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Efficacy and safety of probiotics in neonatal hyperbilirubinemia: Randomized controlled trial

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Abstract

Introduction

There have been many studies evaluating the role of probiotics in the management of necrotizing enterocolitis (NEC), yet few studies related to the role of probiotics in the management of neonatal jaundice. The purpose of this study was to determine the efficacy and safety of utilizing probiotics in the management of neonatal hyperbilirubinemia.

Methods

This study was a single blinded randomized clinical trial conducted on 2–28 day old term and near-term infants (35–42 weeks gestational age) that were hospitalized with neonatal jaundice in Bandar Abbas, Iran in 2016. The primary outcome of this study was to evaluate the duration of hospitalization in neonates with neonatal jaundice. Secondary outcomes were to determine the percentage of infants who needed phototherapy on the 2nd, 3rd, 4th, and 5th days of admission.

Data were analyzed by SPSS software and descriptive statistics and Chi-square and independent samples *t*-test.

Results

One hundred and twenty-six (126) breastfed infants were enrolled in this study and randomly assigned to one of two groups. The non-probiotic group included 61 (48.4%) patients and the probiotic group included 65 (51.6%) patients. Duration of hospitalization was 3.10 ± 0.569 days in the non-probiotic group versus 3 ± 0.901 in the probiotic group ($p = 0.469$). The percentage of patients discharged in the probiotic group was significantly higher in comparison to the non-probiotic group on the 3rd day of admission ($p = 0.008$) and Discharged early. The percentage of patients discharged were similar between the two groups on the 2nd, 4th, and 5th days of admission ($p > 0.05$).

Conclusion

Probiotics are not effective in lowering the duration of phototherapy in infants with hyperbilirubinemia. Although probiotics can increase the rate of discharge on the 3rd day of admission in infants with neonatal hyperbilirubinemia, the rate of hospital discharge was not different in the probiotic and non-probiotic groups on the 2nd, 4 th, and 5 th days of admission. ClinicalTrials.gov Identifier: NCT03266913.

Introduction

Bilirubin is a substance that is produced by breaking down red blood cells, which is taken up by the liver and is digested by enzymes in the liver and then secreted in the urine or the stool. These enzymes may have a slow or insufficient function in newborns to help eliminate bilirubin, resulting in jaundice (Weng et al., 2016; Tomerak et al., 2016; Yu et al., 2015). It is characterized by yellowing of the skin and sclera of the infant, which is usually physiologic and does not require treatment, but can be pathologic and abnormally high in the blood, and can lead to kernicterus in the infant (Yang et al., 2015; Wu et al., 2015; Shapiro et al., 2017). Indirect Hyperbilirubinemia (jaundice) is a common phenomenon in preterm infants. In these infants, the path to conjugation has not evolved. Also, the later onset of feeding in these

infants has led to a decrease in intestinal flow and a decrease in bacterial colonization in the intestine, which has led to an increase in the enterohepatic bilirubin cycle, all of which are major causes of hyperbilirubinemia in preterm infants.

Neonatal Jaundice occurs in 60% of term infants and 80% of premature infants (Al-Omran et al., 2017). Although it is transient, it is associated with a high rate of readmission of patients in the first week of infancy (Al-Omran et al., 2017; Seidman et al., 1995). It is important to note that neonatal jaundice is one of the conditions requiring special attention in pediatric medicine and neonatal medicine because although in most infants it is a physiological phenomenon, it may increase significantly in some infants and it can cause neurological complications and brain damage caused by the deposition of bilirubin in the brain and the creation of kernicterus (Bernstein and Landing, 1962; Bhutani et al., 2005). Severe hyperbilirubinemia is one of the most common causes of newborn hospitalization. Despite the many efforts that have been made to identify newborns at high risk of jaundice before hospital discharge, recent increases in early discharge and increased breast-feeding have led to an increase in neonatal jaundice and kernicterus. Probiotic is a living microorganism that has beneficial effects in the treatment and prevention of certain pathological conditions. Probiotics can reduce the intestinal transit time and improve the quality of intestinal wall contraction and increase the amount of mitosis in enterocytes, as well as decrease the enterohepatic cycle in addition to other benefits in infants (Zhang et al., 2017; Thomas et al., 2017; Uberos et al., 2017; Xiao et al., 2017; Strunk et al., 2017; Thukral and Sankar, 2017).

In a study in 2013, it was shown that Saccharomyces boulardii is safe and effective in very low birth weight infants with hyperbilirubinemia in lowering the duration of phototherapy and improving nutrition tolerance (Demirel et al., 2013). Serce et al. (2015) have shown that Saccharomyces boulardii can not decrease the duration of phototherapy and level of bilirubin in patients with neonatal hyperbilirubinemia.

Another study by Suganthi et al., in 2016 have reported statistically significantly lower bilirubin levels in infants with hyperbilirubinemia treated with Saccharomyces boulardii in comparison to placebo. They reported that usage of Saccharomyces boulardii has no side effects in these patients (Suganthi and Das, 2016).

The main goal of this trial was to see if probiotics might reduce the duration of time hospitalization for newborn hyperbilirubinemia. The study's secondary goals were to assess the efficacy of probiotics on the percentages of patients discharged from the hospital on the second, third, fourth, and fifth days of their hospitalization. In addition, we looked at the drug's adverse effects in two groups.

Section snippets

Study design and setting

This study is a prospective single-blinded randomized controlled trial which was carried out at the Children's Hospital in 2016 in Bandar Abbas in Iran, which lasted from April 2016 up to the end of the completion of the sample.

Study population, sampling, and sample size

A total of 126 infants 2–28 days old with neonatal jaundice with a gestational age of 35–42 weeks who were hospitalized at Bandar Abbas Children Hospital from April 2016 are the statistical population of this study.

Inclusion criteria

The inclusion criteria of the study included the

Demographic information and baseline characteristics

In this study, we enrolled 126 breastfed infants. The patients were randomly assigned into two groups. We included 61 (48.4%) patients in no probiotic group and 65 (51.6%) in probiotic group.

Table 1 summarizes the baseline characteristics of the study population in two groups.

Main study results

The primary outcome of the study was a duration of hospitalization. Duration of hospitalization was 3.10 ± 0.569 days in non-probiotic group versus 3 ± 0.901 in probiotic group (p = 0.469). The difference was not

Discussion

Neonatal jaundice is one of the common causes of infant admission and readmission in the first days of life. The main treatment for hospitalized neonates is phototherapy however, some studies have suggested alternative therapies for these patients. Among these treatments are the use of probiotics. Several studies have examined the role of Saccharomyces boulardii in the treatment of neonatal jaundice (Demirel et al., 2013; Serce et al., 2015; Suganthi and Das, 2016). Because the results of these

Authors' contributions

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

Declaration of competing interest

There is no conflict of interest to be declared.

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