

DISERTASI

**PENGARUH PEMBERIAN DADIH TERHADAP DURASI DIARE
AKUT, KADAR *SECRETORY IMMUNOGLOBULIN A*, *TUMOR
NECROTIC FACTOR ALFA*, KESEIMBANGAN MIKROFLORA DAN
TINGGI VILI ILEUM**

Penelitian eksperimental laboratorium pada mencit putih



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ABSTRAK

PENGARUH PEMBERIAN DADIH TERHADAP DURASI DIARE AKUT, KADAR SECRETORY IMMUNOGLOBULIN A, TUMOR NECROTIC FACTOR ALFA, KESEIMBANGAN MIKROFLORA DAN TINGGI VILI ILEUM

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Diare merupakan penyebab kedua kematian pada anak usia dibawah 5 tahun dimana setiap tahunnya 760.000 anak meninggal dunia karena diare. Saat ini dikembangkan paradigma baru bahwa probiotik dapat menjadi suplemen terapi diare. Probiotik mengandung bakteri asam laktat (BAL) yang berpotensi meningkatkan imunitas dan meningkatkan proses absorpsi oleh vili usus. Di Sumatera Barat sendiri dikenal probiotik tradisional yaitu dadih yang merupakan produk susu kerbau fermentasi. Tujuan dari penelitian ini adalah untuk menilai pengaruh pemberian dadih terhadap durasi diare, kadar *secretory Immunoglobulin A*, kadar *Tumor Necrotic Factor Alfa*, keseimbangan mikroflora, tinggi vili ileum pada mencit diare yang diinduksi *Enteropathogenic Escherichia coli* (EPEC).

Penelitian ini menggunakan metode eksperimental dengan rancangan *Randomized Post Test Only Control Group*. Sampel sebanyak 30 ekor mencit diinduksi dengan bakteri EPEC. Penelitian dilakukan pada Juni 2016 sampai Mei 2017. Subyek dibagi dalam 3 kelompok yang terdiri dari kelompok kontrol negatif (diberi aquades ad libitum dan pakan standar), kontrol positif (mencit tidak diberi dadih), perlakuan (mencit diberi dadih 112mg/20grBB/hari). Pengamatan dilakukan selama 14 hari. Uji statistik menggunakan *Dependent Sample T Test*, *Independent Sample T Test*, *Shapiro- Wilk*, *One Way Anova* dan *Post Hoc Bonferroni*.

Hasil penelitian menunjukkan kelompok perlakuan yang diberi dadih memiliki rerata durasi diare yang lebih singkat (4,10 hari) dibandingkan dengan kontrol positif yang tidak mendapat dadih (8,80 hari) dengan nilai $p = 0,007$, bermakna secara statistik ($p < 0,05$). Rerata kadar sIgA meningkat pada kelompok perlakuan yang diberi dadih (8,69 ng/ml) dibandingkan dengan kontrol negatif (6,22 ng/ml) dan kontrol positif (8,29 ng/ml) dengan nilai $p = 0,142$, tidak bermakna secara statistik ($p > 0,05$). Rerata kadar TNF- α menurun pada kelompok perlakuan yang diberi dadih (173,18 pg/ml) dibandingkan dengan kontrol positif (238,10 pg/ml) dengan nilai $p = 0,422$, tidak bermakna secara statistik ($p > 0,05$). Rerata total koloni bakteri asam laktat meningkat pada kelompok perlakuan (100,70 cfu/gram) dibandingkan dengan kontrol positif (34,90 cfu/gram) dan kontrol negatif (53,30 cfu/gram) yang tidak mendapat dadih dengan nilai $p = 0,001$, bermakna secara statistik ($p < 0,05$). Rerata total koloni bakteri patogen menurun pada kelompok perlakuan (1,60 cfu/gram) dibandingkan kelompok kontrol positif (8,10 cfu/gram) dan kontrol negatif (3,40 cfu/gram) dengan nilai $p = 0,001$, bermakna secara statistik ($p < 0,05$). Rerata total koloni *E.coli* menurun pada kelompok perlakuan (1,00 cfu/gram) dibandingkan dengan kontrol positif (3,30 cfu/gram) dan kontrol negatif (2,10 cfu/gram) dengan nilai $p = 0,001$, meningkat secara statistik ($p < 0,05$). Tinggi vili ileum meningkat pada kelompok kontrol positif (0,26 μm) dibandingkan kontrol negatif (0,24 μm) dan kelompok perlakuan yang diberi dadih (0,25 μm) dengan nilai $p = 0,707$, tidak meningkat secara statistik ($p > 0,05$). Pada gambaran histopatologis vili ileum pada kelompok kontrol positif yang tidak mendapatkan dadih terjadi 75% destruksi epitel, banyak sebum dan kelompok limfosit serta leukosit polimorfonuklear (PMN) dilapisan lamina propria. Tetapi pada kelompok perlakuan yang mendapatkan dadih destruksi epitel hanya 30% dan hanya ada sebum ringan kelompok limfosit dan leukosit PMN pada lapisan lamina propria. Terjadinya reaksi imunologis terhadap infeksi EPEC dibuktikan dengan ditemukannya proliferasi limfoid dilapisan submukosa vili ileum pada kelompok perlakuan ini.

