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The effectiveness of pleuran in treatment of acute gastroenteritis in children- a randomised, placebo-controlled, double-blind trial

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu w dyscyplinie nauki medyczne

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Summary

The effectiveness of pleuran in treatment of acute gastroenteritis in children- a randomised, placebo-controlled, double-blind trial

The present thesis comprises three publications on the use of β-glucans in the treatment of acute infectious diarrhoea in children.

Acute gastroenteritis (AGE) is a significant global health concern, representing one of the foremost causes of morbidity and mortality in paediatric population. While oral and intravenous rehydration have proven effective in reducing mortality associated with AGE, they do not address the progression of the disease itself. Consequently, there is an urgent need for new therapeutic strategies that can not only alleviate symptoms, but also impact the course of the illness. In this context, pleuran, a β-(1,3/1,6)-D-glucan, has been selected as a potential therapeutic agent for diarrhoea. Pleuran belongs to β-glucans, a group of high-molecular-weight polysaccharides found in various natural sources such as fungi, bacteria, and cereals, which have demonstrated a range of beneficial effects, including immunomodulatory properties. Pleuran is recognized for its immunomodulatory properties, which have been shown to enhance the body's natural immune response. It is also known to present a strong safety profile. Previous studies have demonstrated its efficacy in treating viral and bacterial infections. Notwithstanding its extensive range of beneficial effects, the effectiveness of pleuran in the treatment of AGE has not yet been investigated. Presented series of articles aims to evaluate the anti-infective activity of β-glucans, basing on pleuran in gastrointestinal infections in children.

The initial publication was a scoping review on anti- infective properties of β-glucans in children. We summarized the current literature on the topic focusing exclusively on clinical trials. We used the PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses, Extension for Scoping Reviews) to prepare the review. We performed an electronic search of PubMed, Embase, and Cochrane databases up to May 2021, identifying 6,232 relevant studies, of which twelve were ultimately included in the analysis. The type of preparation, doses and study designs varied between studies, which was the reason for summarizing results in design of scoping review instead of systematic review. Ten out of twelve trials demonstrated the effectiveness of β-glucans in reducing the incidence of respiratory tract infections or alleviating symptoms of upper respiratory tract infections. Ten out of twelve studies have reported a good tolerance and safety profile.

We concluded that good tolerance of β-glucans shows a favourable benefit-risk ratio of this type of intervention in the treatment of acute respiratory infections in children. Although it is known that β-glucans primarily act by stimulating the immune system within the gut-associated lymphoid tissue, previous studies have not evaluated their effectiveness in the treatment of acute gastrointestinal infections in children. Our literature review not only identified this important research gap but also supported determining the appropriate dose of β-glucan used in our study.

The second manuscript is a protocol for a study that aimed to evaluate the efficacy of pleuran in reducing the duration and symptoms of diarrhoea. The present study has been designed as a fully blinded, placebo-controlled, randomised clinical trial. The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT checklist) was used when writing the protocol. Before recruitment, the trial was registered in the Clinical Trials database. The study group comprised children aged between 2 and 10 years who presented to the hospital with diarrhoea lasting between 24 and 72 hours. Children eligible for the study were randomised to the active treatment group, which received the pleuran preparation, and the placebo group, which received a placebo preparation. All participants received daily study preparation until the diarrhoea subsided. The primary endpoint was defined as the duration of diarrhoea, measured from the onset to the normalization of stool consistency and frequency. The study's recruitment started in June 2018 and was completed in December 2022. Due to the unsatisfactory pace of patient recruitment, the study protocol was modified three times during the course of the trial. The changes included expanding the age range of eligible participants from the original 2–6 years to 2–10 years, as well as adding two additional recruitment centres. Each modification was approved by the Bioethics Committee of the Medical University of Warsaw.

The results of this study were presented in the third manuscript. The study was reported in accordance with the CONSORT Statement. We have enrolled 27 children, who were randomly assigned to either the experimental group (Group A, 13 patients) or the control group (Group B, 14 patients). One patient was excluded from the analysis due to a loss of contact with caregiver. The study assessed the duration of diarrhoea, intravenous rehydration, hospitalization, and symptoms improvement but did not find any significant differences in clinical outcomes between the two groups. One mild adverse event (rash) was reported in the experimental group. We demonstrated that pleuran was ineffective in shortening the duration of AGE and alleviating its symptoms in a paediatric population.

To the best of our knowledge, this was the first and only randomised controlled trial (RCT) to evaluate the efficacy of pleuran or other β-glucans in the treatment of acute gastroenteritis in children. The strength of this trial lies in its randomised, fully blinded, placebo-controlled design. The implementation of both the SPIRIT Checklist and the CONSORT Statement ensured the correct methodology of study commencement and result reporting. The stratified randomisation process was utilised to ensure an equal distribution of children with shorter and longer durations of diarrhoea between the experimental and control groups. Despite the small sample size, this study serves as a pilot for future research. Based on our experience and existing literature, we have identified key areas for future research on the management of acute gastroenteritis.