COLOSTRUM POWDER SUPPLEMENTATION IN THE TREATMENT OF ACUTE WATERY, NON BLOODY DIARRHEA IN CHILDREN 6 MONTHS TO 36 MONTHS OF AGE WITH SOME SIGNS OF DEHYDRATION: A RANDOMIZED DOUBLE BLIND PLACEBO CONTROLLED CLINICAL TRIAL

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OBJECTIVE: To determine the efficacy and safety of colostrum powder supplementation among pediatric patients 6 months to 36 months old with acute watery, non-bloody diarrhea in a Pediatric Ward of a Tertiary Government Hospital

STUDY DESIGN: Randomized, double-blinded, placebo controlled clinical trial

SETTING: Pediatric Ward of a Tertiary Government Hospital

PARTICIPANTS: Eighty subjects 6 months to 36 months old with acute non-bloody diarrhea of six days duration or less, with some signs of dehydration based on WHO-CDD protocol

INTERVENTION: Subjects were randomized to either colostrum powder (Group A) or placebo (Group B)

OUTCOME MEASURES: Efficacy of colostrum powder as treatment to acute watery diarrhea was measured in terms of stool characteristics, frequency and volume and duration of hospital stay.

RESULTS: A total of 80 diarrheal cases 6 months to 36 months of age were enrolled to the study. The two groups were essentially similar in terms of age (P value 0.345) and sex (P value 0.135). Mean age was 12.8 months for Group A and 14.5 months for Group B. The character of the stool was described as either watery, semi-formed and formed stool. The stools significantly differ in the two groups by day 3, 62% of subjects in Group A showed formed stools and 16% in Group B (P value – 0.00003). The volume of the stools was significantly higher in Group B than in Group A at all days of observation (P value 0.0001). Group A had lesser frequent stools on days 1-3. The cumulative rate of discharged was higher in Group A than in Group B starting day 3. On day 5, 92% of patient in Group A was discharged while 69% on Group B. The length of hospital stay was 2.21 days in Group A and 3.21 days in Group B (P value 0.0001).

CONCLUSION: Colostrum powder supplementation in the management of acute diarrhea enabled majority of the subjects in this study to have earlier formed stools and reduce volume of stool, reduce frequency of stooling, earlier discharge and shorter hospital stay. There was no adverse effect reported

KEYWORDS: colostrum, acute watery, non-bloody diarrhea, children, randomized controlled study

INTRODUCTION

Diarrheal disease is one of the leading causes of illness and death among young children in developing countries.[1] Children below 5 years of age are mostly affected with deaths occuring in the first two years of life. [2]

In the Philippines, diarrhea is one of the leading cause of morbidity and mortality for all ages. It is the second leading cause of morbidity among children under five years of age. Death due to acute diarrhea is secondary to severe dehydration which can be prevented with proper management.[3]

Over the past years, several measures at improving the health conditions of children were implemented. Oral rehydration therapy, improved nutrition, breastfeeding and immunization contributed to the reduction in the incidence of mortality and morbidity caused by diarrrhea.[2] Deaths from diarrhea in the first five years of life decline from the previous estimates of 13.6 to 5.6 per 1000 per year in a decade.[4] Based on the 2011 Family Health Survey, the estimated under-five mortality rate (U-5MR) or the probability of a child born on a specified year and dying before reaching the age of five years is lower than the estimated deaths per 1,000 live births compared to the 2006 Family Planning Survey (FPS). Under-five mortality levels in the Philippines continue to improve, falling from 64 deaths per 1,000 live births in 1993 to 40 deaths in 2003.[5] This reflects progress at improving the health conditions of children.

The management of diarrhea is primarily supportive and is directed at preventing or treating dehydration. Several measures were implemented to decrease the number of cases. There has been much interest on the use of probiotics, zinc and folic acid supplementation in modifying diseases of the gastrointestinal tract.[6,7] Recently, the use of bovine colostrum as adjunct in the management of diarrheal disorder is receiving attention among child health workers. However, the efficacy of bovine colostrum as supplement in the management of diarrhea is based on testimonials, anecdotal reports and the marketing efforts of its manufacturers and distributors.

