Clinical Outcomes and Adverse Drug Events Identified in Patients Treated with Hydroxychloroquine and Azithromycin

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Abstract

Aim To assess clinical outcomes and adverse drug events in patients hospitalised with COVID -19 treated with off- label hydroxychloroquine and azithromycin. Methods We performed a retrospective analysis of hospitalised COVID-19+ patients who received hydroxychloroquine plus azithromycin over a 2 week period. The primary end point was clinical improvement on day 7 defined as either hospital discharge or an improvement of two points on a six-category ordinal scale. Secondary outcomes evaluated included mortality at day 28, ICU admission, requirement for mechanical ventilation and incidence of adverse drug events. Results Data from a total of 82 patients with laboratory confirmed SARS-CoV-2 infection was evaluated. Clinical improvement was seen in 26.8% of patients at Day 7. 31% of patients were admitted to ICU, 16 (19.5%) underwent mechanical ventilation and Day 28 mortality was 28%. Age over 70, history of cardiovascular disease and 3 or more comorbidities were risk factors for mortality. The incidence of adverse drug events was 42%. No patient experienced a Grade 4 or 5 toxicity. Over a fifth of patients (23) had raised LFTs (65% had raised LFTs at baseline), 11 patients experienced prolonged QT and 1 patient experienced grade 1 hypoglycaemia. Treatment was stopped early in 6(7.3%) patients due to prolonged QT interval or LFT elevations. Conclusion This descriptive study details the clinical outcomes of COVID-19 positive patients treated with these agents and highlights the importance of monitoring all repurposed agents for adverse drug events.

Title

Clinical outcomes and adverse drug events identified in COVID-19 patients treated with hydroxychloroquine and azithromycin.

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PI statement

The authors confirm that the Principal Investigator for this paper is Professor Colm Bergin and that he had direct clinical responsibility for patients. The PI confirms that we have complied with our institution's policies concerning research involving human subjects and the NREC policies for protection of human subjects.

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- MK and RO'C undertook data collection, wrote the manuscript and edited the manuscript after reviewer's comments.
- LT and MC performed statistical analysis and advised on clinical parameters. All authors read and approved the final manuscript.
- BC, GM, MM and ER provided advice on consultation regarding adverse events to choose to monitor in this patient cohort and provided final article review.
- CD, ROR, SC, CM and C Bannan provided on clinical parameters (oxygen requirements) and provided final article review.
- Prof C Bergin undertook responsibility of PI, advised on structure and parameters of research and provided final sign off.

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What is already known about this subject:

- There are currently no licensed antiviral medications for the treatment of COVID-19.
- Hydroxychloroquine has shown some antiviral efficacy in some in-vitro studies.
- Hydroxychloroquine and azithromycin have a well-defined side effect profile including risk of QT prolongation, hypoglycemia and liver function test elevation.

What this study adds:

- When repurposing medications for new indications we need to be mindful that safety data cannot always be extrapolated to the new indication.
- In a small cohort 42% of patients experienced at least one adverse event from treatment with hydroxychloroquine and azithromycin and 7.3% had to stop treatment.
- Clear protocols should be in place to ensure all patients initiated on novel treatments are monitored closely for adverse events.

Data Availability Statement:

Data available on request due to privacy/ethical restrictions

Hosted file

`Submission.docx` available at https://authorea.com/users/324490/articles/452662-clinical-outcomes-and-adverse-drug-events-identified-in-patients-treated-with-hydroxychloroquine-and-azithromycin