

LAMPIRAN

Lampiran 1. Lembar persetujuan dan pengesahan

PERSETUJUAN PEMBIMBING

Proposal skripsi yang berjudul studi literatur efektivitas terapi antibiotik pada pasien demam tifoid dewasa dibuat oleh Siti Hawa, 1648201110046 telah diujikan didepan tim penguji pada Seminar Proposal Program Studi S1 Farmasi Fakultas Farmasi Universitas Muhammadiyah Banjarmasin pada tanggal

Banjarmasin, 17 Mei 2020

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PENGESAHAN PROPOSAL

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Analisis Efektivitas Biaya Penggunaan Antibiotik pada Pasien Demam Tifoid di RS SMC Periode 2017

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Abstract

Typhoid fever is an acute infection of the small intestine with symptoms of fever more than one week can cause a digestive disorders and reduce the level of consciousness. Treatment of typhoid fever can be done by administering antibiotic therapy. The use of antibiotics at a relatively high cost may not necessarily guarantee the effectiveness of the patient's recovery. The purpose of this study was to determine the cost effectiveness of antibiotics from typhoid fever patients in Samarinda Medika Citra (SMC) Hospital. The method of data collection was conducted retrospectively based on medical records of typhoid fever patients hospitalized for the period January to December 2017. Cost effectiveness data for antibiotic treatment analysed by ACER value. The results of 79 patients showed that most typhoid fever sufferers were women with a percentage of 53.16% and happened at 6 to 11 years and 26 to 35 years with the same percentage as much as 17.72% with 4 days of hospital stay and antibiotics that have better effectiveness are ampicillin which can reduce fever temperature by 36.70 °C at a cost of Rp. 46,695.77 for 4.3 days with ACER value of Rp. 398,543.00.

Keywords: Typhoid Fever; Cost Effectiveness Analysis; Ampicillin; Antibiotics.

Lampiran 3. Limpitikul *et al*, 2013

Cost effectiveness in treatment of typhoid

PUBLIC HEALTH RESEARCH

Costs and Effectiveness of Ciprofloxacin and Ceftriaxone in Treatment of Typhoid Fever in Children in Thailand

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ABSTRACT

Accepted 12 December 2012

Introduction The burden of typhoid fever remains high in impoverished settings, and increasing antibiotic resistance is making treatment costly. The purposes of this study were: to compare the costs and the effectiveness of typhoid programs between oral and injection treatments in pediatric patients at Songkla Hospital.

Methods This study was an incidence-based cost-of-illness analysis from providers' perspective. Micro-costing approach was employed for calculating patient-specific data. The study was conducted in Songkla Hospital in the southern part of Thailand from 2009 to 2010. The total number of the cases was 78. Patients taking antibiotics for 48 hours, and those suspected of having complicated typhoid fever like peritonitis, ileus, toxic encephalopathy were excluded. We collected and reviewed medical records. In all provisionally selected children, blood was drawn for complete blood count, widal test and blood culture. The statistics used in data analysis were descriptive statistics and the cost-effectiveness of typhoid treatment with the two methods was compared using independent t-test.

Results The results of the study revealed that the average cost of typhoid treatment with oral Ciprofloxacin calculated with DRG was 3,301.88 baht which was lower than that of injection Ceftriaxone treatment calculated with DRG (3,015.05 baht). When the operation costs were considered, the results of the study remained the same, i.e. the treatment cost of typhoid with oral Ciprofloxacin was two times lower than that with injection Ceftriaxone. The average cost of the oral treatment was 2,844.45 baht, and that of the injection treatment was 5,305.10 baht. Regarding the effectiveness of typhoid treatment with Ciprofloxacin measured from the time the fever was reduced, it was found that the body temperature of the two methods of treatment were used was not significantly different ($p < .05$). The patients on oral medications had a fever for an average of 3.36 days while those on injection treatment had a fever for an average of 3.76 days. However, the lengths of stay (LOS) of the two groups of patients were significantly different.