The nutritional value of milk is undisputed. Bovine colostrum (BC) is the “early” milk produced by cows during the first several days post-parturition. This “early” milk has a nutrient profile and immunological composition that differs substantially from “mature” milk. In addition to macronutrients found in milk, BC contains oligosaccharides, growth factors, antimicrobial compounds, and immune-regulating constituents either not present in milk or present in substantially lower concentrations.[8] Bovine colostrum is proven to be the most efficacious as it contains much higher levels of Immunoglobulin-G (IgG) than human colostrum (which predominantly contains IgA) and because it is produced in large volumes by cows above and beyond what their calves require.[9]

Preliminary evidence suggests that bovine colostrum might help prevent and

and possibly treat infectious diarrhea. A double-blind, placebo-controlled trial of 80 children with rotavirus diarrhea found that hyperimmune colostrum had significantly less daily total stool output and stool frequency compared to children who received placebo (p value <0.05). The clearance of Rota virus was also earlier in hyperimmune bovine colostrum group (p value <0.001). There were no adverse effects noted in the study.[10]

A double-blind trial done by Mitra, et.al showed similar results. Patients who received bovine colostrum had shorter duration of diarrhea compared to the control (p value <0.001). They have greater reduction in stool output (p value <0.04) with no untoward effects noted in either groups.[11]

In a multi-center study by Rump, et. al., immunodeficient patients with chronic diarrhea were treated with oral Lactobin Immunoglobulin (LIG), an immunoglobulin from bovine colostrum. Among 29 patients, 21 gave good results leading to transient (10 days) or long-lasting (more than 4 weeks) normalisation of the stool frequency. The mean daily stool frequency decreased from 7.4 to 2.2. Intestinal cryptosporidiosis disappeared in 5 patients. [12]

Twenty-five HIV-positive patients suffering from chronic diarrhea were given colostrums bovine colostrum. Participants had negative stool cultures for microbial pathogens with the exception of Cryptosporidium. Seven were positive for Cryptosporidia and 18 were negative for diarrhea-causing organisms. In the 18 subjects with negative stool culture, complete remission of diarrhea occurred in seven cases (39%) and a reduction of 50 percent or more in frequency of diarrhea occurred in an additional four cases (22%). In the persons with positive stool culture for Cryptosporidia, three experienced complete remission and two had partial remission. Stool frequency in the seven cases decreased from an average of 9.4 to 3.7 daily by the end of the 10-day intervention.[13]

The therapeutic effect of bovine milk IgG antibody showed clinical importance demonstrated in a few studies. It is therefore of interest to conduct further study to determine its clinical usefulness among pediatric patients.

The result of this study will give us insights on the use of bovine colostrum as adjunct treatment to acute watery diarrhea to improve the health conditions of Filipino children. This study will provide pediatricians an option to give their patients the bovine colostrum as a safe and accessible adjunct in the treatment of diarrhea. If proven effective and safe, the drug will lessen the number of hospital stay of patients thus days absence from work of parents and relatives resulting to lesser expense, not to forget the ease of psychological burden from illness and hospitalization. The result of the study can guide the health policy makers to come up with an option to improve the treatment of diarrhea in order to achieve the Millennium Development Goal of Reduction in Child Mortality by 2015.

This study was conceptualized with

the following objective: to determine the efficacy and safety of colostrums powder supplementation among pediatric patients 6 months to 36 months old with acute watery, non-bloody diarrhea with some signs of dehydration admitted in a Tertiary Government Hospital. It further aims to compare the effects of colostrum powder supplementation versus the placebo as to: character of stools; volume of stools; frequency of stool passage; duration of hospital stay; and to determine the adverse effect of colostrum powder supplementation.

METHODS AND PROCEDURE

The study is a randomized, double-blind placebo controlled clinical trial conducted at the Pediatric Ward of a Tertiary Government Hospital.

The subjects were screened for the inclusion and exclusion criteria through interview of parents and guardians and physical examination of the patients. The study population included children 12 months to 36 months old with acute watery, non bloody diarrhea of six days duration or less; with some signs of dehydration based on WHO-CDD protocol. Excluded in the study were children with diarrhea of more than six days duration; with severe dehydration; bloody diarrhea; severe malnutrition; history of allergy to milk; history of seizure; postoperative and immunocompromised patient; intake of antidiarrheal medication and stool analysis positive for helminths, amoeaba and occult blood.

