ORIGINAL RESEARCH

Assessment of adverse drug reaction profile of oseltamivir

Dr. Sharad Jaiswal

Assistant Professor, Department of Pharmacology, Gold Field Institute of Medical Sciences, Faridabad, Haryana, India

Corresponding Author
Dr. Sharad Jaiswal
Assistant Professor, Department of Pharmacology, Gold Field Institute of Medical Sciences, Faridabad, Haryana, India

Received: 11 July, 2014 Accepted: 20 August, 2014

ABSTRACT

Background:H1N1 influenza A, commonly known as swine flu, is a respiratory illness caused by the H1N1 influenza virus. The present study was conducted to assess adverse drug reaction profile of oseltamivir. **Materials & Methods:**84 suspected or confirmed cases of H1N1 influenza A, close contacts of cases H1N1 influenza A of both genders were enrolled. Oseltamivir was administered 75 mg twice a day for 5 days in group I (therapeutic) and 75 mg once a day for 10 days in group I (prophylactic). Causality assessment by Naranjo's scale was done. **Results:** In group Iand group II, adverse drug reactions were nausea in 25% and 22%, vomiting in 14% and 11%, gastritis in 19% and 11%, weakness in 32% and 19%, headache in 11% and 9%, abdominal pain in 7% and 2%, vertigo in 5% and 3% and urgency of micturition in 4% and 5% respectively. The difference was significant (P< 0.05). Adverse drug reaction by Naranjo's scale were possible and probable such as nausea14%and 11%, vomiting10% and 4%, gastritis8% and 11%, weakness13% and 12%, headache8% and 3%, abdominal pain7%, vertigo4% and 1% and urgency of micturition in 3% and 1% respectively. The difference was significant (P< 0.05). **Conclusion:** Oseltamivir is well tolerated; however, gastrointestinal adverse drug reactions (ADRs) are the most common and can be easily avoided by taking the medication with antacids and/or H2 receptor antagonists after a meal.

Keywords:H1N1 influenza A, Oseltamivir, Causality assessment

INTRODUCTION

H1N1 influenza A, commonly known as swine flu, is a respiratory illness caused by the H1N1 influenza virus. It gained attention in 2009 when it emerged as a novel strain of influenza virus that caused a global pandemic. Swine flu is called so because it was initially thought to be spread by pigs, although later studies showed that human-to-human transmission was the primary mode of spread.[1] Swine flu is caused by the H1N1 influenza virus, which is a subtype of the influenza A virus.The virus spreads from person to person through respiratory droplets produced when an infected person coughs or sneezes. It can also spread by touching contaminated surfaces and then touching the mouth, nose, or eyes.[2]

The antiviral medications available for prophylaxis and treatment of H1N1 influenza A are zanamivir and oseltamivir. Since zanamivir needs to be inhaled, oseltamivir is now thought to be the most appropriate medication that can be taken orally among them.[3] The release of newly generated viral particles from the infected cells is dependent on the potent selective neuraminidase enzyme inhibitor oseltamivir, which cleaves sialic acid residues on newly formed virions. In order to prevent and treat infection, oseltamivir blocks this enzyme, which prevents the release of progeny virions from the infected cells.[4] For prophylaxis, a recommended treatment regimen consists of 75 mg taken twice daily for five days and 75 mg taken once day for at least one week. In the phase III trial of oseltamivir, common adverse drug reactions (ADRs) were nausea, vomiting, diarrhea, abdominal discomfort, bronchitis, vertigo, exhaustion, and headache.[5]The present study was conducted to assess adverse drug reaction profile of oseltamivir.

MATERIALS & METHODS

The present study consisted of 84 suspected or confirmed cases of H1N1 influenza A, close contacts of cases H1N1 influenza A of both genders. All gave their written consent to participate in the study.

Data such as name, age, gender etc. was recorded. Oseltamivir was administered 75 mg twice a day for 5 days in group I(therapeutic) and 75 mg once a day for 10 days in group I (prophylactic). Causality assessment by Naranjo's scale was done. Assessment

of preventability was done by modified Schumock and Thornton scale.Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Adverse drug reaction in both groups

Adverse drug reaction	Group I	Group II	P value
Nausea	25%	22%	0.05
Vomiting	14%	11%	
Gastritis	19%	11%	
Weakness	32%	19%	
Headache	11%	9%	
Abdominal pain	7%	2%	
Vertigo	5%	3%	
Urgency of micturition	4%	5%	

Table I, graph I shows that in group I and group II, adverse drug reactions were nausea in 25% and 22%, vomiting in 14% and 11%, gastritis in 19% and 11%, weakness in 32% and 19%, headache in 11% and 9%, abdominal pain in 7% and 2%, vertigo in 5% and 3% and urgency of micturition in 4% and 5% respectively. The difference was significant (P< 0.05).

