



To determine safety profile of azithromycin in Covid-19 patients

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Abstract

At the end of the year 2019, a novel virus named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV or COVID-19) first appeared in the Chinese city of Wuhan and the WHO declared the novel coronavirus disease as a global pandemic on March, 11th 2020. Corona Virus is RNA virus, major virus that affects respiratory system and can result in acute respiratory distress syndrome, so there emerged several management strategies to combat the challenge of the disease. Azithromycin is one of those treatment options. Azithromycin have been used widely and generally considered as safe medication. The design of this study is Cross-Sectional Study. The 80 Covid-19 positive in ICU were given Azithromycin along with other standard treatment, Side effects were divided into mild serious and allergic reactions. These were noted down in pre designed proforma. Data analysis was done in SPSS version 25. 80 patients were studied 38 (46.2%) patients experienced side effects, majority of which were mild in nature, Out of 80 patients Abdominal Pain was 37.5%, diarrhea 22.7% nausea 25%, transaminitis 2.5%, anorexia 26.3%, taste perversion 36.3%, dyspepsia 15%, vomiting 17.5%, headache 6.3% and somnolence 1.3%. Only 1 (1.25%) patients had arrhythmia and 1 (1.25%) had urticaria that was successfully treated. After this study this can be concluded that Azithromycin is safe drug as majority of side effects experienced were mild in nature and it can be safely used to treat Covid-19 positive patients.

Keywords: 2019-nCoV, azithromycin, COVID-19, SARS-CoV-2

1. Introduction

The Wuhan City of China experienced Covid-19 virus upsurge for the first time late in December 2019, became a pandemic, it has been treated as pneumonia with unknown etiology (1, 2). One of the major target of corona virus is pulmonary system of the humans (3). It was named as 2019-nCoV by Chinese experts (4) and Later, it was named by the International Committee on Taxonomy of Virus as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) (5). Rapid and accurate detection of COVID-19 is crucial to control outbreaks in the community and in hospitals (6). Current diagnostic tests for coronavirus include reverse-transcription polymerase chain reaction (RT-PCR), real-time RT-PCR (RRT-PCR), and reverse transcription loop-mediated isothermal amplification (RT-LAMP) (7). The need of an hour is to find effective therapeutic agents for the treatment of COVID-19 whether inpatient or outpatient as the devastating effects of the coronavirus designated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) demands an urgent attempt to combat situation. (8) It has been demonstrated by few studies that hydroxychloroquine sulfate (HCQ) inhibits SARS-CoV-2 in vitro (9) and one of study proves that the combination of HCQ and azithromycin (AZ) inhibits SARS-CoV-2 *in vitro*. (10)

modified from erythromycin. Like other macrolides, azithromycin has activity against *Moraxella catarrhalis* and *Streptococcus pneumoniae* and also against atypical microbes (11). It has been showing activity against Zika and Ebola viruses in vitro and has immunomodulatory action as demonstrated by in vivo activity in the prevention of severe respiratory tract involvement in viral infections (12). Azithromycin works by inhibiting protein synthesis and experimentally reduces viral replication and inflammation possibly because viruses and cytokines are both made of proteins and use cellular ribosomes for protein translation. In addition, inhibiting virus production can reduce viral transmission to others, which is an important additional benefit (13).

The COVID-19 pandemic has resulted in over 144 million confirmed cases and over 3.06 million deaths globally. Corona Virus is RNA virus, major virus that affects respiratory system and can result in acute respiratory distress syndrome, so there emerged several management strategies to combat the challenge of the disease. Azithromycin is one of those treatment options. Azithromycin have been used widely and generally considered as safe medication.

Azithromycin is a macrolide antibiotic it has a structure

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2. Materials and Methods

In Intensive Care Unit of Allied Hospital Faisalabad, from 1 December 2020 to 31 January 2021. Eighty (80) patients were taken through non probability purposive sampling. Patients were taken according to inclusion a criterion that is Covid-19 PCR patients admitted in ICU, Both genders included, Age range was 18 to 85 years, and all grades of severity of disease were included. The patents who has documented known allergy to macrolides. Females who were pregnant, those with prolonged QT interval documented on Baseline ECG. Patients cardiac issue, were excluded from study. After Ethical Committee approval of the proposal of the study, patient according to inclusion and exclusion criteria were recruited. After taking informed consent, all patients received a standardized clinical examination, all baseline and specific investigations according to their clinical condition and Baseline ECG at day 0 and they were regularly followed up daily during their stay in hospital. All of them given Tab Azithromycin 500mg oral daily, they were observed and asked questions regarding side effects of Azithromycin and side effects were noted down on tenth day.

The side effects has been divided in three major groups, Mild Side Effects, Serious Side effects and Allergic Reactions. All findings and self-reported side effects were noted down in pre designed proforma. Data Analysis was done with SPSS version 25.0 that was used to enter and analyzed the data. Quantitative data like age were presented as means and standard deviation and qualitative data like gender, diarrhea was presented as frequency and percentages.