Children with informed consent were included in the list of the participants. A minimum of 80 subjects were sampled based on the following assumption: 95 % Confidence level; 80 % Power; SD of 2 and a Difference of 2 days duration of diarrhea based on the study of Martinez, et. al.[8] The formula to determine the sample size for 2 groups comparing means is based on the distribution function of a standardized normal deviate by Julious SA.[15]

$$n = \frac{(z \times 1\text{-}\beta)^2 \times 2 \times SD2}{(d')^2}$$

$$n = \frac{(1.96 \times .84)^2 \times 2 \times SD2}{(2)^2}$$

n = total sample size

z = the standard normal deviate, set at 1.96

Power = 1 - = Probability of rejecting the null hypothesis when it is false

SD = Standard deviation

d' = difference between two samples

Subjects were randomized to two treatment groups. Group A were given colostrum powder, Group B were given placebo powder.

The colostrums powder was commercially available in the market. Its important components are 1.5% Lactoferrin (42mg), 25% Immunoglobulins (720 mg IG) and 3% Proline-Rich Polypeptides (87 mg PRP) per regular daily serving of 3 grams. The colostrums

Powder was repacked into 10 grams per pack which is the recommended daily dose in times of illness or stress. The placebo had the same appearance, color and taste as the colosturm powder. It was kept in a sachet similar to the test drug. The test drug and the placebo was repackaged and prepared, respectively by the Derpartment of Industrial Pharmacy, University of the Philippines, Manila.

Random allocation of the subjects to one of the two treatment groups was done using pre-drawn block random assignment. The randomization list was prepared using letters A and B. Six 4-letter combinations (which serve as blocks) was made using these 2 letters which include ABAB, ABBA, AABB, BABA, BAAB, and BBAA. These 6 combinations were the basis for treatment assignment through substitution with the corresponding number generated from random numbers. The predrawn treatment assignments were placed in a sealed envelope.

The study was done according to the Principles in the Declaration of Helsinki. Parents of the children were informed about the nature, procedures, benefits and risks related to the study. An informed consent was obtained for their inclusion. The study was approved by the Ethics Review Committee prior to its implementation.

CONDUCT OF THE STUDY

A research orientation was conducted by the principal investigator among the members of the research team prior to the start of the study. An assistant investigator did the baseline history and physical examination upon admission. He classified the degree of dehydration according to the WHO/CDD assessment of dehydration **(Appendix A)**. Parents of the subject were informed about the purpose, benefits, and risks related to the study **(Appendix B)**. Patient informed consent were obtained prior to their inclusion **(Appendix C)**. Patient who fulfilled the criteria, was randomly assigned to either group A (intravenous fluid and Colostrum powder) or Group B (intravenous fluid and placebo powder).

A randomnization list was prepared using letter A for Group A; and letters B for Group B. A total of six (6) combinations of the two (2) letters in random order was formed and was written on separate sheets of paper properly sealed (Appendix D). Each random order has an equal chance of being drawn and assigned to each group.

Group A and group B children were given intravenous fluid of D5 0.3 NaCl at 3050cc/kg per 8 hours as deficit therapy. Replacement as maintenance therapy was instituted accordingly. Group A children were given 10g of Colostrum powder dissolved in 20 ml water, given for four days based on the study done by Sarker et al. Group B children were given 10g of placebo powder dissolved in 20 ml water, given for four days. The placebo is of the same appearance, color and taste. It was kept in a container similar to that of Colostrum powder.

An assistant investigator who was blinded of the study evaluated the duration of patient's diarrhea, frequency of stool passage, volume and character of stool (Appendix E). Adverse reactions were also observed by the investigators (Appendix F). A nurse unknowleadegable of the study objective and treatment assignment administered the Colostrum powder and the placebo. Figure 1 outlines the study procedure.

