The safety of hydroxychloroquine in paediatric populations: Analysis of worldwide pharmacovigilance reports

Introduction/background & aims: Hydroxychloroquine was widely promoted as a treatment for COVID-19. Although its use for treatment of COVID-19 is not supported by the evidence from randomised clinical trials,1 there are ongoing studies considering its use for prophylaxis. Paediatric patients experience a generally milder disease phenotype than older adults, and the risks of this treatment need to be considered specifically in this population. This study set out to detail adverse effect reports of hydroxychloroquine use in paediatric patients.

Method/summary of work: The study entailed a search of VigiBase, the World Health Organisation's (WHO) global database of individual case safety reports (ISCRs) received from >130 countries worldwide. Included ISCRs were from patients <19 years of age at the time of the adverse event, listing hydroxychloroquine as the suspect drug. Outcomes were the types, and severity, of the adverse events reported.

Results/discussion: VigiBase contained 536 reports of adverse events to hydroxychloroquine in patients <19 years from 1971 to 2020. Gender was predominantly female (377, 70.3%), and median age 14 years. ISCRs originated most frequently from Europe (204 reports, 38.1%), least frequently Africa (2, 0.4%). There were 547 different reasons for using hydroxychloroquine,

the five most common reasons were “unknown reason” (221, 40.4%), systemic lupus erythematosus (112, 20.5%), rheumatoid arthritis (27, 4.9%), juvenile idiopathic arthritis, (20, 3.7%) and lupus nephritis (9, 1.6%). For adverse events, a total of 1707 were reported, with 555 different ones specified. The most commonly reported adverse effects for hydroxychloroquine were “Drug ineffective” (51, 9.5%), nausea (29, 5.4%), diarrhoea (28, 5.2%), rash (28, 5.2%), vomiting (27, 5.0%). Reporters classified 292 (54.5%) of ISCR as “serious.” Overall, there were 42 (7.8%) deaths associated with reported adverse events.

In deaths, where a reason for use was provided, “Intentional Overdose” was the most commonly recorded (nine reports, 6.9%). The most common adverse events noted in the fatal reports were completed suicide (n = 13), toxicity to various agents (n = 11), intentional overdose (n = 9), cardiac arrest (n = 9), pulmonary oedema (n = 8), renal failure (n = 8) and metabolic acidosis (n = 6).

Conclusion(s): Hydroxychloroquine carries with it a degree of risk that would need to be balanced against the expected severity of COVID- 19 if considered for use in paediatric patients. Experimental medications for COVID-19 should ideally be provided in the context of a clinical trial.