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Research Article

Role of Antiviral Therapies in Laboratory Confirmed Influenza Cases in Egypt 2010-2012/Single Center Experience Study

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Abstract

Rationale: Many studies have studied the role of antiviral therapy in reducing the severity and reducing the both morbidity and mortality, also emphasized its role in reducing the length of stay. In Egypt Data is very limited about the role of different antiviral drugs and its role and impact on the treatment of influenza , so the significance of this study is to explain what are the most frequently prescribed antiviral medications and try to address its impact on outcome of the laboratory confirmed influenza cases.

Methods: The current study was conducted at Cairo University Hospitals over 2 years from 2010 - 2012. It was conducted on hospitalized patients both adult and pediatric age group. All the patients who fulfilled the WHO case definition of severe acute respiratory infection (SARI) were enrolled and admitted. Criteria used were; fever of ≥ 38°C or history of fever plus cough within the last 10 days. Demographic data, co-morbid conditions, outcome and data about antiviral treatment received were collected. Nasopharyngeal and oropharyngeal swabs were collected and analyzed for the pandemic influenza 2009 A (H1N1), seasonal A H1N1, seasonal A H3N2 with influenza B and C by using PCR.

Results: Influenza virus has been detected in 81 cases distributed as follows; 48 cases of influenza A (28 cases of pandemic 2009 H1N1, 20 cases H3N2) while 30 cases were influenza B subtype while 3 cases were non A non B subtype. only one case was combined A and B subtype.

Mean age for these patients was 19.2 years and 50% were below age of 5 years (41/81), while only 5% were above age of 65 years. Female was accounted for 43% of the cases and two were pregnant in 2nd trimester. None the current study patients received flu vaccine during the preceding year prior to this episode of infection. Only 2.5% (2/81) cases had received the oseltamivir treatment. One patient was male patient 55 years old with seasonal influenza H3N2, he was asthmatic with no other risk factors, he has no consolidation on CXR received 75 mg twice daily orally for 5 days from within the 48 hours from onset of the symptoms, he has been discharged from the hospital without need for either ICU admission nor need for mechanical ventilation (MV). The other patient who received oseltamivir was 9-month boy with pandemic 2009 H1N1, he had consolidation on CXR, he received oseltamivir according to his weight for 5 days, also this patient discharged without need for ICU nor need for MV. None of them have been complicated during hospital stay. both of these cases have been discharged after of average 4 days from admission.no side effects from oseltamivir treatment had been reported from both conditions. Neither zanamivir nor peramivir or adamantanes have been tested during this study.

Conclusion: Only 2.5% cases who had laboratory confirmed influenza infection had been received antiviral therapy in the first 48 hours. Oseltamivir was the only available and the only prescribed antiviral therapy. Neither zanamivir nor peramivir or adamantanes was prescribed. Oseltamivir prescribed into usual standard dose. Further randomized studies are needed to properly assess the role of different antiviral therapies on influenza outcomes.

Keywords: *Antiviral Therapies; Influenza; Mechanical Ventilation (MV); Zanamivir; Oseltamivir*

Introduction

Influenza is an acute respiratory infection that caused by either influenza A or B viruses. Influenza occurs in outbreaks and epidemics worldwide, mainly during the winter season. influenza is usually a self-limited disease. However, in certain high risk group may cause significant morbidity and mortality [1].

Many studies have studied the role of antiviral therapy in reducing the severity and reducing the both morbidity and mortality, also emphasized its role in reducing the length of hospital stay [2-11].

Antiviral treatment against influenza which is available in Egypt are neuraminidase inhibitors mainly oseltamivir and zanamivir which is active against influenza A and B while the other group is the adamantanes; amantadine and rimantadine. The latter group is active against influenza A only and is not frequently used nowadays due to high rate of resistance [12-14].

According to our knowledge; in Egypt data is very limited about the role of different antiviral drugs in the treatment of influenza, their side effects and its impact on outcome. So the value of this study is to try to explain role of these antiviral therapies in treatment of influenza confirmed cases and try to fulfill this gap of knowledge about its impact on outcome.

Material and Methods

The current study was conducted at Cairo University Hospitals over 2 years from 2010 - 2012. It was conducted on hospitalized patients both adult and pediatric age group. All the patients who fulfilled the WHO case definition of SARI [15] were enrolled and admitted. Criteria used were; fever of ≥ 38°C or history of fever plus cough within the last 10 days. Demographic data, co-morbid conditions, outcome and data about antiviral treatment received were collected. Date related to antiviral therapy included: type of antiviral used, dosage, duration, complications and any reported side effects. Nasopharyngeal and oropharyngeal swabs were collected and analyzed for the pandemic influenza 2009 A (H1N1), seasonal A H1N1, seasonal A H3N2 with influenza B and C by using PCR (MagMAX Total Nucleic Acid Isolation Kit (Cat No. ARE 1840; Applied Biosystems, Foster City, California, USA).