Conclusions The results of this study showed that the cost-effectiveness of oral treatment was better than injection. Besides, the patient and caregiver spent less time when oral treatment was administered than when injection treatment was used. Therefore, the direct cost for treatment was reduced and the indirect cost as a result from LOS was also reduced. Above all, the patient did not get pain from injection while the effectiveness of fever reduction was not different.

Keywords Costs-Effectiveness-Ciprofloxacin-Ceftriaxone-Typhoid Fever-Children

Lampiran 4. Rampengan 2013

Antibiotik Terapi Demam Tifoid Tanpa Komplikasi pada Anak

Novie Homenta Rampengan

Bagian Ilmu Kesehatan Anak, Fakultas Kedokteran Universitas Sam Ratulangi/RSU Prof.Dr.R.D. Kandou, Manado

Latar belakang. Demam tifoid masih merupakan masalah kesehatan khususnya di Indonesia. Kloramfenikol merupakan obat pilihan lini pertama untuk terapi demam tifoid tanpa komplikasi pada anak sampai saat ini. Antibiotik lain yang dipergunakan adalah tiamfenikol, sefiksime dan azitromisin.

Tujuan. Melakukan evaluasi respon antibiotik yang digunakan dalam terapi demam tifoid tanpa komplikasi di Bagian Ilmu Kesehatan Anak RSU Prof.Dr.R.D.Kandou, Manado.

Metode. Penelitian kohort retrospektif dilakukan di Bagian Ilmu Kesehatan Anak RSU Prof.Dr.R.D.Kandou, Manado, Juli 2007-Juni 2012 pada anak usia 6 bulan-15 tahun dengan diagnosis demam tifoid. Data diperoleh dari rekam medik pasien. Waktu bebas demam dan lama rawat pada tiap kelompok antibiotik di data. Analisis statistik dilakukan dengan menggunakan ANOVA dengan uji F dengan program SPSS 17.

Hasil. Didapatkan 161 kasus yang memenuhi kriteria inklusi. Antibiotik terbanyak dipakai adalah kloramfenikol (31,1%), tiamfenikol (27,3%), sefiksime (23%), dan azitromisin (18,6%). Waktu bebas demam paling pendek dicapai pada kasus yang diberikan azitromisin yaitu 37,9 (SB 32,8) jam, diikuti oleh kloramfenikol 40,3 (SB 28,3), tiamfenikol 45,3 (SB 38,1) dan sefiksime 50,8 (SB 32,3). Rerata lama rawat paling cepat ditemukan pada kelompok kloramfenikol yaitu 4,4 (SB 1,3) hari, diikuti dengan azitromisin 4,6 (SB 1,3), tiamfenikol 4,8 (SB 1,7) dan sefiksime 4,8 (SB 1,6). Tidak terdapat perbedaan bermakna rerata waktu bebas demam dan lama rawat keempat jenis antibiotik.

Kesimpulan. Pemberian antibiotik kloramfenikol, tiamfenikol, sefiksime, dan azitromisin pada demam tifoid anak tidak terdapat perbedaan bermakna pada rerata waktu bebas demam dan lama rawat inap.

Sari Pediatri 2013;14(5):271-6.

Kata kunci: demam tifoid, antibiotik, waktu bebas demam, lama rawat inap

Lampiran 5. Yusrizal, 2011

Analisis Efektivitas Biaya Kloramfenikol Dan Seftriakson Pada Pengobatan Pasien Demam Tifoid di Instalasi Rawat Inap RSUD.Abdul Moeloek Tahun 2011

