

ABSTRAK

PENGARUH PEMBERIAN ZINK TERHADAP DIARE PADA TIKUS YANG DIINDUKSI LIPOPOLISAKARIDA (LPS) DARI *ESCHERICHIA COLI*

Kajian terhadap kadar sitokin proinflamasi (TNF- α , IL-1, IL-6),
Zink, SOD, Hb dan jumlah sel goblet mukosa usus

Sulaiman Yusuf, Srisuparyati Soenarto, M. Juffrie, Wiryatun Lestariana

Latar belakang: Proses inflamasi di usus yang menyebabkan diare akibat peningkatan pelepasan sitokin proinflamasi TNF- α , IL-1, dan IL-6 yang dipicu oleh adanya paparan LPS dari *E. coli* dengan sel epitel mukosa usus, serta status zink dalam plasma yang rendah misalnya pada bayi atau anak yang sedang mengalami diare. Jika sitokin proinflamasi ini dikendalikan dengan zink, proses inflamasi di usus yang menyebabkan diare akan membaik atau cepat sembuh.

Tujuan: Mengetahui pengaruh pemberian zink terhadap diare pada tikus yang diinduksi LPS dari *E. coli* dengan mengkaji status imun (sitokin proinflamasi: TNF- α , IL-1, dan IL-6), kadar zink, SOD, Hb serta jumlah sel goblet epitel mukosa usus.

Metode: Penelitian menggunakan rancangan eksperimental (*controlled trial design*) di laboratorium. Sebanyak 20 ekor tikus putih *Sprague Dawley* jantan dibagi secara acak dalam 4 kelompok: 1). Kelompok tikus kontrol hanya diberi pakan standar, 2). Kelompok tikus diberi LPS *E. coli* 2,5 mg/kgBB/oral 1x pada hari I, 3). Kelompok tikus diberi LPS *E. coli* 2,5 mg/kgBB/oral 1x pada hari I + zink 30 mg/kgBB/oral setiap hari selama 12 hari (kelompok preventif), 4). kelompok tikus diberi LPS *E. coli* 2,5 mg/kgBB/oral 1x pada hari I $\rightarrow$ diare + zink 30 mg/kgBB/oral setiap hari selama 12 hari (kelompok terapi). Semua tikus diambil darah melalui sinus orbita dan jaringan epitel mukosa usus (duodenum, jejunum, ileum dan kolon) pada 0 jam, 5 jam (setelah diberi LPS *E. coli*), 10 jam, hari-4, 8, dan 12 masing-masing 1 tikus setiap kelompok untuk dianalisis variabel sitokin proinflamasi: TNF- α , IL-1, dan IL-6 dengan tehnik pemeriksaan ELISA. Pemeriksaan kadar zink serum, kadar SOD dan Hb dalam darah. Pemeriksaan sel goblet epitel mukosa usus dengan pewarnaan hematoksilin-eosin (HE). Data hasil pengukuran setiap kelompok didistribusikan berdasarkan waktu perlakuan dan disajikan dalam bentuk tabel dan gambar grafik.

Hasil penelitian: Lebih tinggi kadar zink, SOD dan Hb pada tikus kelompok preventif dan kelompok terapi setelah pemberian zink dari pada kelompok + LPS terutama pada hari-4, 8 dan 12 yang mengalami diare dan tidak diberi zink. Terdapat pengaruh antara pemberian zink terhadap kadar sitokin proinflamasi, semakin tinggi kadar zink maka semakin rendah kadar sitokin proinflamasi terutama TNF- α . Tetapi kadar IL-1 dan IL-6 pada hari-8 terjadi peningkatan pada kelompok preventif dan kelompok terapi yang disertai penurunan kemampuan mengkonsumsi pakan. Disamping itu terdapat pengaruh antara kadar sitokin proinflamasi TNF- α , IL-1 dan IL-6 terhadap timbulnya

diare pada tikus kelompok + LPS. Jumlah sel goblet meningkat ketika tikus diare. Tidak terdapat pengaruh antara kadar zink dan jumlah sel goblet epitel mukosa usus. Semakin banyak kadar zink maka semakin banyak jumlah sel goblet dan sebaliknya.