Ethical standards

Formal written consent was obtained either from patients themselves or by patients sponsors. Study protocol was approved by Cairo university ethics committee and is consistent with Helsinki Declaration of Bioethics protocol [16].

Statistical analysis

Data were statistically described in terms of mean ± standard deviation (± SD), median and range, IQR, or frequencies (number of cases) and percentages when appropriate. All statistical calculations were done using computer program IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows.

Results

Influenza virus had been detected in 81 cases distributed as follows; 48 cases of influenza A (28 cases of pandemic 2009 H1N1, 20 cases H3N2) while 30 cases were influenza B subtype while 3 cases were non A non B subtype (mainly C subtype). Only one case was combined A and B subtype.

Mean age for these patients was 19.2 years. They are distributed as follows: 50% (41/81) were below age of 5, were 11% (9/81) were between 5 - 18, 33% (27/81) were between 18 - 65 years while only 5% (4/81) were above 65. Figure 1 showed the age group distribution. Female was accounted for 43% of cases (35/81) and two were pregnant in 2nd trimester. None the current study patients received flu vaccine during the preceding year prior to this episode of infection. Consolidation on CXR had been detected on 25%(22/81) of the cases.

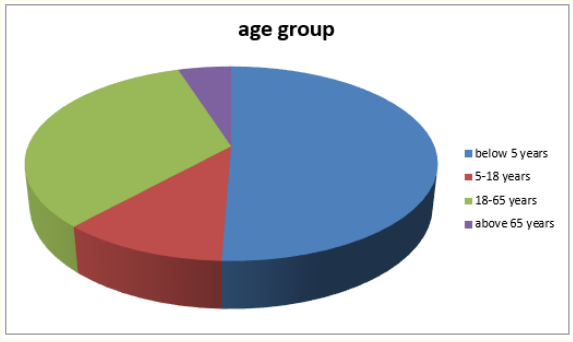

Figure 1: *Age distribution between the study population.*

In the current study oseltamivir treatment had been received by 2.5% (2/81) cases. One patient was male patient 55 years old with seasonal influenza H3N2, was asthmatic with no other risk factors, has no consolidation on CXR received 75 mg twice daily orally for 5 days within the 48 hours from onset of the symptoms. This patient had been discharged from the hospital without need for either ICU admission or need for mechanical ventilation (MV). The other patient who received oseltamivir was 9 month boy with pandemic 2009 H1N1, has consolidation on CXR, received oseltamivir according to the actual weight for 5 days, also the patient had been discharged without need for ICU nor need for MV. None of them have been complicated during hospital stay. Both of these cases had been discharged after of average 3 days from admission.no complications from oseltamivir treatment had been reported in both cases. No other antiviral therapy had been prescribed nor tested like zanamivir, peramivir or adamantanes. As regard the remaining 79 cases who did not receive any antiviral therapy; almost half of the influenza confirmed cases in the present study reported chronic co morbid conditions where 16 were asthmatic while none had COPD and 11 had non sp. respiratory problems, 14 patients were cardiac, 16 patients had endocrinal problems, 1 had renal problelms, 5 had neurological problems, 2 patients had hepatic problems. One patient had hematological problems. Figure 2 showed the distribution of co morbidities. 21 of these patients had consolidation of CXR. About 19%(15/79) developed respiratory failure that necessities MV to be applied. MV average days were 8.6 days, 5 cases developed severe acute respiratory failure with acute lung injury and 1 case developed heart failure. 92%(73/79) have been discharged while 6.3% (5/79) patient died and 1 patient did discharge against medical advice. The outcome for the study population had been shown into figure3. The 5 cases mortality reported into this study were as follows: 4 were male, one case above 76 years old, one case 60 years while the other 3 cases were below age of 5 years. All of these cases presented after 5 days from the symptoms onset. 3 cases had chronic comorbid conditions (respiratory/renal/cardiac/neurological/endocrinal)while the other two cases had no comorbid conditions. All of the cases developed severe acute respiratory failure with acute lung injury. In the current study did not test for oseltamivir resistance.

