A Randomized Double Blind Controlled Study on the Efficacy of Spirulina as an Adjunct Therapy in the Management of Pediatric Community Acquired Pneumonia-C in Patients 6 Months to 5 Years Old Admitted in a Tertiary Government Hospital*

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ABSTRACT

Objective: To determine the effect of Spirulina among patients with community acquired Pneumonia–C (PCAP-C) based on the resolution of the following symptoms; fever, respiratory rate, chest indrawings, rales, oxygen saturation and compare their length of hospital stay.

Design: A randomized-double blind, placebo controlled clinical trial

Setting: The study was done at a tertiary government hospital

Patients/Participants: Children 6 months to 5 years old with PCAP-C were randomized to either treatment group A or B. The two groups received the standard treatment for pneumonia and adjunct treatment of Spirulina for group A and placebo for group B.

Results: A total of 147 patients participated in the study. Seventy four patients were randomized to group A and 73 patients to group B. Respiratory rate showed greater improvement with Spirulina supplementation starting day 3, 4 and 5. Resolution of chest in-drawing was significant in Spirulina group on day 2 (p- value < 0.05), day 3 (p – value < 0.05) and day 4 (p – value <0.05). There were more patients in Spirulina group with decreased to absent rales on day 2 (p-value 0.02), day 3 (p-value 0.039), day 4 (p-value 0.01) and day 5 (p-value 0.01). Temperature and oxygen saturation on both groups had almost similar trends. The mean hospital stay in Spirulina group (3.09 days) is shorter as compared to the placebo group (p-value 0.02).

Conclusion: Spirulina supplementation showed positive effects in PCAP-C. Its immune-modulating effect played a positive role in the treatment outcome of pneumonia.

Keywords: pneumonia, Spirulina, PCAP-C

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INTRODUCTION

Pneumonia is a leading cause of death in children worldwide. In 2013, the World Health Organization (WHO) reported that Pneumonia killed an estimated 1.1 million children less than 5 years of age accounting for 18% of all deaths in children worldwide. Antibiotic remains the core of treatment for Pneumonia. However, despite good antibiotic coverage for pneumonia the mortality and morbidity remain high.[1]

In 2004, there were an estimated 12 million deaths in the Asia–Pacific region, of which approximately one quarter (2.8 million) was attributable to respiratory causes. In this region, COPD and lung cancer accounted for 70% of all deaths attributable to respiratory disease. Infection is the other major cause of mortality, with pneumonia comprising 475,000 (16.8%) and TB with 305,000 deaths (10.8%).[2]

The World Health Organization (WHO) reported that about 156 million new episodes of childhood clinical pneumonia occurred globally in 2000, of which 95% occurred in developing countries. Nine percent of the pneumonia cases occurring in these countries are severe enough to be life-threatening and require hospital admission. In the African and South-East Asian Regions it was estimated that about 2 million deaths from pneumonia occur each year in children less than five years of age. Globally, the Philippines ranks number 10 among fifteen countries with 3 million reported cases. [3]

In the Philippines, the Department of Health reported that it is the leading cause of mortality and ranks the 2nd most common cause of morbidity in 2010.[4] Pneumonia also topped the list of 20 illnesses that the Philippine Health Insurance Corporation paid for in claims annually, costing at least 2 billion pesos in 2010. In the first half of 2011 alone, the Philippine Health insurance had spent at least 1.2 billion pesos in pneumonia claims. [5]

Pneumonia can be diagnosed based on clinical signs and symptoms such as tachypnea, chest in drawings, fever and other abnormal chest findings. Chest radiograph and laboratory tests can be used to confirm the presence of pneumonia and identify the causative pathogen. Fever of 38.5 ^{0}C and above, a chest x-ray findings of consolidation or atelectasis are features suggestive of bacterial pathogen. Patients with pneumonia of bacterial etiology should be treated with appropriate antibiotic. Oral Amoxicillin given for an average of 7 days is recommended for an outpatient cases while intravenous Penicillin or Ampicillin for hospitalized patients. [6]