Kesimpulan: Pemberian zink berpengaruh terhadap kadar sitokin proinflamasi, kadar zink, SOD dan Hb, tetapi tidak berpengaruh terhadap jumlah sel goblet epitel mukosa usus. Kemampuan mengkonsumsi pakan berpengaruh terhadap kadar zink, SOD, Hb dan sitokin proinflamasi.

Kata kunci: Zink, LPS dari *E.coli*, TNF- α , IL-1, IL-6, SOD, Hb, sel goblet.

ABSTRACT

THE EFFECT OF ZINC ON DIARRHEA IN ESCHERICHIA COLI LIPOPOLYSACCHARIDE (LPS) INDUCED MICE

The study on the levels of proinflammatory cytokines (TNF- α , IL-1, IL-6),
zinc, SOD, Hb and the number of goblet cells of the intestinal mucosa

Sulaiman Yusuf, Srisuparyati Soenarto, M. Juffrie, Wiryatun Lestariana

Background: Inflammatory process in the intestine that causes diarrhea due to increased release of proinflammatory cytokines TNF- α , IL-1 and IL-6 which are triggered by the exposure of E. Coli LPS to epithelial cells of the intestinal mucosa as well as zinc status in low plasma such as in infants or children who are experiencing diarrhea. If these proinflammatory cytokines are controlled by the use of zinc, the inflammatory process in the intestine that causes diarrhea will improve or recover quickly.

Objective: Determining the effect of zinc on diarrhea in E. Coli LPS induced mice by assessing the immune status (proinflammatory cytokines: TNF- α , IL-1 and IL-6), the levels of zinc, SOD, Hb and the number of goblet cells of the intestinal mucosa.

Methods: This study used a controlled trial experimental design in the laboratory. A total of 20 white male Sprague Dawley mice were randomly divided into 4 groups: 1). The control group was only given standard foods, 2). Groups of mice was given LPS 2.5 mg/kg body weight per oral of E. Coli LPS once on day 1, 3). The preventive group was given 2.5 mg/kg body weight per oral of E. Coli LPS once on day 1 + 30 mg/kg body weight per oral of zinc once every day for 12 days. 4). The therapy group was given 2.5 mg/kg body weight per oral of E. Coli LPS once on day 1, mice that had diarrhea was given 30 mg/kg body weight per oral of zinc once every day for 12 days. Blood samples of all the mice were taken through the orbital sinus and the epithelial tissues of the intestinal mucosa (duodenum, jejunum, ileum and colon) in which one mouse from each group were analyzed on the 0 hour, 5th hour (post E. Coli LPS induction), 10th hour, 4th day, 8th day and 12th day for the proinflammatory cytokines variables: TNF- α , IL-1 and IL-6 by using ELISA test, the levels of Zinc, SOD, Hb and the number of goblet cells of the intestinal mucosa by using hematoxylin-eosin (HE) staining. Measurement data of each group are distributed based on the time of treatment and presented in tables and graphics.

Results: There was an increase in the levels of zinc, SOD and hemoglobin in mice preventive group and therapy group after administration of zinc with increased ability to consume feed and decreased levels of zinc, SOD and hemoglobin in mice + LPS group had diarrhea and was not given the zinc. There is influence between zinc levels with SOD. The more levels of zinc, the more levels of SOD and vice versa. There is the effect of zinc administration on levels of proinflammatory cytokines, the higher levels of zinc, the lower levels of the proinflammatory cytokines TNF- α especially.

But the levels of IL-1 and IL-6 on day 8 there was an increase in the preventive group and treatment group were accompanied by a decrease in the ability to consume feed addition, there is the influence of the proinflammatory cytokines TNF- α , IL-1 and IL-6 on the incidence of diarrhea in + LPS group mice. The number of goblet cells increased when mice diarrhea. There is no influence between zinc levels and the number of goblet epithelial cells of the intestinal mucosa. The more levels of zinc, the more the number of goblet cells and vice versa.

Conclusions: The use of zinc has a significant effect on the levels of proinflammatory cytokines, zinc, SOD and Hb but has no effect on the number of goblet cells of the intestinal mucosa. The ability to consume feed effects on the levels of Zinc, SOD, Hb and proinflammatory cytokines.

Keywords: Zinc, E. Coli LPS, TNF- α , IL-1, IL-6, SOD, Hb, Goblet Cells