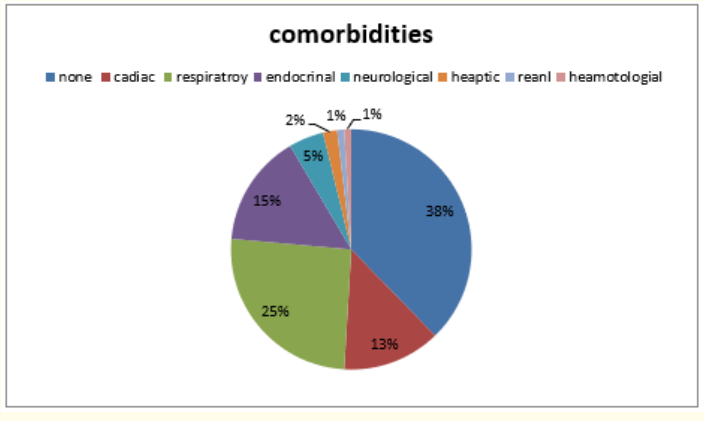

Figure 2: *Comorbid conditions associated with lab confirmed influenza cases.*

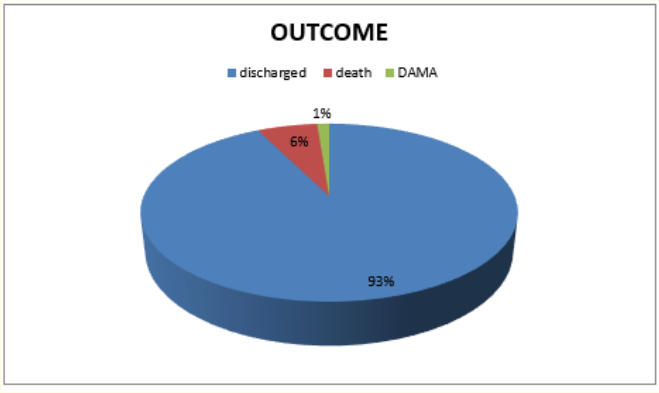

Figure 3: *Outcome between lab confirmed influenza cases.*

Discussion

According to our knowledge this study Is the first study that discussed the role of different antiviral therapies in treatment of laboratory confirmed influenza cases in Egypt. According the results shown here, we addressed that only two cases from 81 cases who had laboratory confirmed influenza infections had received antiviral therapy, During the 1st 48 hours from their illness, one had risk factors while the other did not have any risk factors. None of these cases were that severe enough to receive MV and both of them had been discharged from hospital after average of 3 days. Also 73 cases who did not receive any antiviral therapy had been discharged from the hospital. But the striking issue here is that all of mortality cases did not received oseltamivir treatment during the hospital course, this may be explained by Cairo university hospitals are the main tertiary hospitals in Egypt and most of the time the cases may be transferred late into this facility, all of the 5 cases who reported mortality has been the symptoms onset beyond 5 days duration and have been transferred into Cairo university hospitals after average 6 - 7 days. This may explain that why these patients did not receive any antiviral therapy as many report concluded that if the antiviral therapy could be initiated as early as possible during the first 48 hours from illness, the benefit will be that great than if started late [1,17]. At the study time there were no sufficient reports to support the usage of antiviral therapy in influenza cases beyond the first 48 hours.

Despite we do not have a formal report about how frequent the Egyptian patients seeking medical advice during the 48 hours from the onset of the symptoms, we think that most of the patients do not seek their GPs nor any medical advice during the first 48 hours, this hypothesis may be supported by other reports that concluded between only 13 to 30% of the patients are seeking medical advice during the first 48 hours from their illness [18,19].

On the other side there are recent reports supporting the usage of antiviral therapy even if beyond 48 hours from the onset of the symptoms [20].

We define the high risk groups into our study according the international guidelines as follows: Adults ≥ 65 years of age, Pregnant women and women up to two weeks postpartum, Pulmonary disease, including asthma, Cardiovascular disease, except isolated hypertension Active malignancy, Chronic renal insufficiency, Chronic liver disease, Diabetes mellitus, Hemoglobinopathies, such as sickle cell disease, any neurologic condition that can compromise handling of respiratory secretions (e.g. cognitive dysfunction, spinal cord injuries, seizure disorders, neuromuscular disorders) [1]. We found that about half of our study population had one or more of these risk factors. Despite this observation most of these high risk group did not receive antiviral therapy. We think this may be related to clinical condition they presented with as they were not so severe to start and may be related to time window they presented at as the Cairo university staff who were responsible for prescribing antiviral therapy and responsible for assessment were sticking to the available guidelines and evidence at that time.

Into our study the only available antiviral therapy was oseltamivir. We did use it by usual standard dose 75 mg twice daily for 5 days according the usual international recommendation at study time. We think we need further studies to test the role other antiviral therapies like zanamivir or peramivir as no studies available on these two medications. We do not have any data about the oseltamivir resistance pattern.

Into this study we noticed that none of the two pregnant female receive oseltamivir therapy, this may be related also to late presentation after 48 hours of illness.