The use of adjunct treatment in pneumonia has been the subject of several researches. Studies have shown that adjunct treatment for pneumonia like Vitamin A and C had minimal effect to none. There are no studies available to warrant recommendation for the use of these immune-modulators. Studies on the efficacy of Zinc, in the treatment of Pneumonia are also equivocal to non-beneficial.[7]A recent clinical trial done by Cadete et al revealed that supplementation of Spirulina shortened the duration of fever, significantly decreased the heart rate and provided radiologic improvement in children admitted as severe pneumonia.[8] In the investigators knowledge there are no published studies which use Spirulina as adjunct in the management of pediatric community acquired pneumonia-C (PCAP-C). This study aims to answer the research question; among children six months to five years of age admitted in a tertiary government hospital how effective is Spirulina as an adjunct treatment in PCAP-C.

REVIEW OF LITERATURE

Spirulina is a microscopic and filamentous cyanobacterium that derives its name from the spiral or helical nature of its filaments. It has a long history of use as food and it has been reported that it has been used during the Aztec civilization. Spirulina refers to the dried biomass of Arthrospiraplatensis, an oxygenic photosynthetic bacterium found worldwide in fresh and marine waters. It has been used as a source of protein and vitamin supplement in humans without any significant side-effects. It has the ability to modulate immune functions and exhibits anti-inflammatory properties by inhibiting the release of histamine by mast cells. Multiple studies investigating the efficacy and the potential clinical applications of Spirulina in treating several diseases have been performed.[9]

In a journal article it was stated that Spirulina administered 2000mg/day, significantly reduced IL-4 levels by 32% from phytohemagglutinin (PHA) – stimulated cells. These results indicate that Spirulina can modulate the profile patients with allergic rhinitis by suppressing the differentiation of TH2 cells mediated, in part, by inhibiting the production of IL-4.[10]

Several local studies showed significant improvement in weight gain, increase in height, correct nutritional anemia in preterm and low birth babies. Presently, however, numerous people are looking into the possible therapeutic effects of Spirulina. One local study done in a tertiary hospital in Manila proved that Spirulina powder is efficacious and safe as an adjunct in management of acute non-bloody diarrhea. [11]

To date, there is one local investigation that has been published regarding the use of Spirulina for community acquired pneumonia. The study is a randomized double blind controlled trial done at a tertiary government hospital in Iloilo City. The study determined the efficacy of Spirulina as adjunct therapy among patients with Pneumonia severe. Seventy eight patients 2 months to 5 years old admitted from February to August 2012 were enrolled in the study. Clinical and physiologic parameters measured include severity of cough, fever, fast breathing, chest indrawing, tachycardia, rales, chest x -ray, leukocyte count and hospital stay. Demographic profiles of the two groups were comparable (p>0.050). The result showed a trend towards improvement within 3 days among patients given Spirulina on clinical parameters and physiologic profile compared to placebo. There was a significant drop in temperature on day 2 (p -value 0.038) and significant decrease in mean heart rate on Day 1 (p -value 0.036) and Day 2 (p -value 0.037) among those who were supplemented with Spirulina.

An improvement on the Chest x-ray finding was noted on Day 3 of treatment among Spirulina group (p - value 0.036). The study showed similar hospital stay in both groups. The study recommended a trial of higher dosing of Spirulina to assess significant effect in both clinical and physiologic parameter. [8]

OBJECTIVE

To determine the efficacy of Spirulina as an adjunct therapy in the treatment of PCAP-C in children 6 months to 5 years old admitted in a tertiary government hospital.

SPECIFIC OBJECTIVES

1. To determine the effect of Spirulina among patients with PCAP-C based on the resolution of the following symptoms: fever, respiratory rate, chest in-drawings, rales and oxygen saturation.
2. To determine the duration of hospital stay among patients with PCAP-C given Spirulina as adjunct therapy and those given with placebo.
3. To determine the adverse effect of Spirulina as adjunct therapy in PCAP-C.