Yusrizal

Jurusan Farmasi Politeknik Kesehatan Kemenkes Tanjungkarang

Abstrak

Pengobatan terhadap penyakit demam tifoid terus berkembang. Dari dulu, kloramfenikol merupakan obat pilihan utama untuk pengobatan demam tifoid. Namun seiring dengan kemajuan bidang kedokteran, dikembangkan lagi obat-obat seperti golongan sulfonamida, sefalosporin dan florokuinolon. Seftriakson dianggap sebagai obat yang efektif untuk pengobatan tifoid dalam jangka pendek. Tetapi harga obat tersebut masih cukup mahal. Telah dilakukan penelitian penelitian non eksperimental menggunakan metode *cross-sectional*, untuk melihat efektifitas biaya terhadap pasien demam tifoid yang menggunakan kloramfenikol dan pasien yang menggunakan seftriakson di Instalasi Rawat Inap Rumah Sakit Umum Daerah Abdul Moeloek Provinsi Lampung Tahun 2011. Hasil penelitian menggunakan analisis statistik Uji t menunjukkan bahwa Seftriakson mempunyai efektifitas pengobatan yang lebih baik dibandingkan dengan kloramfenikol pada pengobatan pasien demam tifoid dan Seftriakson mempunyai efektifitas biaya yang tidak berbeda dengan kloramfenikol pada pengobatan pasien demam tifoid

Kata kunci: Kloramfenikol, Seftriakson, Efektivitas pengobatan, Efektivitas biaya

Lampiran 6. Rusmini, 2015

ANALISIS EFEKTIVITAS PENGGUNAAN KLORAMFENIKOL DAN SEFTRIAKSON DALAM PENGOBATAN DEMAM TIFOID ANAK DI RSUD Dr. H. ABDUL MOELOEK PROVINSI LAMPUNG TAHUN 2012-2014

Hetti Rusmini

ABSTRAK

Demam tifoid merupakan penyakit yang disebabkan oleh bakteri *Salmonella typhi* terutama menyerang bagian pencernaan. Kloramfenikol merupakan obat pilihan utama untuk pengobatan demam tifoid. Seftriakson merupakan obat yang efektif untuk pengobatan demam tifoid dalam jangka pendek. Penelitian ini bertujuan untuk mengetahui efektivitas penggunaan kloramfenikol dan seftriakson pada pengobatan demam tifoid anak.

Rancangan penelitian ini menggunakan *cross-sectional* dengan sampel adalah pasien demam tifoid anak yang di rawat inap Rumah Sakit Umum Daerah Dr. H. Abdul Moeloe menggunakan data rekam medik periode tahun 2012-2014. Sebanyak 29 pasien diberi pengobatan kloramfenikol dan 29 pasien diberi pengobatan seftriakson. Analisa statistik menggunakan *Mann Whitney Test*.

Berdasarkan hasil penelitian diperoleh lama perawatan pasien yang menggunakan kloramfenikol adalah $4,18 \pm 1,25$ hari sedangkan pasien yang menggunakan seftriakson adalah $2,38 \pm 0,49$ hari. Hilangnya demam pada pasien yang menggunakan kloramfenikol adalah pada hari ke $2,41 \pm 0,68$ dan pasien yang menggunakan seftriakson adalah pada hari ke $1,98 \pm 0,28$.

Analisis efektivitas pengobatan demam tifoid anak menunjukkan bahwa seftriakson mempunyai efektivitas pengobatan yang lebih baik dibandingkan dengan pengobatan demam tifoid anak menggunakan kloramfenikol.

Kata Kunci : Seftriakson, Kloramfenikol, Demam Tifoid.

Lampiran 7. Susono *et al*, 2014

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COST EFFECTIVENESS ANALYSIS PENGOBATAN PASIEN DEMAM TIFOID PEDIATRIK MENGGUNAKAN CEFOTAXIME DAN CHLORAMPHENICOL DI INSTALASI RAWAT INAP RSUD PROF. DR. MARGONO SOEKARJO