Graph I Adverse drug reaction in both groups

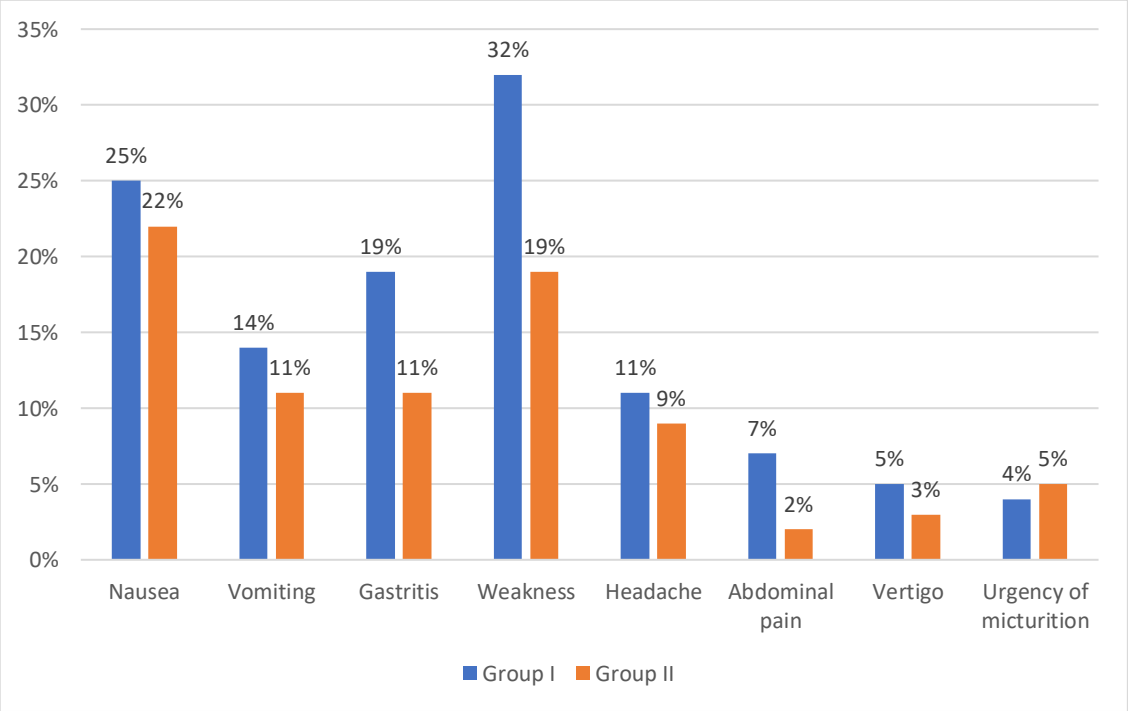

Table II Adverse drug reactions in group I by Naranjo's scale

Adverse drug reaction	Possible	Probable	Definite
Nausea	14%	11%	-
Vomiting	10%	4%	-
Gastritis	8%	11%	-
Weakness	13%	12%-	-
Headache	8%	3%	-
Abdominal pain	7%	-	-
Vertigo	4%	1%	-
Urgency of micturition	3%	1%	-

Table II shows that adverse drug reaction by Naranjo's scalewere possible and probable such as nausea14% and 11%, vomiting10% and 4%, gastritis8% and 11%, weakness13% and 12%, headache8% and 3%, abdominal pain7%, vertigo4% and 1% and urgency of micturition in 3% and 1% respectively. The difference was significant (P< 0.05).

DISCUSSION

Diagnosis of swine flu is primarily based on symptoms, exposure history, and clinical examination by a healthcare provider.[6]Nasal or throat swabs may be collected for laboratory testing, such as reverse transcription-polymerase chain reaction (RT-PCR), to confirm the presence of the H1N1 influenza virus.[7]Antiviral drugs such as oseltamivir (Tamiflu) or zanamivir (Relenza) may be prescribed to treat swine flu, especially for individuals at high risk of complications or with severe illness. These medications work by inhibiting the replication of the influenza virus and can help reduce the severity and duration of symptoms if started early in the course of the illness.[8]Treatment also includes supportive measures such as rest, staying hydrated, and using over-the-counter medications to relieve symptoms such as fever and pain.Hospitalization may be necessary for individuals with severe symptoms or complications, particularly those with pneumonia, respiratory failure, or other medical conditions requiring intensive care.[9,10]The present study was conducted to assess adverse drug reaction profile of oseltamivir.