2.1. Ethical approval

This cross-sectional study was conducted at the Allied hospital (Faisalabad Medical University) Pakistan. This study was approved by the Institutional ethics committee of Allied hospital (Faisalabad Medical University) with approved no. AHF-353-FMU-04/15.

3. Results

Eighty (n=80) patients presented to Covid ICU were studied, all of them were given Azithromycin 500mg daily orally. Their demographic profile is shown in Table 1, there were 56 (80%) male and 24(30%) female patients. Mean Age was 54.9 + 11.28 with Minimum 27 and Maximum 85 years, Out of which 11 (13.7%) were in 18-40 year age group, 46 (57.5%) in 41-60 year age group, 22 (27.5%) in 61-80 years age group and 1 (1.25%) in > 81 year group. All patients were Covid PCR positive 80(100%) and only 4(5%) were smokers. (Table1) Out of 80 patients 11(17.5%) were having mild to moderate Disease, 50(62.5%) patients had sever disease and 16 (20%) were critical. (Table 2) Out of 80 patients 38 (46.2%) suffered from Side effects, of which 36 (45%) out of 80 and 94.7% out of 38 had Mild Side effects, 1(1.25%) out of 80 and 2.6% out of 38 patient had Sever Adverse reaction and 1(1.25%) out of 80 and 2.6% out of 38 patient had Allergic reaction (Table 3a).

Table 1. Demographic profile of patients

| Total No. Patients (n) | | 80 |
|------------------------|-------|------------|
| Male | | 56 (70%) |
| Female | | 24 (30%) |
| Age Group | 18-40 | 11 (13.7%) |
| | 41-60 | 46 (57.5%) |
| | 61-80 | 22 (27.5%) |
| | > 81 | 1 (1.25%) |
| Covid-19 PCR | | 80 (100%) |
| Smokers | | 4 (5%) |

Table 2. Clinical severity

| | |
|--------------------------|------------|
| Mild To Moderate Disease | 14 (17.5%) |
| Sever Disease | 50 (62.5%) |
| Critical Illness | 16 (20%) |

Table 3 (a). Side effects profile of azithromycin in 80 patinets

| Occurrence Of Adverse Events | 38 (46.2%) out of 80 patinets |
|-----------------------------------|--|
| Mild Side Effects | 36 (45%) out of 80 and 94.7% out of 38 |
| Sever Adverse Events | 1 (1.25%) out of 80 and 2.6% out of 38 |
| Allergic Reaction to Azithromycin | 1 (1.25%) out of 80 and 2.6% out of 38 |

Table 3 (b). Side effect profile of azithromycin

| Mild side effects | | |
|------------------------------------|--|---|
| 1 | Abdominal Pain | 30 (37.5%) out 80 and 78.9% out of 38 |
| 2 | Diarrhea | 22 (27.5%) out of 80; 57.8% out of 38 |
| 3 | Nausea | 20(25%) out of 80 and 52.6% out of 38 |
| 4 | Elevated ALT AST | 2 (25%) out of 80 and 5.2% out of 38 |
| 5 | Anorexia | 21 (26.3%) out of 80; 55.2% out of 38 |
| 6 | Taste Perversion | 29 (36.3%) out of 80; 76.3% out of 38 |
| 7 | Dyspepsia | 12 (15%) out of 80 and 31.5% out of 38 |
| 8 | Vomiting | 14 (17.5%) out of 80 and 36.8 % out of 38 |
| 9 | Headache | 5 (6.3%) out of 80 and 13.1% out of 38 |
| 10 | Somnolance | 1 (1.3%) out of 80 and 2.6% out of 38 |
| Serious Adverse Reaction | | |
| 11 | Arrythmia | 1 (1.25%) out of 80 and 2.6 out of 38 |
| 12 | Hypotension | None |
| 13 | QT Prolongation | None |
| 14 | Torsade's de Point | None |
| 15 | Renal and Hepatic Failure | None |
| 16 | Convulsions | None |
| 17 | Neutropenia, Leucopenia and Thrombocytopenia | None |
| Allergic Reactions to Azithromycin | | |
| 18 | Arthralgia | None |
| 19 | Edema | None |
| 20 | Urticaria | 1 (1.25%) out of 80; 2.6% out of 38 |
| 21 | Angioedema | None |

Table 4. Co morbid conditions

| Co Morbid Conditions | 38 (47.5%) out of 80 | |
|----------------------|------------------------|---|
| 2 | Diabetes | 28 (35%) out of 80 and 73.6% out of 38 |
| 3 | Hypertension | 19 (23.7%) out of 80 and 50% out of 38 |
| 4 | Ischemic Heart Disease | 5 (6.25%) out of 80 and 13.1% out of 38 |