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ABSTRAK

Di Indonesia insiden demam tifoid banyak dijumpai pada populasi yang berusia 3-19 tahun. Resistensi luas antibiotik aktif terhadap *Salmonella typhi* banyak ditemui salah satunya *chloramphenicol*. *Chloramphenicol* adalah antibiotik pilihan pertama untuk tifoid pediatrik di RSUD Prof. Dr. Margono Soekarjo Purwokerto. Telah dilakukan penelitian *cost effectiveness analysis* menggunakan metode observasional analitik dengan rancangan *cross sectional*, pengambilan data menggunakan pendekatan retrospektif melalui penelusuran rekam medik pasien. Terdapat 87 pasien yang masuk dalam penelitian ini, 64 pasien mendapatkan *chloramphenicol* dan 23 pasien mendapatkan *cefotaxime*. Total biaya rata-rata pasien demam tifoid pediatrik yang mendapat *chloramphenicol* sebesar Rp1.453.618,00 sedangkan pada pasien yang mendapat *cefotaxime* sebesar Rp1.319.413,00. Berdasarkan waktu bebas demam pasien, nilai ACER *chloramphenicol* sebesar Rp983.969,00 per hari bebas demam, sedangkan *cefotaxime* sebesar Rp761.917,00 per hari bebas demam dengan nilai ICER sebesar Rp-527.535,00 per hari bebas demam. Untuk lama rawat pasien, nilai ACER *chloramphenicol* sebesar Rp299.098,00 per hari rawat sedangkan *cefotaxime* sebesar Rp297.835,00 per hari rawat dengan nilai ICER sebesar Rp312.104,00 per hari pengurangan lama rawat. Sehingga *cefotaxime* lebih *cost effective* dibandingkan dengan *chloramphenicol*.

Kata kunci: demam tifoid pediatrik, *cefotaxime*, *chloramphenicol*.

Lampiran 8. Beatrix *et al*, 2018

PHARMACON Jurnal Ilmiah Farmasi – UNSRAT Vol. 7 No. 2 MEI 2018 ISSN 2302 - 2493

**ANALISIS EFEKTIVITAS BIAYA PENGOBATAN PASIEN
PEDIATRIK DEMAM TIFOID MENGGUNAKAN CEFIXIME
DAN CEFOTAXIME DI RSU PANCARAN KASIH GMIM
MANADO**

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ABSTRACT

The highest prevalence of typhoid fever in Indonesia in the age group of 5-14 years old. The mortality rate of typhoid fever in some areas was 2-5% of patients into asymptomatic carriers, thus providing a new source of infection for the surrounding community. Treatment using antibiotics is the most widely used typhoid fever drug, related to the many incidences of bacterial infection suffered by many people. This study aims to determine which drugs are more effective between Cefixime and Cefotaxime in the treatment of pediatric typhoid fever in GMIM Pacaran Kasih Hospital Manado. Cost Effectiveness Analysis has been done using descriptive observational method with cross sectional design, retrieval data using retrospective approach through patient medical record data search. Based on the results obtained, the average total cost of pediatric typhoid fever patients who received cefixime were Rp. 2.546.912 while at cefotaxime were of Rp. 2.594.693. Based on patient free fever time, the value of ACER Cefotaxime were Rp. 1.179.406 per day of free of fever, while cefixime were Rp. 1.142.113 per dy of free of fever with ICER value of Rp. 1.592.700 per day free of fever. For long patient care, ACER cefotaxime value of Rp. 589.703 per day of care while cefixime of Rp. 585.497 per day treated with ICER value of Rp. 955.620 per day addition of length of stay. So in conclusion, cefixime is more cost effective than cefotaxime.

Keywords : Cost Effectiveness Analysis, Cefixime, Cefotaxime, Typhoid Fever, Pediatrics

Lampiran 9. Haluang *et al*, 2015

PHARMACON Jurnal Ilmiah Farmasi – UNSRAT Vol. 4 No. 3 Agustus 2015 ISSN 2302 - 2493

**ANALISIS BIAYA PENGGUNAAN ANTIBIOTIK PADA PENDERITA
DEMAM TIFOID ANAK DI INSTALASI RAWAT INAP
RSUP PROF. DR. R.D. KANDOU MANADO
PERIODE JANUARI 2013 - JUNI 2014**

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ABSTRACT

Drug costs in health care last few decades have increased sharply. Antibiotics are a group of drugs used to treat infectious diseases one of which is typhoid fever. The use of antibiotics by relatively high costs can not necessarily guarantee the effectiveness of patient care. This study aims to determine the characteristics of patients typhoid fever in children who are treated in inpatient installation of RSUP Prof. Dr. R. D. Kandou Manado and determine the cost effectiveness of antibiotic drugs used patient.

