Imunitas Heterolog Vaksinasi Difteri-Tetanus sebagai Priming Vaksin COVID-19 Inaktif pada Anak: Kajian terhadap Antibodi Spike-Receptor Binding Domain dan Interferon Gama-Sel T Spesifik SARS-CoV-2 = Heterologous Immunity Diphtheria-Tetanus Vaccination as Priming of Inactivated COVID-19 Vaccine in Children: Study of Antibody Spike-Receptor Binding Domain and Interferon Gamma SARS-CoV-2 Specific T Cell

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Abstrak

Golongan usia anak merupakan golongan usia yang paling ringan terdampak infeksi COVID-19. Salah satu kemungkinan penyebab keadaan tersebut adalah perlindungan dari efek nonspesifik vaksinasi rutin yang diterima anak sebelumnya. Vaksinasi rutin yang diterima anak dapat memodulasi sistem imun anak terhadap infeksi lain di luar target imunisasi yang dituju melalui mekanisme imunitas heterolog. Bukti-bukti penelitian terdahulu menimbulkan hipotesis antigen vaksin DTP berpotensi menimbulkan imunitas heterolog dengan SARS-CoV-2. Hal ini berdasarkan kemiripan epitop antara antigen SARS-CoV-2 dengan antigen pada vaksin DTP. Belum diketahui bagaimana pengaruh vaksinasi DT booster terhadap respons imun (antibodi S-RBD SARS-CoV-2 dan IFN--sel T spesifik SARS-CoV-2) pascavaksinasi COVID-19 inaktif pada anak usia 6–7 tahun. Penelitian ini bertujuan mengetahui pengaruh pemberian vaksinasi DT booster pada anak yang mendapat vaksinasi COVID-19 inaktif terhadap respons imun humoral dan selular anak.

Studi potong lintang dilakukan dengan didahului tahapan pengambilan data pada orang tua subjek penelitian di wilayah Senen, Jakarta Pusat. Pengambilan data menggunakan kuesioner yang disebarkan secara luring kepada orang tua melalui guru sekolah anaknya. Dari kuesioner didapatkan data status vaksinasi anak, yang dibedakan dalam 4 kelompok yaitu COVID+/DT+, COVID+/DT–, COVID–/DT+ dan COVID–/DT–, dan diukur antibodi S-RBD, IFN--sel T spesifik SARS-CoV-2 dan IgG antidifteri.

Hasil penelitian menunjukkan 113 dari 154 subjek penelitian (73,4%) telah memiliki status relative immune terhadap difteri, dengan hasil IgG antidifteri > 0,1 IU/mL. Terdapat imunitas heterolog vaksinasi DT booster terhadap COVID-19 dengan adanya perbedaan bermakna kadar antibodi S-RBD SARS-CoV-2 antara anak yang sudah mendapat vaksin DT booster dibanding yang belum (1182 U/mL vs. 612,5 U/mL, p = 0,026), dan perbedaan bermakna IFN--sel T spesifik SARS-CoV-2 pada anak COVID+/DT+ dibanding COVID+/DT– (560,87 mIU/mL vs. 318,03 mIU/mL, p = 0,03). Tidak didapatkan korelasi antara IgG antidifteri dan S-RBD SARS-CoV-2. Selain hasil penelitian data laboratorium, didapatkan pula data keinginan orang tua untuk vaksinasi COVID-19 bagi anaknya adalah sebesar 69,7%.

Disimpulkan vaksin DT booster dapat berperan menguatkan respons imun spesifik SARS-CoV-2 pada anak yang menerima vaksin COVID-19 inaktif.
.....Corona Virus Disease 2019 (COVID-19) in children tends to be mild. A possible cause is existing

protection from the routine vaccination previously received by children. Routine vaccinations can modulate the child's immune system against other pathogen, presumably through a mechanism of heterologous immunity. Previous research had suggested that the Diphtheria-Tetanus-Pertussis (DTP) vaccine antigen has potential to incite heterologous immunity towards SARS-CoV-2, due to similarities between SARS-CoV-2 epitopes and various epitopes found within the DTP vaccine. It was not known whether the Diphtheria-Tetanus (DT) vaccination could modulate the SARS-CoV-2-specific immune response among children aged 6–7 years who received inactivated COVID-19 vaccine.

This study thus aimed to assess the impact of DT booster immunization in SARS-CoV-2-specific humoral and cellular immune responses among children who received two doses of CoronaVac.

A cross-sectional study was performed on children aged 6–7 years old in the Senen area, Central Jakarta. This study was started with data collection from parents of eligible subjects using questionnaire that was distributed to parents via their children' school teachers. Based on the collected demographic data and the child's vaccination status, eligible subjects were further screened. The participating subjects were subsequently classified into 4 groups, i.e., COVID+/DT+, COVID+/DT-, COVID-/DT+ and COVID-/DT-. Blood collections were performed to determine anti-diphtheria toxoid antibodies, anti-S-RBD antibodies and SARS-CoV-2-specific T cell-produced IFN-.

The results showed that 113 of 154 subjects (73.4%) had relative immune-status against diphtheria as the result of the anti–diphtheria toxoid antibodies was > 0.1 IU/mL. There was a heterologous immunity of DT booster and COVID-19 vaccine, as there was significant difference in anti-S-RBD antibody titers between the group with DT booster compared to non-DT booster (1182 U/mL vs. 612.5 U/mL, $p = 0.026$), and a significant difference in IFN- concentration between the group of COVID+/DT+ and COVID+/DT- (560.87 mIU/mL vs. 318.03 mIU/mL, $p = 0.03$). No correlation was found between anti-diphtheria and anti-S-RBD antibodies. In addition, our data indicated that parental intention to vaccinate their children against COVID-19 in the Senen area was 69.7%.

In conclusion, our results suggested that DT booster vaccine might able to enhance SARS-CoV-2-specific immune responses among children who received inactivated COVID-19 vaccine.