Amongst Patients having mild side effects 30(37.5%) out of 80 and 78.9% out of 38 had Abdominal Pain. 22(27.5%) out of 80 and 57.8% out of 38 had Diarrhea, 20(25%) out of 80 and 52.6% out of 38 had Nausea, 2(2.5%) out of 80 and 5.2% out of 38 had Elevated ALT AST, 21(26.3%) out of 80 and 55.2% out of 38 had Anorexia, 29(36.3%) out of 80 and 76.3% out of 38 experienced Taste perversion 12(15%) out of 80 and 31.5% out of 38 had Dyspepsia. 14(17.5%) out of 80 and 36.8% out of 38 had Vomiting. 5(6.3%) out of 80 and 13.1% out of 38 had Headache. 1(1.3%) out of 80 and 2.6% out of 38 had Somnolence. Only 1(1.25%) out of 80 and 2.6% out of 38 had Arrhythmia as serious adverse event and 1(1.25%) out of 80 and 2.6% out of 38 had Urticaria, Amongst Allergic reaction. (Table 3b) Out of 80 patients, 38 (47.5%) had Co Morbid Conditions in the form of Diabetes 28 (35%) out of 80 (73.6% out of 38). Hypertension was present in 19 (23.7%) out of 80 (50% out of 38) and 5(6.25%) out of 80 (13.1% out of 38) had Ischemic Heart Disease (Table 4).

Fig. 1 is bar chart showing frequency of occurrence of side effects was more in Age group 41-60 years that is 25 patients. 2 patients from 18-40 years, 10 from 61-80 years and 1 from > 81 years experienced adverse reaction.

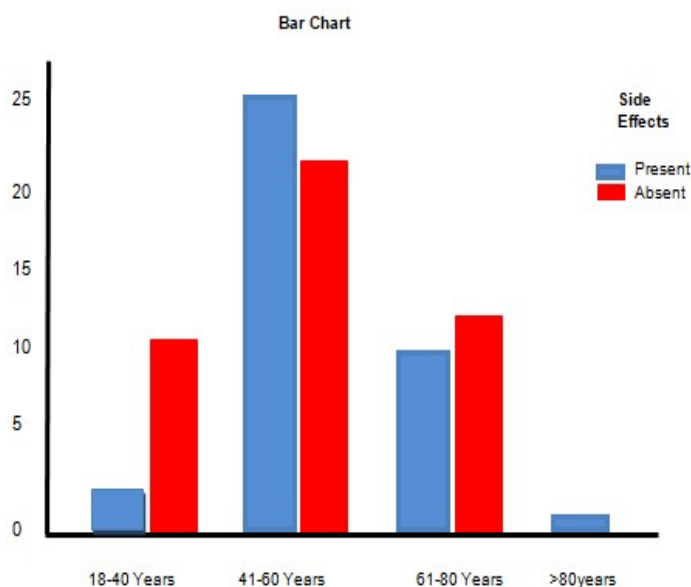


Fig. 1. Showing frequency of side effects according to age groups

4. Discussion

Azithromycin is the prototype of an antimicrobial agent which falls in the class of azalides derived from the macrolides (14). Azithromycin has good tolerance in general, but relatively common adverse effects (1–5 % of patients) include gastrointestinal upset, headache and dizziness (15). Compared to study done by Barbara A. Brown Mean age was 66 years compared to 54.9 in our study. He noted unpropitious event in 32 of 39 patients (84%) while taking Azithromycin compared to 38(46.2%) patients in our study which is quite less. The mostly was GI event (82%) in Barbara's study, GI symptoms included diarrhea (62%) compared to (27.5%) in ours,

abdominal pain (41%) compared to (37.5%) in ours, anorexia (33%) compared to (26.3 %) in ours, unusual taste sensation (33%) compared to (36.3%) in ours, nausea (28%) compared to (25%) in ours, vomiting (18%) compared to (17.5%) in ours and abdominal bloating or dyspepsia (~10%) compared to (15%) in our study (16).

Hence it is demonstrated that generally, Azithromycin remained safe drug option to use in covid positive, ICU admitted patients in Allied hospital (Faisalabad Medical University), majority of side effects were mild and tolerable and resulted in completion of antibiotic course, one patient had episode of arrhythmia, he had multiple co morbid conditions as well, that episode was successfully treated and does not resulted in fatality.

Further research with larger sample size however will definitely enable us to better manage this potentially fatal Novel Corona Virus. We concluded that Azithromycin is a safe drug as demonstrated by results only 38 (46.2%) out of 80 patients experienced side effects, majority of which were mild in nature. Only 1 (1.25%) patients had arrhythmia and one (1.25%) has allergic reaction that was successfully treated.

Conflicts of interest

The authors have no conflicts of interest to declare.

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