Pada penelitian ini disimpulkan bahwa terdapat pengaruh pemberian dadih terhadap durasi diare pada mencit yang mengalami diare akut. Tidak terdapat pengaruh pemberian dadih terhadap kadar sIgA pada mencit yang mengalami diare akut tetapi kadar sIgA terlihat cenderung lebih tinggi. Tidak terdapat pengaruh pemberian dadih terhadap kadar TNF- α pada mencit yang mengalami diare akut, tetapi terlihat bahwa kadar TNF- α cenderung lebih rendah. Terdapat pengaruh pemberian dadih terhadap keseimbangan mikroflora usus dengan meningkatnya total koloni bakteri asam laktat dan

menurunnya total koloni bakteri patogen dan *Escherechia coli* pada mencit yang mengalami diare akut. Tidak terdapat pengaruh pemberian dadih terhadap tinggi vili ileum pada mencit yang mengalami diare akut, tetapi pada mencit yang tidak mendapat dadih terlihat kerusakan epitel mukosa vili ileum.

Kata kunci: dadih, durasi diare, *tumor necrotizing factor alfa*, *secretory immunoglobulin A*, keseimbangan mikroflora, tinggi vili ileum, mencit.



ABSTRACT

THE CORRELATION OF DADIH SUPPLEMENTATION ON ACUTE DIARRHEA DURATION, SECRETORY IMMUNOGLOBULIN A LEVEL, TUMOR NECROTIC FACTOR ALFA LEVEL, INTESTINAL MICROFLORA BALANCE AND HEIGHT OF ILEUS VILLI IN MICE INDUCED WITH *ESCHERICHIA COLI* ENTEROHEPATOGENIC

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Diarrhea is the second leading cause of death among children under 5 years old where every year 760.000 children died because diarrhea. There is new paradigm that probiotic can be a supplement to treat diarrhea. Probiotic consists of lactic acid bacteria (LAB) that has potential to strengthen immunity and increase absorption process in intestinal villi. In West Sumatera, there is traditional probiotic known as dadih from fermented buffalo milk. The objective of this study is to determine correlation of dadih administration with duration of diarrhea, secretory immunoglobulin A, tumor necrotic factor alfa level, intestinal microfloral balance and ileum height in mice with diarrhea which were induced with *Enteropathogenic Escheria Coli* (EPEC).

Design of the study is an experimental with *Randomized Post Test Only Control Group*. The population of this study was all the male white mice (*Mus musculus*) from animal development unit of Pharmacology Laboratory of Andalas University, 6-8 weeks of age, and 20-30 gram of weights, induced with EPEC and took place in Pharmacy Laboratory, pathology Anatomy Laboratory and Biomedic Laboratory of Medical Faculty Andalas University from June 2016 to May 2017. Subjects were divided into three groups, the first group was negative group (mice were given aquades and normal food), the second group was positive group control (mice were not given dadih), and the third group was treatment group (mice were given dadih). The observation was conducted in 14 days. Statistical analysis was done Dependent Sample T Test, Independent Sample T Test, Shapiro- Wilk, One Way Anova dan Post Hoc Bonferroni.

The result showed that the mean of diarrhea duration was shorter in the treatment group (4.10 day) compared with positive control group (8.80 day), with $p= 0.007$, statistically significant ($p<0.05$). Mean of sIgA level was higher in treatment group (8.69 ng/ml) compared with negative control group (6,22 ng/ml) and positive control group (8,29 ng/ml), with $p=0.142$, not statistically significant ($p>0.05$). Mean of TNF- level was lower in the treatment group (173.18 pg/ml) compared with positive control group 238.10 pg/ml), with $p= 0.422$, not statistically significant ($p>0.05$). Study showed dadih administered treatment group had higher mean of LAB colony total (100.70 pg/ml) compared with positive control (34.90 cfu/grams) and negative control (53.30 cfu.grams), with $p= 0.001$, statistically significant ($p<0.05$). Treatment group had lower mean of pathogen colony total (1.60 cfu/grams) compared with positive control (8.10 cfu/grams) and negative control (3.40 cfu/grams), with $p=0.001$, statistically significant ($p<0.05$). Treatment group had lower mean of *E.coli* colony total (1.00 cfu/grams) compared with positive control (3.30 cfu/grams) and negative control (2.10 cfu/grams), with $p=0.001$, statistically significant ($p<0.05$). Mean of ileum height was higher in positive control group (0.26 μm) compared with negative control group (0.24 μm) and treatment group (0.25 μm), with $p=0.707$, not statistically significant ($p>0.05$). Histopathological features of the ileal villi in the untreated positive control group showed 75% of epithelial destruction, many lymphocyte grouping and polymorphonuclear leukocytes (PMN) in lamina propria layer. However, in the treatment group only showed 30 % epithelial destruction, mild cluster of lymphocyte and PMN leucocytes in lamina propria layer. The occurrence of immunological reactions to EPEC infection is evidenced by the proliferation of lymphoid follicle in submucosa of ileal villi in this treatment group.

This study concluded that there is effect of dadih supplementation to duration in mice that suffered from acute diarrhea. There is no effect of dadih supplementation on sIgA levels in mice that suffered from acute diarrhea, but it tends to be higher. There is no effect of dadih supplementation on TNF- levels in mice that suffered from acute diarrhea, but it tend to be lower. There is effect of

dadih supplementation to intestinal microflora balance by increasing total colony of lactic acid bacteria and decreasing total colony of pathogenic bacteria and Escherechia coli in mice with acute diarrhea. There is no effect of dadih supplementation on high ileal villi in mice that suffered from acute diarrhea, but in mice that do not get dadih supplementation seen mucosal epithelial damage of ilium villi.

Keywords: Dadih, diarrhea duration, tumor necrotizing factor alfa, secretory immunoglobulin A, illeum villi height, microfloral balance, mice.