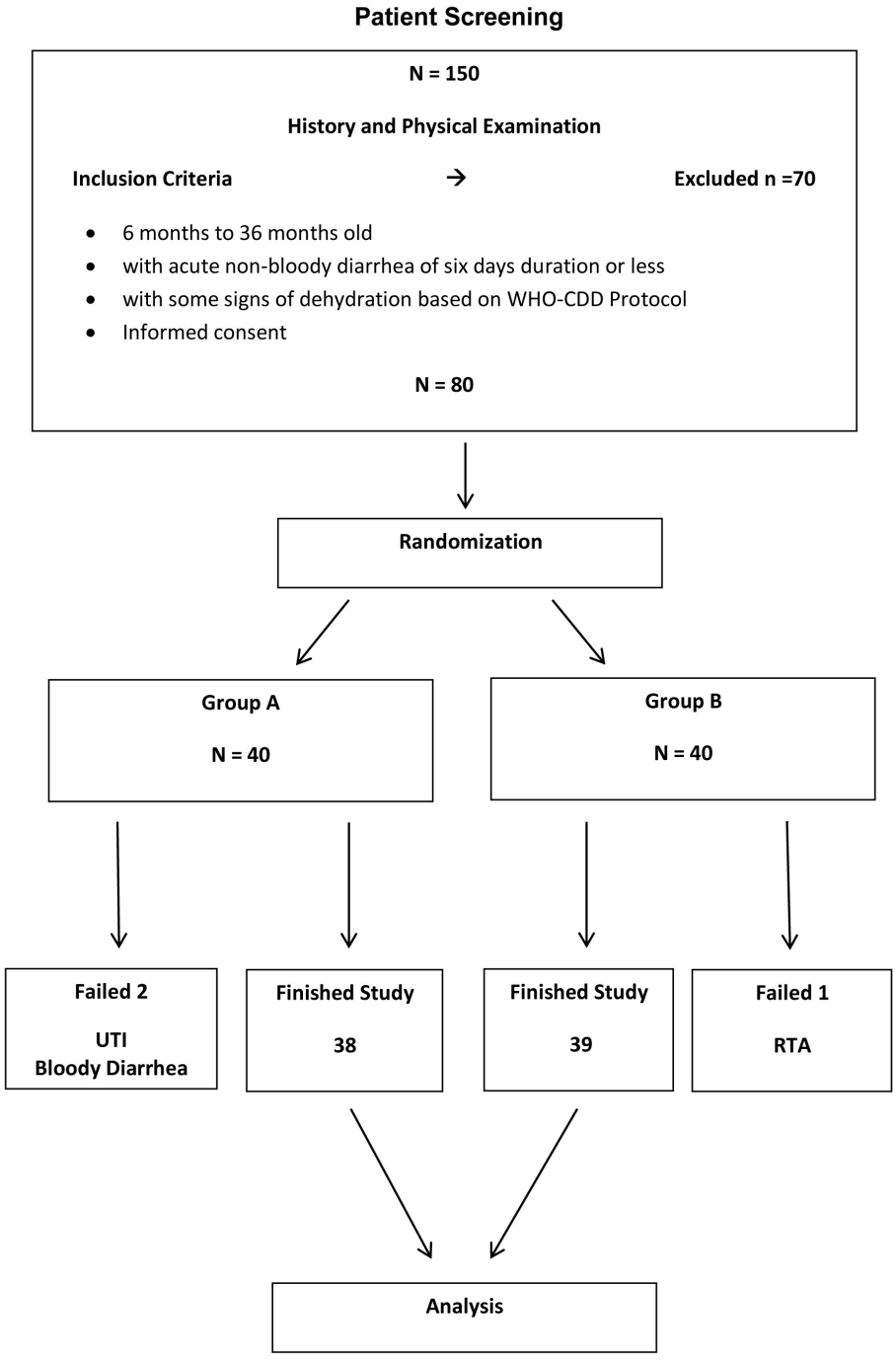

Figure 1: Flow Chart of Study Procedure

DEFINITION OF TERMS

Acute Diarrhea - the passage of loose or watery stools, at least three times in 24 hours period for less than 7 days[16]

Colostrum - the first mammary secretion that a mammal provides for its newborn in the first 24-48 hours of life. It contains numerous immune modulators, growth factors as well as essential nutrients.[9]

Colostrum powder - commercial preparations come which from cows that contain its immune proteins in dry form.

Some Dehydration - degree of dehydration with 5-10% water loss. Patient may present with restlessness or irritability, has sunken eyes, drinks eagerly and skin pinch goes back very slowly[16]

Tolerability - the ability of the subject to ingest a substance without vomiting, nausea and abdominal pain[17]

MEASURES OF OUTCOME

The study outcome measure determined the character, frequency and volume of stool and duration of hospital stay.

The character of stool was determined as follows:

a. Liquid stool - predominantly water.
b. Semi-formed/semi-liquid stool - composed of both liquid and semi liquid stool
c. Formed stool - solid stool

The frequency of the stool was noted and recorded every 8 hours. Mean frequency of stool between treatment group by hospital day was computed.

The volume of stool was weighed and recorded in grams by weighing the diaper before and after each use. A weighing scale (Silvano Brand) was used during the duration of the study. It was calibrated every morning.

