated in swine and The US Centers for Disease Control and Prevention currently recommend antiviral treatment and chemoprophylaxis with either oseltamivir or zanamivir against novel H1N1 influenza for people at high risk of complications, including pregnant women.¹ In this paper we aimed to present our single center experience about the H1N1 during pregnancy, oseltamivir treatment and fetal outcome.

¹Department of Obstetrics and Gynecology, Kecioren Research and Education Hospital, Kecioren, Ankara

²Department of Pediatric Cardiology, Kecioren Research and Education Hospital, Kecioren, Ankara

³Department of Infectious Disease, Kecioren Research and Education Hospital, Kecioren, Ankara

Address of Correspondence: Nermin Akdemir
Vadi Sok, N:5/1, Subayevleri
Kecioren, Ankara
drnerminakdemir@yahoo.com

Submitted for Publication: 08. 10. 2010

Accepted for Publication: 16. 02. 2011

Material and Method

Data of patients who diagnosed swine flu and oceltamivir therapy was started between September 2009 and June 2010 were collected retrospectively. Patients were included if they have symptoms of fever, cough, malaise and impaired general conditions and diagnosed as swine flu included the study among the patients in the outbreak in 2008 and 2009. Exclusion criteria were defined as follows: other diagnosis than H1N1, premature newborns, and known fetal cardiac or other anomalies, pregnant women who have known cardiac disease or who denied the follow up were excluded the study. Maternal events such as death, premature labor, respiratory and/or congestive heart failure were collected. And also, postpartum echocardiography data of both mother and newborns were also collected.

Between September 2009 and June 2010 ten pregnant patients have been diagnosed H1N1 for symptoms such as severe dyspnea, cough, fever, sweating and impaired general condition during pregnancy. Diagnosis of Swine Flu was made using clinical criteria and rapid influenza tests. All patients were hospitalized for further respiratory or obstetric complication.

Oseltamivir treatment was started as 75 mg twice daily for five days until the definite viral test results achieved in central Healthy Ministry Laboratory. Because of adverse effects and complications due to H1N1 and oseltamivir, all patients were followed in Obstetric Ward during the 5-7 days.

Results

Nine patients have an uncomplicated treatment course, but one patient developed a severe respiratory distress and low arterial oxygen saturation. That patient was taken to intensive care unit and intubated for ventilation support. The patient sent to ICU was diagnosed as cardiomyopathy and delivered a normal twin (one female and one male) fetus by C/S. Mother has undergone serial echocardiography follow up and normal Left Ventricular Ejection fraction was reported at 3th month after delivery. Twin's heart was normal at birth and 3th month's echocardiography evaluation. Except last patient, all patients were discharged with cure and had an uncomplicated delivery following days.

Nine patients had an uncomplicated delivery and puerperal period. All newborns were evaluated by echocardiography after delivery. The patient who started osetamivir in 31th week has a newborn Secundum ASD and membranous VSD. Two of the pregnant patients have newborns with Patent Foramen Ovale in which Osetamivir was started at 30th week and in the other was 31th week (Table 1).

Discussion

This retrospective study showed that oseltamivir treatment was uncomplicated during pregnancy in terms of maternal health. Some suspects are existing for newborns of infected pregnant women for structural congenial cardiac pathologies.

This is the largest patient's series which evaluate the early maternal outcome and cardiac structural cardiac abnormalities in the newborns of H1N1 infected and treated by osetamivir

during pregnancy period from our country in the 2009th Pandemic Influenza A (H1N1).

One study showed that, oseltamivir was extensively metabolized by the placenta.² In a study of 90 cases, 1 malformation (1.1%) was reported about oseltamivir usage and it was concluded that incidence of major malformations are similar with general population (1% - 3%)³. There is not any report in the published literature about fetal cardiac malformations associated with oseltamivir treatment for H1N1 infection during pregnancy. We have shown a high incidence of cardiac malformation (3/11, 27.7 %) by echocardiography. Previous reports do not described any fetal malformation during H1N1 infection during pregnancy. Association between osetamivir and cardiac abnormality is unknown because cardiac development is completed in majority of fetuses until 30th week. It is also known that, majority of the fetal cardiac ASD and VSD closes spontaneously in late pregnancy and early period of birth. Oseltamivir may have some role for delaying of spontaneous closure of cardiac septal defects such as indometazin.

Study Limitations:

Most important limitation of this study is the small sample size. Exposure of oseltamivir during second trimester is other limitation because cardiac development has completed.