OPERATIONAL DEFINITION

A. PRIMARY OUTCOME MEASURE

The primary outcome measured was the effect of Spirulina on patients based on the following parameters:

1. Resolution of tachypnea refers to the hospital day when the patient's respiratory rate per minute decrease or returns to normal.
2. Resolution of chest in drawing refers to the hospital day when the absence of inward movement/ retractions of the chest wall and abdomen was not visible as the child breathes.
3. Resolution of rales refers to the hospital day when absence of crackling sound is not audible on auscultation of the chest area.
4. Resolution of fever refers to the hospital day when normalization of the axillary body temperature (36.5 -37.7 ^{0}C) was recorded through a standard digital thermometer.
5. Normalization of oxygen saturation refers to the hospital day when normalization of oxygen level of the body (95% and above) was recorded with a standard finger pulse oximeter.

B. SECONDARY OUTCOME MEASURE

The duration of hospital stay from the time of admission until the time of discharge of the patient.

C. ADVERSE REACTIONS

Refers to any new signs or symptoms such as appearance of maculo-papular rashes, erythema, itchiness that the patient may manifest during the clinical trial, which was absent prior to admission.

METHODOLOGY

This is a randomized, double-blind control clinical study conducted at a tertiary government hospital.

The subjects enrolled were infants and children after 6 months to 5 years old; with a primary clinical diagnosis of PCAP-C based on the "Philippine Pediatric Society Guidelines in the Diagnosis and Management of Pediatric Community Acquired Pneumonia, 2004" with a clinical, laboratory and radiographic findings suggestive of bacterial pathogen; requiring monotherapy and with written informed consent signed by the parent or caregiver.

The study excluded infants and children with other co-morbid conditions like pulmonary tuberculosis, measles, meningitis, sepsis, those with hemodynamic instability; those patients with completed Hib vaccination; children with severe malnutrition, severe dehydration, with chronic illness and on maintenance medications and supplement. (i.e. Primary Koch's infection, Leukemia, Nephrotic syndrome, among others)

The sample size was computed based on the study of Cadete et al, where in a 63.16% (60% conservative rate) rate of radiologic improvement was noted in Spirulina group vs. 38.50% (30% conservative rate) rate of radiologic improvement in placebo group after three days of treatment. This study required a sample size of 60 per group with 1:1 allocation. The assumed difference of patients' improvement was tested at 80% power and at 95% (0.05α) level of significance.

Patients who met the inclusion criteria were randomized to Spirulina (Group A) or placebo (Group B) based on the randomization list prepared by a statistician. The list was prepared using MS Excel 2013 software, where it generated random numbers as basis for assigning treatment grouping.

The Spirulina and placebo was provided by Pharmaceia Jimenez the drug company that manufactures "Arthrospiraplatensis (CellLife)". It is distributed in 60mg/sachet and 250mg/tablet available in major pharmaceuticals nationwide. Each sachet and tablet contains 100% Arthrospiraplatensis. The recommended drug intake, if used in conjunction with medications, is 60mg/ kg body weight. There are currently no known side effects, drug interactions or contraindications to this drug. The Spirulina and placebo was of the same color, taste and consistency. The Spirulina and placebo was packed in similar disposable plastic sachet.

The research assistant, subjects, research team was not aware of which group is the Spirulina and which the placebo is. A research assistant, who is a Third Year Resident assigned at the ward determined the primary and secondary outcome measure. A research asssitant noted and recorded any adverse effects. Parents were likewise instructed to report any untoward manifestation to the investigator. The principal investigator verifies the accuracy and completeness of the data. Analysis of data was performed to determine the efficacy of Spirulina.