Duration of hospital stay is computed as the length of hospital stay of patient in treatment group A and B.

Cumulative rate of discharged is computed to compare the proportion of discharges between two groups.

DATA ANALYSIS

Means and standard deviations, frequency counts and percentage were used to describe the data. T-test for independent samples was used to compare continuous variables and chi-square and Fischer's exact test for categorical variables. Odds ratio were computed. A 95% confidence level or P value of < 0.05 was considered significant. Minitab version 16 was used as statistical software.

RESULTS

A total of 80 patients 6 months to 36 months of age qualified to the inclusion criteria. All patients gave consent and were randomized to either treatment Group A,

Colostrum Powder and treatment Group B, Placebo powder. There were two dropouts in the treatment Group A, one had UTI started on IV antibiotics and one developed bloody diarrhea.

The two groups did not significantly differ in terms of age (P value 0.345) and sex (P value 0.135). The mean age was 12.8 months for Group A and 14.5 months for Group B. (See Table I)

TABLE I. AGE AND SEX DISTRIBUTION OF STUDY PARTICIPANTS OF TREATMENT GROUP A (COLOSTRUM) AND TREATMENT GROUP B (PLACEBO)

	Treatment Group A	Treatment Group B	P Value
Age, Mean + SD	12.8 + 7.5	14.5 + 8.1	0.345
Sex			0.135
Male	8	15	
Female	3024		

The character of the stool was compared between the two treatment groups. It was described as either watery, semiformed, and formed stool (Table 2). On day 1, all subjects in the two groups had liquid stools. On day 2, the proportion of subjects with formed stools was significantly higher in treatment Group A (16%) than in treatment Group B (2.5%). On day 3 of observation, there was no patient in treatment Group A with liquid stool as compared with 12 (31%) patients in treatment Group B. Twenty three (61%)patients in treatment Group A already had formed stools, and 10 (26%) subjects in treatment Group B. There was a significant difference in character of stool between two treatment group on day 3 (p value <0.005).

TABLE II. COMPARATIVE FREQUENCY AND PERCENTAGE DISTRIBUTION OF STOOL CHARACTER BETWEEN TREATMENT GROUP A AND TREATMENT GROUP B BY HOSPITAL DAYS

	Treatment Group A	Treatment Group B	P Value
Day 1	N %	N %	1.00
1 - Liquid	38	39	
2 - Semiformed	0	0	
3 - Formed	0	0	
Day 2			0.0098
1 - Liquid	14 (37%)	30 (77%)	
2 - Semiformed	18 (47%)	8 (21%)	
3 - Formed	6 (16%)	1 (2.5%)	
Day 3			0.00003
1 - Liquid	0	12 (31%)	
2 - Semiformed	9 (24%)	16 (41%)	
3 - Formed	23 (61%)	10 (26%)	
Discharged	6 (16%)	1 (2.5%)	
Day 4			0.728
1 - Liquid	0	4 (10%)	
2 - Semiformed	3 (8%)	8 (21%)	
3 - Formed	6 (16%)	6 (41%)	
Discharged	29 (76)	6 (41%)	
Day 5			1.00
1 - Liquid	0	0	
2 - Semiformed	1 (2.6%)	6 (15%)	
3 - Formed	2 (5.3%)	6 (15%)	
Discharged	35 (92%)	27 (69%)	

We did the comparative analysis of the volume of the stool measured in grams between treatment group A and treatment group B. The volume of stool was significantly higher in treatment Group B than in treatment Group A at all days of observation with P values of <0.0001 (Table 3). Shown in figure 2 is a comparative figure of volume of stool in grams by hospital days.

TABLE III: COMPARISON OF VOLUME OF STOOL IN GRAMS, MEAN + SD BETWEEN TREATMENT GROUP A AND TREATMENT GROUP B BY HOSPITAL DAYS

	Treatment Group A	Treatment Group B	P Value
Day 1	N = 38	N = 39	0.0001
	428.1 + 200.7	578.3 + 159.1	
Day 2	N = 38	N = 39	<0.0001
	198.6 + 102.7	390.4 + 147.4	
Day 3	N = 32	N = 38	
	138.7 + 84.2	293.8 + 133.0	<0.0001
Day 4	N = 9	N = 28	
	137 + 60.3	241.1 + 111.1	

