

Probiotics for the prevention of pediatric antibiotic – associated Diarrhea (AAD)

Khoa Dịch vụ 3

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Background

- A balance of more than 400 species of bacteria in the human gut is important for normal gastrointestinal function.
- Antibiotic treatment may disturb gastrointestinal flora -> a range of symptoms, most notably, diarrhea.
- The incidence of diarrhea in children receiving broad spectrum antibiotics is 11% - 40%.

- Probiotics are microorganisms intended to have a health benefit when consumed
- Probiotics: improve microbial balance in the intestinal tract and display both antibacterial and immune regulatory effects in humans
- Probiotics commonly administered in RCTs of ADD are: Bacillus spp., Bifidobacterium spp., Lactobacilli spp., Lactococcus spp., Leuconostoc cremoris, Saccharomyces spp., Streptococcus spp. alone or in combination

Clinical questions

1. Do probiotics co-administered with antibiotic reduce the incidence of AAD ?
2. Is there any adverse event of probiotics when co-administered with antibiotics ?
3. Which probiotic strain(s) and dose(s) are more efficacious in preventing AAD?
4. Do probiotics co-administered with antibiotics (any agent) reduce the duration of AAD?
5. Do probiotics co-administered with antibiotics (any agent) reduce the daily stool frequent?

1. Do probiotics co-administered with antibiotic reduce the incidence of AAD in children ?

- a) *M-A of 6 RCTs (n = 766) (J.Pediatr 2006)* : treatment with probiotics compared with placebo reduced the risk of AAD 28,5% → 11,9%, (RR 0,44, 95% CI 0,25 - 0,77) → NNT 7, 95% CI 5-10.
- b) *M-A of 15/16 RCTs (n = 2874) (Cochrane 2011)* : incidence of AAD in the probiotic gr. 9%, control gr. 18% (RR 0,52 95% CI 0,38-0,72).
- c) *M-A of 16/82 RCTs (JAMA 2012)*: probiotics reduced the incidence of AAD by 45% (RR 0,55; 95% CI 0,38-0,80) → NNT 11

2. Is there any adverse event of probiotics when co-administered with antibiotics in children?

- a.** *M-A of 11/16 RCTs (n=1583) (Cochrane 2011) : NO statistically significant differences in the incidence of adverse events (RD 0,00; 95% CI -0,01 - 0,02).*
- b.** *M-A of 6 RCTs (766 participants)(J.Pediatr 2006): no adverse effects due to the use of probiotics were observed.*
- c.** *M-A of 23/82 RCTs (JAMA 2012): no adverse effect*

3. Which probiotic strain(s) and dose(s) are more efficacious in preventing AAD?

Cochrane 2011

- a. M-A of 4 RCTs used *L. rhamnosus* alone (n=611): statistically significant indicating a protective effect (RR 0,35; 95% CI 0,22-0,56 I₂=0%).
- b. M-A of 3 RCTs used the yeast *S. boulardii* (n=1328) was not statistically significant (RR 0,45; 95% CI 0,14-1,48, I₂=88%).

J. Pediatric 2006

- a. M-A 2 RCTs Lactobacillus GG (n=307): were statistically significant indicating a protective effect (RR 0,3; 95% CI 0,15-0,6)
- b. 1 RCT Saccharomyces boulardii (n=246) : were statistically significant indicating a protective effect (RR 0,2; 95% CI 0,07-0,6)
- c. 1 RCT B. lactic & Streptococcus thermophilus (n=157): statistically significant indicating a protective effect (RR 0,5; 95% CI 0,3-0,95)

JAMA 2012 :

- M-A 17 RCTs used Lactobacillus alone:
36% decreased risk of ADD
(RR 0,64; 95%CI 0,47-0,86)
 - M-A 15 RCTs used Saccharomyces alone
52% decreased risk of AAD
(RR 0,48; 95% CI 0,35-0,65)
- >Indirect comparisons between the studies did not find a significant difference in the risk of AAD based upon the specific organism used

Dose of probiotic

Cochrane 2011

- 7 RCTs providing children with 5-40 billion CFU/yeast per day: incident of AAD in the probiotic gr. 8% control gr. 22% (RR 0,40; 95% CI 0,29-0,55; $I^2 = 29\%$)
 - 7 RCTs providing children <5 billion CFU/yeast per day: incident of AAD in the probiotic gr. 8% control gr. 11% (RR 0,8; 95% CI 0,53-1,21; $I^2 = 36\%$)
- > effect is based on dose (≥ 5 billion CFU/day), the number needed to treat to prevent 1 case of diarrhea is seven (NNT 7 95% CI 6-10)

4. Do probiotics (any specified strain or dose) co-administered with antibiotics (any agent) reduce the duration of AAD?

Cochrane 2011

M-A of 5 RCTs (n=897): probiotics decreased the mean duration of ADD by almost three quarters of a day , a statistically significant difference (WMD -0,60; 95% CI -1,18 – 0,02)

5. Do probiotics (any specified strain or dose) co-administered with antibiotics (any agent) reduce the daily stool frequency ?

Cochrane 2011

M-A of 4 RCTs (n=425) : differences were not statistically significant (WMD -0,30; 95% CI -0,06 – 0,00)

Conclusion

- The overall evidence suggests a protective effect of probiotics in preventing AAD.
- The subgroup effect based on dose (≥ 5 billion CFU/day): based on high-dose probiotic \rightarrow NNT 7; 95% CI 6-10
- More trials are also needed to evaluate the efficacy of other probiotic strains, the optimal dose of the probiotic preparation and safety of probiotics