We think we have some Limitations: (1) The small no of the patients who received antiviral therapy making the comparison with the patients who did not receive difficult. (2) We could not assess the viral shedding into the patient who receive antiviral therapy to compare it with the patient who did not receive the antiviral therapy.

But we have also some strength points as (1) This is the first study that tried to address the role of antiviral therapies in both adults and pediatric Egyptian patients. (2) We defining the risk group according the international guidelines at that time.

Despite we could not address properly the impact of antiviral therapies on outcome due to small number of the treatment group, we think that this study may be the initial nucleus for further randomized control trial to compare the effect of different antiviral therapy against influenza.

Conclusion

Only 2.5% cases who had laboratory confirmed influenza infection had been received antiviral therapy during the 48 hours. oseltamivir is the only prescribed antiviral therapy. oseltamivir prescribed into usual standard dose. further randomized studies are need to properly assess the role of different antiviral therapy therapies on influenza severity and outcome.

Acknowledgment

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Bibliography

1. Fiore AE., *et al*. "Antiviral agents for the treatment and chemoprophylaxis of influenza --- recommendations of the Advisory Committee on Immunization Practices (ACIP)". *MMWR Recommendations and Reports* 60.1 (2011): 1-24.

2. "Randomised trial of efficacy and safety of inhaled zanamivir in treatment of influenza A and B virus infections. The MIST (Management of Influenza in the Southern Hemisphere Trialists) Study Group". *Lancet* 352.9144 (1998): 1877.

3. Dobson J., *et al*. "Oseltamivir treatment for influenza in adults: a meta-analysis of randomised controlled trials". *Lancet* 385.9979 (2015): 1729-1737.

4. Jefferson T., *et al*. "Antivirals for influenza in healthy adults: systematic review". *Lancet* 367.9507 (2006): 303-313.

5. Treanor JJ., *et al*. "Efficacy and safety of the oral neuraminidase inhibitor oseltamivir in treating acute influenza: a randomized controlled trial. US Oral Neuraminidase Study Group". *Journal of the American Medical Association* 283.8 (2000): 1016-1024.

6. Kaiser L., *et al*. "Impact of oseltamivir treatment on influenza-related lower respiratory tract complications and hospitalizations". *Archives of Internal Medicine* 163.14 (2003): 1667-1672.

7. Hernán MA and Lipsitch M. "Oseltamivir and risk of lower respiratory tract complications in patients with flu symptoms: a meta-analysis of eleven randomized clinical trials". *Clinical Infectious Diseases* 53.3 (2011): 277-279.

8. Lee N., *et al*. "Factors associated with early hospital discharge of adult influenza patients". *Antiviral Therapy* 12.4 (2007): 501-508.

9. Chaves SS., *et al*. "Impact of Prompt Influenza Antiviral Treatment on Extended Care Needs After Influenza Hospitalization Among Community-Dwelling Older Adults". *Clinical Infectious Diseases* 61.12 (2015): 1807-1814.

10. McGeer A., *et al*. "Antiviral therapy and outcomes of influenza requiring hospitalization in Ontario, Canada". *Clinical Infectious Diseases* 45.12 (2007): 1568-1575.

11. Bowles SK., *et al*. "Use of oseltamivir during influenza outbreaks in Ontario nursing homes, 1999-2000". *Journal of the American Geriatrics Society* 50.4 (2002): 608-616.

12. Centers for Disease Control and Prevention. "Influenza antiviral medications: summary for clinicians" (2018).

13. Uyeki TM. "Influenza". *Annals of Internal Medicine* 167.5 (2017): ITC33-ITC48.

14. Ghebrehewet S., *et al*. "Influenza". *British Medical Journal* 355 (2016): i6258.

15. WHO. "Global epidemiological surveillance standards for influenza" (2014).

16. World Medical Association. "WMA Declaration of Helsinki. Ethical principles for medical research involving human subjects". Revised by the 59th WMA General Assembly, Seoul (2008).

17. Ng S., *et al*. "Effects of oseltamivir treatment on duration of clinical illness and viral shedding and household transmission of influenza virus". *Clinical Infectious Diseases* 50.5 (2010): 707-714.

18. Gaglia MA Jr., *et al*. "Patient knowledge and attitudes about antiviral medication and vaccination for influenza in an internal medicine clinic". *Clinical Infectious Diseases* 45.9 (2007): 1182-1188.

19. Havers F., *et al*. "Use of influenza antiviral medications among outpatients at high risk for influenza-associated complications during the 2013-2014 influenza season". *Clinical Infectious Diseases* 60.11 (2015): 1677-1680.

20. Centers for Disease Control and Prevention. "Guidance for clinicians on the use of RT-PCR and other molecular assays for diagnosis of influenza virus infection" (2015).

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