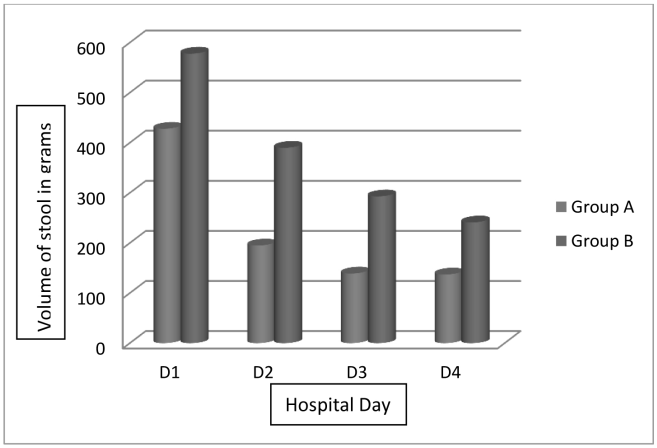

Figure 2. Comparison of Volume of Stools in grams Between Treatment Group A and Group B by hospital days

A comparative analysis of frequency of stool between treatment group A and treatment group B by hospital day is reported as mean and standard deviation in table IV. The result showed that treatment Group B had more frequent stools than treatment Group A from days 1 to 3 of observation. There is a significant difference in mean frequency of stool between two treatment groups with a P value of <0.0002.

TABLE IV: COMPARISON OF STOOL FREQUENCY, MEAN + SD BETWEEN TREATMENT GROUP A AND TREATMENT GROUP B BY HOSPITAL DAYS

Variable	Treatment Group A	Treatment Group B	P Value
Day 1	N = 38	N = 39	0.0008
	2.92 ± 1.3	3.97 ± 1.33	
Day 2	N = 38	N = 39	0.0001
	1.50 + 1.2	2.66 + 1.1	
Day 3	N = 38	N = 39	
	1.22 + 0.444	2.18 + 0.945	<0.0002

The cumulative rate of discharge between the two treatment groups was also compared (see table V and figure 3). It showed that starting at day 3, the cumulative Rate of discharge was significantly higher in Group A than in Group B. At day 5 of the study, 35 (92%) patients in Group A were already discharged compared to 27 (69%) patients in Group B (p value <0.005).

TABLE V. CUMULATIVE RATE OF DISCHARGE BETWEEN TREATMENT GROUP A AND TREATMENT GROUP B

	Treatment Group A	Treatment Group B	P Value
D1	0	0	<0.0001
D2	0	0	
D3	6 (16%)	1 (3%)	
D4	29 (76%)	11 (28%)	
D5	35 (92%)	27 (69%)	
D6	38 (100%)	33 (87%)	
D7		37 (95%)	

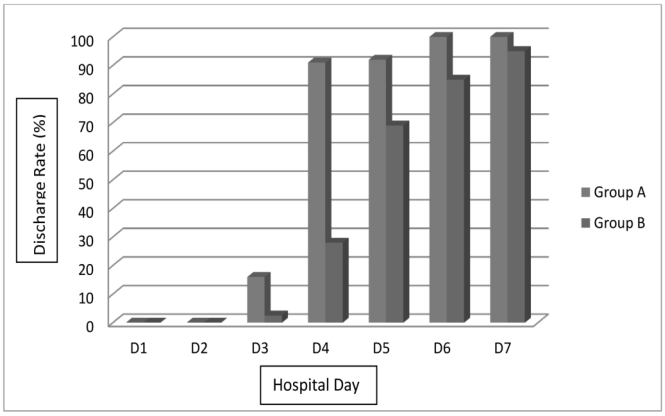

Figure 3. Cumulative Rate of Discharge in Percent Between Treatment Group A and Treatment Group B by Hospital Days

Table VI and figure 4 outline the comparative length of hospital stay between treatment group A and treatment group B. The mean length of hospital stay in treatment Group A was 2.21 days. It is shorter as compared to treatment Group B with a mean hospital stay of 3.21 days. The P value was <0.0001 which is statistically significant.