We found that in group Iand group II, adverse drug reactions were nausea in 25% and 22%, vomiting in 14% and 11%, gastritis in 19% and 11%, weakness in 32% and 19%, headache in 11% and 9%, abdominal pain in 7% and 2%, vertigo in 5% and 3% and urgency of micturition in 4% and 5% respectively. Anodavidya et al[11]analyzed the pattern of adverse drug reactions (ADRs) of oseltamivir and its comparison with available data.Suspected or confirmed cases of H1N1 influenza A on therapeutic regimen and close contacts of cases H1N1 influenza A on prophylactic regimen of oseltamivir were included. Data were collected by personal interview after obtaining written informed consent. Causality, severity, and preventability assessments were done by using Naranjo's scale, modified Hartwig and Siegel's scale, and modified Schumock and Thornton Scale, respectively. Total 294 patients were interviewed. In prophylactic group, 107 of 257 (41.63%) and in therapeutic, group 23 of 37 (62.16%) developed ADRs. ADRs reported in therapeutic group was significantly (P = 0.029) higher as compared with prophylactic group. Frequently observed ADRs in both the groups were gastritis, nausea, vomiting, diarrhea weakness, sedation, loneliness, sadness, headache, and abdominal pain. Naranjo's algorithm showed all ADRs in probable category in prophylactic group, 27.78% probable and 72.22% possible reactions in therapeutic group. Severity assessment showed 76% mild and 24% moderate reactions in therapeutic group, 89% mild and 11% moderate reactions in prophylactic group. Severity of ADRs was significantly higher in therapeutic group. Most of ADRs were in nonpreventable category, except gastritis, nausea and vomiting were in definitely preventable category.

We found that adverse drug reaction by Naranjo's scale were possibleand probable such as nausea14%and 11%, vomiting10% and 4%, gastritis8% and 11%, weakness13% and 12%, headache8% and 3%, abdominal pain7%, vertigo4% and 1% and urgency of micturition in 3% and 1% respectively. Schirmer et al[12]reviewed the antiviral agents and specifically the neuraminidase inhibitor, oseltamivir, for use in treatment and prophylaxis of influenza infection.Oseltamivir is effective in reducing symptom burden in those with influenza A or B infection, and is preventative against developing infection after exposure. Emergence of naturally occurring or post-treatment oseltamivir-resistant influenza as well as an avian influenza pandemic may limit its future use as a monotherapeutic antiviral treatment agent.

The limitation of the study is the small sample size.

CONCLUSION

Authors found that Oseltamivir is well tolerated; however, gastrointestinal adverse drug reactions (ADRs) are the most common and can be easily avoided by taking the medication with antacids and/or H2 receptor antagonists after a meal.

REFERENCES

1. Madhu K, Neha G, Ankit G, Vijayan V K. Influenza A (H1N1) 2009: A pandemic alarm. J Biosci. 2009;34:481–9.
2. McKinney WP, Volkert P, Kaufman J. Fatal swine influenza pneumonia during late pregnancy. Arch Intern Med. 1990;150:213–5.
3. Bardsley-Elliot A, Noble S. Oseltamivir. Drugs. 1999;58:851–60.
4. Shigeta S. Oseltamivir (Guest Commentaries) Drugs. 1999;58:861–2.
5. Tamiflu (oseltamivir phosphate) capsules and for oral suspension [package insert] Nutley (NJ): Roche Laboratories Inc. 2008. [last cited 2010 May 28]. Available from: http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM147992.pdf .
6. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruis I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30:239–45.
7. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm. 1992;49:2229–32.
8. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm. 1992;27:538.
9. Central Drugs Standard Control Organization. List of drugs approved during 2005. [last cited on 2010 May 29]. Available from: http://www.cdsco.nic.in/list_of_drugs_approved_during_2005.htm .
10. Rokuro H. Fatal neuropsychiatric adverse reactions to oseltamivir: Case series and overview of causal relationships. Int J Risk Saf Med. 2008;20:5–36.
11. Anovadiya AP, Barvaliya MJ, Shah RA, Ghori VM, Sanmukhani JJ, Patel TK, Tripathi CB. Adverse drug reaction profile of oseltamivir in Indian population: A

prospective observational study. Indian journal of pharmacology. 2011 May 1;43(3):258-61.

12. Schirmer P, Holodniy M. Oseltamivir for treatment and prophylaxis of influenza infection. Expert Opin Drug Saf. 2009;8:357–71.