The study was performed in accordance with the Principles in the Declaration of Helsinki. An approval from the Hospital Research Committee and Institutional Review Board was obtained before the implementation of this study. An informed written consent was explained to the parents or caregiver before their inclusion in the study. Complete information on the nature, objectives, benefits and risks related to the study was discussed with the parents or caregiver.

CONDUCT OF THE STUDY

The principal investigator conducted an orientation among the members of the research team. The members of the team were assigned specific duties and responsibilities. The research assistant assigned at the Emergency Department screened and performed a complete history and physical examination to all prospective subjects. The parents or guardians of patients that met the inclusion criteria were oriented on the purpose, benefits and possible risks related to the study. A voluntarily signed informed consent and data information form was secured prior to the study implementation (Appendix A).

The subjects in Group A were given 60mg per kilogram bodyweight of Spirulina three times a day for seven days and subjects in Group B received 60 mg per kilogram bodyweight of placebo three times a day for seven days. The two groups received standard treatment of Ampicillin at 100mg/kg body weight in 4 divided doses until discharged.

The clinical response on both groups were assessed and recorded by the research assistant in the ward every 8 hours based on the following: tachypnea, chest in-drawing, rales, axillary temperature and oxygen saturation until the time the patient is discharged. A standard calibrated digital axillary thermometer and oxygen finger pulse oximeter was used to measure temperature and oxygen saturation,

respectively. Batteries of both thermometer and pulse oximeter were replaced every 10 patients monitored to assure accuracy of temperature and oxygen saturation determination. Adverse reactions were also observed by the research assistant. Patients with marked improvement and positive response to the treatment based on the primary outcome measure was discharged and given oral Amoxicillin 40-50mg/kg in three divided doses as switch therapy based on the recommendation in the "Clinical practice guidelines in the evaluation and management of pediatric community acquired pneumonia, 2004". However, patients who still had presence or worsening signs and symptoms of pneumonia on the third day of treatment was either shifted to another antibiotic or added another antibiotic to the regimen and was considered treatment failure from the study.

The principal investigator collected all the data recorded in the monitoring sheet (Appendix B). Collected data was then analyzed by the statistician. The overall flow of this study is shown in Appendix C.

DATA MANAGEMENT AND STATISTICAL ANALYSIS

Data gathered was encoded in Microsoft EXCEL 2013. Categorical data were expressed in frequency and percentage distribution. Continuous data were presented in mean and standard deviation.

Paired t-test was used to test whether the mean values of continuous variables would significantly change from baseline to post-treatment period. In comparing mean values between the two groups, Z test of mean difference was utilized while Chi square test with 2x2 Fischer exact tests was conducted in comparing categorical data. Any associated p-values lesser than 0.05alpha was considered significant. IBMSPSS ver.21 was used as statistical software in processing the data.

Results

A total of 153 patients met the inclusion criteria. One hundred forty seven of the 153 patients gave an informed consent. Seventy four subjects were randomized to Spirulina Group (Group A) and seventy three subjects were randomized to Placebo Group (Group B). Two (2) of the 74 patients enrolled in Spirulina Group were transferred to the Pediatric Intensive Care Unit (PICU) in less than 24 hours after admission for pneumonia severe. Four (4) patients were considered unimproved after three days and were shifted to a different antibiotic which was completed for seven days. Ten of the 73 patients enrolled in Placebo Group were dropouts. Two (2) patients were transferred to PICU for progression to severe pneumonia, six (6) patients were considered unimproved after three days and was shifted to another antibiotic which was completed for seven days and two (2) patients went home against medical advised.

The data in this study were analyzed as per protocol. As shown in Table 1, there were more males (57%) in the Spirulina Group as compared to Placebo Group (43%). In comparison, there were more females in the Placebo Group (57%) as compared to the Spirulina Group (43%). The differences in rates of dominant gender in both groups were not statistically significant. (p - value 0.097).