TABLE VI. COMPARATIVE LENGTH OF HOSPITAL STAY BETWEEN TREATMENT GROUP A AND TREATMENT GROUP B

	Treatment Group A	Treatment Group B	P Value
Length of Hospital stay			
Mean + SD	2.21 + 0.875	3.21 + 1.17	<0.0001
			95% confidence interval of the difference between means -0.994 + 0.468 Or from 0.53 to 1.4 Days

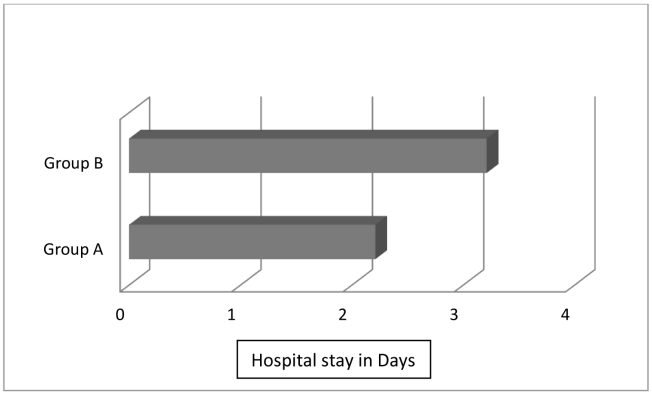

Figure 4. Comparative Length of Hospital Stay in Days Between Treatment Group A and Treatment Group B

There is no adverse reaction noted in both study group.

DISCUSSION

This study conducted among children with acute watery non-bloody diarrhea with some signs of dehydration aim to evaluate the clinical efficacy of orally administered

bovine colostrum. The result of the study has demonstrated a positive effect in the treatment of acute watery, non-bloody diarrhea. The children who received bovine colostrum had lower stool volume similar to the studies done by Sarker et al[11] and Mitra et al[12]. Reduction in stool frequency was also consistent with the study done by Sarker, et al[11]. Although Mitra et al[12] was able to come up with the findings of a shorter duration of diarrhea, it can be deduced from this study that the duration of diarrhea was shorter based on the result of shorter hospital stay.

Although the results of this study are consistent with the findings of Mitra et al and Sarker et al, there were certain important differences to be considered. The study populations in the two studies were confirmed cases of rotavirus diarrhea and used hyperimmune bovine colostrum preparation from immunized cows of human rotavirus. In contrast, the present study was conducted in children with acute watery, non -bloody diarrhea of unspecified cause and was given standard colostrum containing immunoglobulins, lactoferrin, and proline-rich polypetides as the major components. The success of bovine colostrum in this study could be attributed to its major components.

Some studies have focused in the use of colostrum to treat diarrhea, specifically on the advantages of bovine colostrum as an efficient medium in the process of passive immunity in immunocompetent patients.[13,14] Rump et al[13] and Plettenberg et al,[14] studies are also in agreement with the findings in this study in terms of reduction in stool frequency in patients with chronic diarrhea using the standard colostrum preparation.

A noteworthy finding of this study is an earlier formed stool which was not measured in the previous researches.

The clinical benefits of bovine colostrum might be attributed to the presence of intrinsic growth factors and immune factors. Growth factors in bovine colostrum reduce gastrointestinal damage during diarrheal episodes by stimulating cell and tissue growth and are capable of increasing T-cell production. Broad-spectrum antimicrobial factors such as lactoferrin that may have a beneficial effect on the health of the intestinal mucosa by modulating cytokine release which is an important event in immune response.[16,17,18] Immumoglobulins, which are the most abundant immune factors found in colostrum, neutralizes toxins and microbes in the lymph and circulatory system, destroys bacteria and are highly antiviral. Proline-Rich Polypeptide (PRP) regulates the thymus gland, stimulating an underactive immune system or down regulating an overactive immune system. They fuction as signaling peptides produced by activated macrophages and activated T-cells that control the production of all cytokines. Other colostrum components include lysozymes, cytokines, trypsin, lymphokines, orotic acid, oligopolysacharides and conjugates. They also act as agents to boost the immune system. Oligopolysaccharides and glycoconjugates attract and bind to pathogens preventing them from attaching or entering the mucous membranes.[19, 20, 21, 22]

CONCLUSION

Colostrum powder supplementation in the management of children 6 months to 36 months of age with acute watery, non-bloody diarrhea with some dehydration resulted to an: earlier formed stool on day 2 (p value <0.005) and day 3 (p value <0.005); a lower volume of stool at all days of observation (p value <0.005); a higher cumulative rate of discharge (p value <0.001) and shorter mean length of stay (2.21 + 0.875 days), p value 0.001. There was no associated adverse effect noted in all children given colostrum powder.

This study concludes that colostrum powder supplementation given at 10 grams daily for 4 days among children with acute watery, non-bloody diarrhea is effective, safe and can shorten hospital stay.

