medical sciences forum

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Proceedings Paper

Sequence Analysis of Levofloxacin Resistance-Associated Genes—*gyrA* and *gyrB* in Treatment Naïve *Helicobacter pylori* Patients from Malaysia †

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† Presented at the 2nd International Electronic Conference on Antibiotics—Drugs for Superbugs: Antibiotic Discovery, Modes of Action And Mechanisms of Resistance, 15–30 Jun 2022; Available online: https://eca2022.sciforum.net/.

Abstract: Background: Levofloxacin is used as salvage therapy in gastric pathogen *Helicobacter pylori* infection due to its resistance towards first-line therapy antibiotics. Worldwide, the overall prevalence of primary levofloxacin-resistant *H. pylori* was reported at 14%, emerging as a major concern in eradication failure. Mutations in the *gyrA* and *gyrB* genes, especially the quinolone resistance-determining region were reported to be associated with levofloxacin resistance. Therefore, this study aims to identify variants in the levofloxacin-resistance associated genes—*gyrA* and *gyrB* of *H. pylori* in Malaysian patients via sequencing. Methods: A full-length sequencing was performed on *gyrA* (2484 bp) and *gyrB* (2322 bp) using DNA extracted from biopsy samples obtained from 50 treatment-naïve patients infected with *H. pylori*. The identified DNA variants were translated in-silico and the produced protein sequences were used to predict their relative binding affinity towards levofloxacin using the HPEPDOCK webserver. The molecular docking scores between the wild type and mutant were analysed. Results and Discussion: In the *gyrA* gene, three reported mutations (G468E, 80%; P484Q, 76%; A594D, 16%) and two novel polymorphisms (V741I, 80%; S492A, 62%) were identified to have decreased docking scores ranging from 16.36% to 21.25%. For the *gyrB* gene, two commonly reported mutations (R484K, 26%; D481E, 20%) and a novel polymorphism (S240A, 16%) were reported to have decreased in 13.23%, 5.32% and 10.14% docking scores respectively. Decreased docking scores signify a weaker binding affinity between the levofloxacin and the protein binding sites in mutations compared to the wild type, consequently having a potential impact on the efficacy of levofloxacin treatments. Conclusions: The novel variants identified in *gyrA* and *gyrB* might be attributed to levofloxacin resistance in *H. pylori*, therefore, warrant for further investigation.

Acknowledgments: This study was funded by the University of Malaya Impact-Oriented Interdisciplinary Research Grant (IIRG029A/B/C-2019).

Citation: Ng, H.K.; Goh, K.L.; Kee, B.P.; Chua, K.H.; Puah, S.M. Sequence Analysis of Levofloxacin Resistance-Associated Genes—*gyrA* and *gyrB* in Treatment Naïve *Helicobacter pylori* Patients from Malaysia. *Med. Sci. Forum* **2022**, *2*, x. https://doi.org/10.3390/xxxxx

Academic Editor(s):

Published: date