It was noted in Table 1 that the mean age in the Spirulina Group is 1.63, in comparison the mean age in the Placebo Group is 2.70. Those in group B were significantly older than in group (p – value 0.01)

Table 1. Comparative Frequency and Percentage Distribution as to Gender and Age in Spirulina Group and Placebo Group as to Gender

Demographics	Spirulina	Placebo	p-value
	n=68	n=63	
Sex			
Females	29 (43%)	36 (57%)	0.097
Males	39 (57%)	27 (43%)	
Age in years			
mean±SD	1.63±1.33	2.70±1.66	<0.010

The respiratory rate was monitored in both study groups every 8 hours. Table 2 showed that in the Spirulina Group the average respiratory rate in the morning of day 1 is 46.59±8.78 cycles per minute. The respiratory rate decrease in the evening to an average of 42.09±8.37 cycles per minute. The average reduction of respiratory rate in the morning of day 2 was 40.57±8.86 cycles per minute; it continued to decrease in the evening with an average of 37.72±8.27 cycles per minute. A steady decline in respiratory rate was noted at day 3 from 35.59±6.40 t0 32.80±4.31cycles per minute.

The respiratory rate continues to decrease until day 5of observation. Analysis indicated that the reduction of average respiratory rate in Spirulina group was statistically significant (p<0.01).

In comparison, participants in the Placebo Group have a decrease in average respiratory rate at 50.62±7.74 cycles per minute at day 1of observation. The respiratory rate decrease further at 42.02±8.50 cycles per minute at day 2 of the study. The respiratory rate of patients variably changes from 37.71±12.28 cycles per minute to 40.75±6.74 cycles per minute from day 3 to day 4 of the study. The changes in respiratory rate of patients in the placebo Group were statistically significant (p<0.001).

Comparative analysis showed that the average respiratory rate of patients in the Spirulina Group was significantly lower than the patients in the Placebo Group at day 1, day 3, and day 4.

Table 2. Comparison of Mean and Standard Deviation of Respiratory Rate between Spirulina Group and Placebo Group at Different Days and Time Intervals

Respira-tory rate	No. of Cases Monitored	SPIRULINA mean±SD	No. of Cases Monitored	PLACEBO mean±SD	p-value
Day 1					
AM	68	46.59±8.78	63	50.62±7.74	0.006
PM	68	43.22±9.54	63	50.05±9.32	<0.010
Evening	68	42.09±8.37	63	46.59±9.08	0.004
Day 2					
AM	68	40.57±8.86	63	42.02±8.5	0.344
PM	68	38.34±8.16	63	41.21±9.41	0.064
Evening	65	37.72±8.27	63	37.52±8.26	0.892
Day 3					
AM	59	35.59±6.4	3	48±0.00	0.001
PM	59	34.49±5.99	21	37.71±12.28	0.121
Evening	44	32.8±4.31	21	38.29±12.67	0.012
Day 4					
AM	12	29±3.77	12	40.75±6.74	<0.010
PM	12	31.25±3.08	9	39±5.27	<0.010
Evening	9	29.33±4.36	9	37.89±2.42	<0.010
Day 5					
AM	3	22±0.00	6	35.83±4.58	0.001
PM	3	19±0.00	3	38±0.00	1.000

Paired t-test mean change; Group A: p<0.01, Group B: p<0.01

The resolution of chest in-drawing was observed in the two groups at different days and time interval. Table 3 showed that in Spirulina group, 96% of patients had chest in-drawing at day 1, 74% had chest in-drawing at day 2, and 9% had chest in-drawing at day 3. The reduction implied that there was resolution of patients' chest in-drawings beginning at day 2 to 3.

In the placebo group, the rate of chest in-drawings was at 100% at day 1, 90% at day 2, 29% at day 3, and 10% day 4. The trends indicated that there was a slow resolution of chest in-drawing among the Placebo Group. Analysis revealed that Spirulina demonstrated better effect in the resolution of chest in-drawings at day 2, 3, and day 4 (p<0.01).