RECOMMENDATION

In this study, the effectiveness and safety of colostrum powder supplement was assessed during the duration of the participant's hospital stay. It is then recommended that study participants be evaluated and followed up at home and at the out-patient department.

Further studies be conducted on the effectiveness of colostrum powder supplementation in the management of chronic diarrhea and intestinal parasitism.

APPENDIX A

Assessment of Diarrhea patients for Dehydration Based on WHO/CDD Protocol

	No Signs of Dehydration	Some Dehydration	Severe Dehydration
CONDITION	Well, alert	Restless, irritable	Lethargic or unconscious
EYES	Normal	Sunken	Sunken
THIRST	Drinks normally, not thirsty	Thirsty, drinks eagerly	Drinks poorly, or not able to drink
FEEL Skin Pinch	Goes back slowly	Goes back slowly	Goes back very slowly

APPENDIX B

Letter to Parents

Minamahal na mga magulang,

Ako po si _____, isang residente sa Departamento ng Pediatrics, Quirino Memorial Medical Center. Nagsasagawa ako ng pag-aaral na "Colostrum Powder Supplement in the Treatment on Acute Watery Diarrhea in Children 12 months to 36 months: a Double Blind, Randomnized Controlled Trial." Nais kong malaman sa pag-aaral na ito kung ang mga batang bibigyan ng colostrum supplement ay mas mapapadali ang paggaling kumpara sa mga batang walang colostrum supplement.

Ang pagsali sa programang ito ay libre at walang makukuhang pinansyal na bayad. Bilang mga magulang o taga-pag-alaga, gusto kong ipaalam na magiging bahagi ang inyong anak sa programang ito. Maaaring ang inyong anak ay makakatanggap ng colostrum supplement at maari rin naming hindi. Ang pagpili ng kung sino ang bibigyan ay random na parang pagbunot sa tambiolo.

Magpapapirma ako ng "informed consent" sa inyo bilang patunay na kayo ay sumasang-ayon sa pagsali ng inyong anak sa programa.

Maraming salamat po.

Gumagalang,

Tagapagsaliksik

APPENDIX C

Katibayan sa Pagpayag

Ako _____ nasa hustong gulang, may asawa, at kasalukuyang naninirahan sa _____ay nagpapatunay na:

1. Ako ang magulang/ tagapagsubaybay ni _____ .

2. Lubos na napaliwanagan tungkol sa kahalagahan at pakay ng pag- aaral na may kinalaman sa epekto ng "colostrum powder" sa ikabibilis at ikadadali ng paggaling sa sakit na "gastroenteritis" ("pagtatae"). Pati na ang pagsusuri at pamamaraan na kinakailangang gawin. Ako ay sumasang ayon na maisama ang aking anak sa pag aaral na ito.

3. Ang aking anak ay lubos na nasuri at napag alamang may saki na gastroenteritis ("pagtatae") at walang kaakibat na ibang karamdaman.

4. Ako ay nangangako na magbibigay ng lubos na partisipasyon sa pagtatala ng karakter at dami ng dumi ng aking anak sa loob ng tatlo hanggang limang araw (3-5).

5. Alam ko na ang aking anak ay bibigyan ng "colostrum powder" 10g, isang beses (1) sa isang araw, sa loob ng apat na araw (4) na walang kapalit na halaga.

6. Ako ay bibigyan ng kasiguraduhan na lahat ng resulta ng pag-aaral na ito at mananatiling lihim at konpidensyal, na ako ay maaring tumiwalag sa pag aaral na ito sa anumang oras aking naisin.

7. Ako ay may karapatang magtanong ng mga bagay-bagay na may kinalaman sa pag-aaral na ito at ako ay nabigyan ng kasagutan na nagbigay liwanag sa aking kaisipan.

8. Ako ay nabigyan ng kopya ng katibayan na ito.

_____ _____

Magulang/ Tagapagsubaybay Petsa

APPENDIX D

Randomization Table

1	A	B	A	B
2	A	B	B	A
3	A	A	B	B
4	B	A	B	A
5	B	A	A	B
6	B	B	A	A

APPENDIX E

Patient Data Form

Name of Patient_____ Age/Sex_____

Date/Time	Character of Stools	Volume of Stools	Frequency of Stools

APPENDIX F

Adverse Reaction Checklist

Name of Patient_____ Age:_____

Date	Vomiting	Abdominal pain	Hypersensitivity reaction	Others

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