As conclusion, osetamivir treatment for H1N1 infection of pregnant patients is safe but, may be associated with fetal cardiac anomalies such as ASD, VSD and PFO. Exact mechanism of occurrence of these cardiac malformations is unknown.

Gebelikte H1N1 Enfeksiyonu Nedeniyle Oseltamivir Kullaniminin Sonuçları: Geriye Dönük Bir Çalışma

AMAÇ: Oseltamivir bir antiviral ajan olup gebelik gibi yüksek komplikasyon riski bulunanlarda H1N1 enfeksiyonu tedavisi ve

Table 1: Table shows patient characteristics

patients	age	gravide parite status	Ocelt Treat Week	Delivery week	Delivery Type	Fetal Gender	Fetal Weight	Fetal Echo
1	24	G2P1Y1	30	38	NSD	Male	3490	PFO
2	23	G1POYO	26	40	NSD	Male	3300	Normal
3	29	G2P1Y1	37	40	NSD	Male	3000	Normal
4	24	G4P2Y2A.1	31	38,5	NSD	Male	3380	PFO
5	30	G1POYO	32	36	NSD	Male	2910	Normal
6	19	G1POYO	31	40	NSD	Male	3660	Normal
7	25	G1POYO	36	36,2	NSD	Male	2000	Normal
8	28	G1POYO	31	36	SECTİO	Male	3320	ASD,VSD
9	27	G3P2Y2	34	35	SECTİO	Fem, Male	1950-2300	Normal
10	24	G3P2Y2	28	40	NSD	Male	3300	Normal

kemoproflaksisinde kullanılabilir. Bu çalışmada gebelik sırasında H1N1 enfeksiyonu geçiren ve tedavide oseltamivir kullanımı hakkında merkezimizin tecrübesini ve anne-bebek sonuçlarını sunmayı amaçladık.

GEREÇ VE YÖNTEM: Eylül 2009 ve Haziran 2010 tarihleri arasında, domuz gribi tanısı konan ve oseltamivir tedavisi alan toplam 10 hasta çalışmaya alındı. Oseltamivir her hastaya günde 75 mg 2 doz 5 günlük bir sürede verildi. H1N1 enfeksiyonuna bağlı komplikasyonlar veya oseltamivir tedavisine bağlı yan etkiler nedeniyle hastalar 5-7 gün hastanede yatırıldı. Anne ve yenidoğana ait veriler geriye dönük olarak değerlendirildi. Tüm annelere ve yenidoğanlara doğum sonrası ekokardiyografi yapıldı.

BULGULAR: 10 hastanın verileri geriye dönük incelendi. Domuz gribine ve oseltamivir tedavisine bağlı anne veya bebek ölümü yoktu. Erken membran rüptürü de yoktu. Fakat bir hastada peripartum kardiyomyopati saptandı ve başarılı bir şekilde tedavi edildi. Ancak bu hastalık H1N1 enfeksiyonuna bağlanmadı. Bir yenidoğanda atriyal ve ventriküler septal defekt ve 2 hastada da PFO saptandı.

SONUÇ: Bu geriye dönük çalışmada, gebelikte H1N1 enfeksiyonu geçirmenin anne sağlığı bakımından ciddi bir komplikasyonla ilişkili olmadığını göstermiştir. Her ne kadar anne sağlığı

için güvenli olsa da, gebeliği sırasında H1N1 enfeksiyonu nedeniyle oseltamivir tedavisi gören annelerin yenidoğanlarında ilişkili olabilecek yapısal kardiyak defektler görülebilir.

Anahtar Kelimeler: Domuz gribi, H1N1, Oseltamivir, Fetal malformasyon, Ekokardiyografi

References

1. Tanaka T. Nakajima K. Murashima A. et al. Safety of neuraminidase inhibitors against novel influenza A (H1N1) in pregnant and breastfeeding women. CMAJ 2009;7:181(1-2):55-8
2. Worley KC. Roberts SW. Bawdon RE. The metabolism and transplacental transfer of oseltamivir in the ex vivo human model. Infect Dis Obstet Gynecol 2008;2008: 927574.
3. Hayashi M. Yamane R. Tanaka M. et al. Pregnancy outcome after maternal exposure to oseltamivir phosphate during the first trimester: a case series survey. Nihon Byoin Yakuzaishi Gakkai Zasshi 2009;45:547-50.