Table 3. Comparative Frequency and Percentage Distribution of Chest in-drawings in Spirulina Group and Placebo Group at Different Days and Time Intervals

Chest in-drawings	SPIRULINA Group A N=68	PLACEBO Group B N=63	p-value
Day 1			
AM	65 (96%)	63 (100%)	0.137
PM	65 (96%)	63 (100%)	0.137
Evening	65 (96%)	56 (89%)	0.289
Day 2			
AM	50 (74%)	57 (90%)	0.010
PM	12 (18%)	39 (62%)	<0.01
Evening	9 (13%)	21 (33%)	0.008
Day 3			
AM	6 (9%)	18 (29%)	0.006
PM	0 (0%)	12 (19%)	<0.01
Evening	6 (9%)	6 (10%)	<0.01
Day 4			
AM	0 (0%)	6 (10%)	0.017
PM	0 (0%)	6 (10%)	0.017
Evening	0 (0%)	0 (0%)	1.000

The auscultation findings at different days among patients in Spirulina Group and Placebo Group are shown in Table 4. There were more patients in Spirulina group with absent rales on day 2 (31% vs. 10%, p-value 0.02), day 3 (35% vs. 33%, p-value 0.039), day 4 (100% vs. 38%, p-value 0.01) and day 5 (100% vs. 62%, p-value 0.01).

Table 4.Comparative Frequency and Percentage Distribution of Auscultation Findings in Spirulina Group and Placebo Group at Different Days of Study

Auscultation Findings Resolution	Spirulina N=68 n (%)	Placebo N=63 n (%)	p-value
Day 1	0 (0%)	0 (0%)	1.000
Day 2	21 (31%)	6 (10%)	0.002
Day 3	24 (35%)	21 (33%)	0.039
Day 4	68 (100%)	24 (38%)	<0.01
Day 5	68 (100%)	39 (62%)	<0.01

A comparative analysis of mean axillary temperature among patients in Spirulina and placebo group is shown in Table 5. There is no significant difference in mean axillary temperatures in both study groups on day 1 (37.87 vs. 38.00, p-value > 0.05α). Further analysis showed a significant difference in mean axillary temperature on day 2 of morning temperature determination (36.97 vs. 37.24, p-value 0.050), day 3 of afternoon temperature determination (36.60 vs. 36.82, p-value 0.013), day 4 of afternoon temperature determination (36.53 vs. 36.23, p-value 0.011) and day 5 of afternoon temperature determination (36.50 vs. 36.13, p-value 0.001). Temperature trends in the two groups showed slight reduction from day 1 to day 4. Despite low average reduction, the changes of temperature in both groups were statistically significant (p-value <0.01).

Table 5.Comparison of Mean and Standard Deviation of Axillary temperature in Spirulina Group and Placebo Group at Different Days and Time Intervals

Axillary Temperature	No. of Cases Monitored	SPIRULINA mean±SD	No. of Cases Monitored	PLACEBO mean±SD	p-value
Day 1					
AM	68	37.87±1.19	63	38±0.94	0.519
PM	68	37.49±1.09	63	37.72±0.77	0.159
Evening	68	37.41±0.88	63	37.47±0.53	0.677
Day 2					
AM	68	36.97±0.72	63	37.24±0.91	0.055
PM	68	37.22±0.98	63	37.18±0.69	0.806
Evening	65	37.07±1.02	63	37.13±0.57	0.702
Day 3					
AM	59	36.58±0.53	60	36.54±0.56	0.667
PM	59	36.6±0.49	60	36.82±0.44	0.013
Evening	41	36.63±0.72	58	36.57±0.58	0.611
Day 4					
AM	12	36.73±0.86	18	36.47±0.37	0.266
PM	12	36.53±0.36	18	36.23±0.23	0.011
Evening	9	36.73±0.48	12	36.45±0.48	0.193
Day 5					
AM	3	36.8±0.00	9	37.27±0.59	0.214
PM	3	36.5±0.00	9	36.13±0.13	0.001
Evening			9	36.17±0.10	1.000
Day 6					
AM	0	-	3	36.3±0.00	1.000
PM	0	-	3	36.7±0.00	1.000

