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International Conference on Public Health for Tropical and Coastal Development

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International Conference on Public Health for Tropical and Coastal Development (ICOPH-TCD 2016)

October 15-17, 2016
Semarang, Indonesia

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SK Rektor : 853/UN7.P/HK/2016

SKP of IAKMI : 6 SKP Letter No : 3879/UN7.3.9/KP/2016
SKP of PERSAKMI : 4 SKP Letter No : 189/PP-PERSAKMI-SKP/IX/2016

ISBN 978-602-74235-5-8

Abstract Book

ICOPH-TCD

International Conference on Public Health for Tropical and Coastal Development

International Conference on Public Health for Tropical and Coastal Development (ICOPH-TCD 2016)

Organized by :
Faculty Of Public Health
Diponegoro University

October 15-17, 2016
Patra Jasa Semarang Convention Hotel

ABSTRACT BOOK
INTERNATIONAL CONFERENCE OF PUBLIC HEALTH FOR TROPICAL AND COASTAL DEVELOPMENT 2016

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This abstract book is published by

FKM UNDIP PRESS
Jl. Prof. Soedarto, SH, Tembalang
Semarang 50275
Phone: +62-24-7460044
E-mail: fkmundip.press@gmail.com

ISBN 978-602-74235-5-8

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REDUCE SPLEEN-IFN-γ CORRELATED WITH CXCL9 LEVELS DURING CEREBRAL MALARIA PHASE IN ANNONA MURICATA-TREATED SWISS MOUSE STUDY

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Abstract

Background: Cerebral malaria (CM) cause malaria mortality. Anti-plasmodial and immunomodulatory properties of *A. muricata*-leaf extract (AME) may provide benefices for CM-patients. IFN-γ, a pivotal cytokine in the CM-immunopathology, is modulated by CXCL9, IL-10 and IL-12. The aim was to determine factors correlated with spleen-IFN-γ production in healthy and CM phase with/without ethanolic AME treatment.

Method: A post-test only control group design study using 36 swiss mice randomly devided in 6 groups was performed. The *Plasmodium berghei* ANKA (PbA)-inoculated and healthy mice were grouped in C(+) and C(-). The healthy mice treated with AME 100 and 150 mg/Kg BW/day were grouped in X1 and X2. The PbA-inoculated and received either AME dose were grouped in X3 and X4. Phytohemaglutinin (PHA) induced spleenocyte IFN-γ production, while lipopolysacharide (LPS) induced IL-10, IL-12 and CXCL9. Elisa was used to measure the observed cytokine production. One-way ANOVA and post hoc test were done in normally distributed data; otherwise Kruskal-Wallis and Mann-Whitney test were used.

Results: IFN-γ were significantly lower in C(+), X3 and X4 than C(-) group, and this was also observed in CXCL9. IL-10 were significantly higher in X3 and X4 than C(+) group (p=0.003 and p=0.004). IL-12 were not different among all six groups (p=0.071). Spearman correlation test showed a correlation between IFN-γ and CXCL9 produced during CM-phase regardless AME treatment (r=0.581; p=0.009), while IFN-γ was correlated with IL-10 levels in healthy groups with/without AME treatment (r=0.544; p=0.029).

Conclusion: The conclusions were the reduce spleen-IFN-γ production might regulate differently in healthy and CM phase

Keywords: *Annona muricata*, cerebral malaria,IFN-γ, CXCL9.

ANNONA MURICATA ASSOCIATED WITH INCREASE-PHYTOHEMAGLUTIN INDUCED SPLEEN IL-10 PRODUCTION OF SWISS MICE DURING CEREBRAL MALARIA PHASE

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Abstract

Background: Cerebral malaria (CM) prompts patient death. *A. muricata*-leaf extract (AME) having anti-plasmodial and immunomodulatory properties may provide advantages for malaria-endemic communities. Anemia during CM-patients is possibly due to reduce interleukine (IL)-10, and increase macrophage migration inhibitory factor (MIF) production which interfere erythropoiesis. The objective was to determine whether AME influenced spleen-IL-10 and MIF production during CM-phase which then increased Hb or erythrocyte counts.

Method: A post-test only control group design study was done by using 30 swiss mice which were randomly devided in 6 groups. The C(+) and C(-) groups were *Plasmodium berghei* ANKA (PbA)-inoculated and healthy-mice. Healthy-X1 and X2 groups received ethanolic-AME 100 and 150 mg/Kg BW/day. PbA-inoculated X3 and X4 groups received either AME dose. IL-10 and MIF produced by splenocytes stimulated with phytohemaglutinin (PHA) or lipopolysacharide (LPS) *ex-vivo*, were measured by Elisa. Hb and erythrocyte counts were measured by automatic haematology analyzer.

Results: IL-10 was tested by Kruskal-Wallis ($p<0.0001$), then Mann-Whitney showed a significantly higher IL-10 of X3, X4 than C(+) group ($p=0.003$ and $p=0.017$). PHA and LPS-induced splenocyte MIF production were tested by One-way ANOVA and Kruskal-Wallis ($p=0.176$ and $p=0.413$). Mann-Whitney test showed a lower Hb of C(+), X3 and X4 than C(-) groups ($p=0.045$, $p=0.038$, and $p=0.016$). Erythrocyte counts were not different among 6 group studied ($p=0.072$). IL-10 and MIF had no correlation with Hb or erythrocyte counts during CM-phase. The conclusion is that AME associates with increase spleen-IL-10 production during CM-phase. The spleen-IL-10 and MIF might not influence Hb and erythrocyte counts during CM-phase.

Conclusion: AME associates with increase spleen-IL-10 production during CM-phase. The spleen-IL-10 and MIF might not influence Hb and erythrocyte counts during CM-phase

Keywords: *Annona muricata*, cerebral malaria, MIF, IL-10.