This study is a descriptive and retrospective during the period January 2013 - June 2014 in the Section of Medical Record and Medical Warehouse RSUP Prof. Dr. R. D. Kandou Manado. The study was conducted on 45 patients with a medical record of typhoid fever in children who are hospitalized. The results showed, that majority of patients with typhoid fever in children is aged 6 - 11 years (35,6 %), the male sex (58%), of the JKN patient status (71%), with oral antibiotics (66,7%) and the type of generic antibiotic drugs (84%). Antibiotics that have the lowest cost-effectiveness on the JKN patient status is amoxycilin Rp. 762 / day and the general patient status is chloramfenicol Rp. 360 / day.

Keywords : Antibiotic, Typhoid Fever Children, Cost Effectiveness.

Lampiran 10. Agnes *et al*, 2019

PHARMACON—PROGRAM STUDI FARMASI, FMIPA, UNIVERSITAS SAM RATULANGI,
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ANALISIS EFEKTIVITAS BIAYA PADA PASIEN ANAK DEMAM TIFOID DI RUMAH SAKIT BHAYANGKARA MANADO

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ABSTRACT

Typhoid fever is an endemic disease which its incidence rate is still high in Indonesia. Administering antibiotic therapy can do treatment of typhoid fever. This study was conducted since there are several pediatric patients diagnosed with typhoid fever but have different antibiotic therapies, namely cefotaxime and ceftriaxone therapy, so it is necessary to do calculations to determine the comparison and determine which treatment is more efficient in cost and effectiveness. The method used in this study is CEA (Cost-Effectiveness Analysis) with the design of retrieving medical record data of children with typhoid fever in Bhayangkara Manado Hospital retrospectively from January to December 2018. The samples obtained were 28 pediatric patients, consisting of 12 patients using cefotaxime therapy and 16 patients using ceftriaxone therapy. The result of ACER (An Average Cost Effective Ratio) obtained by ceftriaxone were Rp. 526.609,-/day and cefotaxime Rp. 484.789,-/day. In this study, if patients under cefotaxime therapy want to switch treatment to ceftriaxone therapy, ICER calculation (Incremental Cost-Effectiveness Ratio) is carried out the result are Rp.340.528,-.

Keyword: Typhoid fever, Antibiotics, CEA (Cost-Effectiveness Analysis)

Lampiran 11. Zmora *et al*, 2018

PLOS | NEGLECTED
TROPICAL DISEASES

RESEARCH ARTICLE

Open label comparative trial of mono versus dual antibiotic therapy for Typhoid Fever in adults

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Abstract

OPEN ACCESS

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Data Availability Statement: All relevant data are within the paper and its Supporting Information files.

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Background

Emerging resistance to antibiotics renders therapy of Typhoid Fever (TF) increasingly challenging. The current single-drug regimens exhibit prolonged fever clearance time (PCT), imposing a great burden on both patients and health systems, and potentially contributing to the development of antibiotic resistance and the chronic carriage of the pathogens. The aim of our study was to assess the efficacy of combining third-generation cephalosporin therapy with azithromycin on the outcomes of TF in patients living in an endemic region.

Methods

An open-label, comparative trial was conducted at Dhulikhel Hospital, Nepal, between October 2012 and October 2014. Only culture-confirmed TF cases were eligible. Patients were alternately allocated to one of four study arms: hospitalized patients received either intravenous ceftriaxone or a combination of ceftriaxone and oral azithromycin, while outpatients received either oral azithromycin or a combination of oral azithromycin and cefixime. The primary outcome evaluated was PCT and the secondary outcomes included duration of bacteremia.

Results

105 blood culture-confirmed patients, of whom 51 were treated as outpatients, were eligible for the study. Of the 85 patients who met the inclusion criteria for PCT analysis 41 patients received a single-agent regimen, while 47 patients received a combined regimen. Results showed that PCT was significantly shorter for the latter (35 versus 55 hours, respectively, $p = 0.004$), and this effect was exhibited in both the hospitalized and the outpatient subgroups. Repeat blood cultures, drawn on day 3, were positive for 5/47 (17%) patients after