Paired t-test mean change; Group A: p<0.01, Group B: p<0.01

Table 6 outlines the comparative mean oxygen saturation of Spirulina group and placebo group. There is no significant difference in mean oxygen saturation in day 1 at different time intervals (96.17 vs. 96.67, p-value >0.05). Oxygen saturation was noted to be significantly different on day 2 of the afternoon determination (97.82 vs. 97.0, p-value <0.01), day 3 of morning and afternoon determination (98.60 vs. 98.05, p-value <0.05), day 4 of afternoon and evening determination (98.50 vs. 96.86, p-value <0.05) and day 5 of the morning determination (99.00 vs. 98.00, p-value <0.05).

Table 6.Comparison of Mean Oxygen and Standard Deviation of Oxygen Saturation in Spirulina Group and

Oxygen Saturation	No. of Cases Monitored	SPIRULINA mean±SD	No. of Cases Monitored	PLACEBO mean±SD	p-value
Day 1					
AM	68	96.17±1.89	63	96.67±1.37	0.089
PM	68	96.56±1.71	63	96.95±1.95	0.227
evening	68	97±1.57	63	96.9±1.28	0.707
Day 2					
AM	66	97.2±1.53	63	97.48±1.23	0.257
PM	66	97.82±1.02	63	97±1.24	<0.01
evening	63	93.71±19.13	63	97.67±1.85	0.105
Day 3					
AM	57	98.6±0.73	63	98.05±0.79	<0.01
PM	57	98.49±0.76	63	97.86±1.22	0.001
evening	40	98.58±0.5	61	98.31±0.79	0.063
Day 4					
AM	12	98.75±0.45	21	98.43±0.51	0.079
PM	12	98.5±0.9	21	96.86±1.01	<0.01
evening	9	98.67±0.5	12	97.5±0.52	<0.01
Day 5					
AM	3	99±0.00	9	98±0.00	0.001
PM	3	100±0.00	9	97.33±1	1.000
evening	0	-	9	98.67±0.5	
Day 6					
AM	0	-	3	99±0.00	
PM	0	-	3	98±0.00	

Paired t-test mean change; Group A : p<0.01, Group B: p<0.01

As shown in Table 7, the mean hospital stay in Spirulina group (3.09 days) is shorter as compared to the placebo group (4 days). Analysis showed a significant difference in the mean length of hospital stay (p-value 0.02).

Table 7. Comparison of Mean and Standard Deviation of the Length of Hospital stay in Spirulina Group and Placebo Group

Hospitalization Stay in days	SPIRULINA Group A		PLACEBO Group B		p-value
mean (SD)	3.09	±0.67	3.52	±0.86	0.002
Range (min-max)	2	5	3	6	

There were no reported adverse events noted in both study groups during the study period.

DISCUSSION

Pneumonia is one of the leading causes of death globally among children younger than 5 years of age. The incidence of pneumonia and the childhood related deaths from pneumonia is more than 10 fold higher in developing countries than in developed countries.[12] However, in the Philippines, it still remain as one of the leading causes of morbidity and mortality for children younger than five years of age.

At present, there are still no proven additional interventions in the treatment of pneumonia to ensure early recovery from the disease. In this study, Spirulina supplementation among patients six months to five years of age with PCAP-C had significant results in terms of improvement in respiratory rate, chest in-drawing, auscultation findings and length of hospital stay. The significant improvement in the clinical parameter of the patients' in Spirulina group is explained by the presence of an active ingredient called C-phycocyanin that selectively inhibits the cyclooxygenase 2, a critical enzyme in the biosynthesis of prostaglandin. C-phycocyanin could also enhance the immunologic mechanisms of the lung, which include macrophages in the alveoli and bronchioles, secretory IgA and other immunoglobulins that limit the pathogenic organisms of pneumonia.[13]

Review of literature revealed that Spirulina acts as an immune-modulator. The aqueous extract of Spirulina was found to have a major impact on the immune system by increasing the phagocytic activity of macrophage, stimulating the natural killer (NK) cells. It also played a role in the activation and mobilization of T and B cells due to its stimulatory effects in the production of cytokines and antibodies which are likely accountable for the beneficial effects noted in this clinical trial.[13] The present study have demonstrated that Spirulina supplementation in children with PCAP-C resulted in a shorter length of hospital stay.

A shorter hospital stay would decrease the risk of infants and children to acquire health care associated infections. Furthermore, a shorter hospital stay would mean a decreased number of missed school days for the patient and work days for the caregiver.

CONCLUSION

Spirulina supplementation in the treatment of PCAP C at a dose of 60 mg per kilogram per day showed clinical benefits in terms of earlier normalization of respiratory rate, resolution of chest in-drawing, improvement in chest auscultatory findings, a faster reversal of oxygen saturation to normal and ensuing a shorter length of hospital days as compared to placebo.

There were no reported side effects with the use of Spirulina supplementation in this study. This study proves that Spirulina supplementation is beneficial, safe, and effective adjunct in the treatment of PCAP C in infants and children.

RECOMMENDATION

This study provided evidence that Spirulina can be used as an adjunct therapy to infants and children with PCAP C. It is recommended to determine the safety and efficacy of Spirulina as an adjunct therapy in the management infants and children with Pneumonia (PCAP A and B) in an outpatient setting, infants and children with underlying malnutrition and Primary Koch's Infection. A research with bigger sample size is recommended for implementation in the future.

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APPENDIX A

DATA COLLECTION FORM

General data:

Name: _____

Age: _____ **Sex:** _____ **Wt.** _____ **HC:** _____ **CC:** _____ **AC:** _____ **Ht.** _____

Address: _____

Parents/Guardian: _____

Consent: _____ **Date of consent:** _____

Date and time of Admission: _____ **Admitting Diagnosis:** _____

Admitting MD: _____ **Group assignment:** _____

Variables	PCAP-A	PCAP-B	PCAP-C	PCAP-D
Co-morbid illness	None	Y/N	Y/N	Y/N
Compliant caregiver	Y/N	Y/N	Y/N	Y/N
Ability to follow-up	Y/N	Y/N	Y/N	Y/N
Presence of dehydration	Y/N	Y/N	Y/N	Y/N
Ability to feed	Y/N	Y/N	Y/N	Y/N
Age		>11mos	< 11 mos	<11 mos
Respiratory rate 2-12 mos 1-5 yrs >5 yrs	 >50/min >40/min >30/min	 >50/min >40/min >30/min	 >60/min >50/min >35/min	 >70/min >50/min >35/min
Signs of respiratory failure: Retraction Head bobbing Cyanosis Apnea Sensorium	 Y/N Y/N Y/N Y/N Y/N	 Y/N Y/N Y/N Y/N Y/N	 Inter/subcostal Y/N Y/N Y/N Y/N	 Supraclavicular/ intercostal Y/N Y/N Y/N Y/N
Complications (effusions, pneumothorax)	Y/N	Y/N	Y/N	Y/N

APPENDIX B

Name: _____ Age: _____

Date admitted: _____ Date discharged: _____

Daily Patient Assessment Form

Clinical Parameters	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Respiratory rate	AM						
	PM						
	Evening						
Chest in-drawings	AM						
	PM						
	Evening						
Auscultation findings	AM						
	PM						
	Evening						
Axillary temperature	AM						
	PM						
	Evening						
O2 saturation	AM						
	PM						
	Evening						
Adverse reaction							

APPENDIX C

STUDY PROCEDURE FLOW CHART