EFFECT OF USE OF PROBIOTICS DURING ANTIBIOTHERAPY
A COMPARATIVE STUDY BETWEEN DANISH AND PORTUGUESE POPULATIONS

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INTRODUCTION

Antibiotic-associated diarrhea (AAD) is a type of diarrhea that occurs in association with an antibiotic treatment and with no other apparent cause,(1–3) due to acute disturbance of normal gut flora.(4,5) During treatment with antibiotics, 5-39% of patients experience diarrhea, up to 12 weeks after treatment,(1,3) depending on the type of the antibiotic,(6,7) and it is also associated with old age.(3,5) The broad spectrum antibiotics are the ones that most often cause diarrhea, such as clindamycin, cephalosporins, penicillins (penicillin resistant beta-lactamase, aminopenicillins) and quinolones. (1,3,5,8) About 15-39% of cases of AAD are caused by *C. difficile,*(1,3,9) and the symptoms can be mild or result in colitis, toxic megacolon and even high mortality.(7,9)
Diarrhea is defined by World Health Organization (WHO, 2015) as "the passage of 3 or more loose or liquid stools per day, or more frequently than is normal for the individual".(10) Some antibiotics cause increased intestinal motility leading to diarrhea.(1) AAD is mostly caused by the breakdown of the commensal intestinal flora.(1) This leads to the disruption and manifestation of osmotic or secretory diarrhea by changing the short fatty acid, carbohydrate and bile acid metabolism. These changes impair the resistance to colonization by intestinal pathogens, facilitating its emergence.(1,3)
According the report of a joint Food and Agriculture Organization (FAO)/WHO Expert Consultation on evaluation of health and nutritional properties of probiotics in food including powder with live lactic acid bacteria defined probiotics as “live microorganisms which when administered in adequate amounts confer a health benefit on the host".(11) Its administration must be made together with the antibiotic and not after diarrhea have triggered.(2) The results of a meta-analysis study suggest that the intake of probiotics together with the antibiotic reduces the risk of AAD.(12)
Despite there are many studies, the potential of probiotics is not yet known and their efficacy has not yet fully proven. The AAD is still unclear and the development of this study is an important mean to enlighten some gaps, proving the efficacy of probiotics in this situation. Moreover, there are no studies conducted in Portugal on the subject, or at a community level.

AIM

To characterize the incidence of antibiotic associated diarrhea (AAD) and evaluate the effect of probiotics in gastrointestinal disorders among to samples from Denmark (DK) and Portugal (PT) consumers.

METHODS

Study design - A prospective cross-sectional and observational study was conducted on both populations. Data were collected by questionnaire in PT and by interview in DK from patients to whom had been prescribed antibiotics. Personal and therapeutic profile of each patient was drawn as well as the use of probiotics. The prevalence of diarrhea was surveyed post-treatment.

Study population - the target population included patients to whom antibiotics were prescribed, regardless of concurrently intake of probiotics, in two community pharmacies in Portugal and one in Denmark, by a non probabilistic approache. The main inclusion criteria included people who were prescribed antibiotics and who accepted to participate in the study, regardless of the age. The study excluded ones who experienced episodes of diarrhea, by the time they started the antibiotic treatment, as well as those who declined to participate.

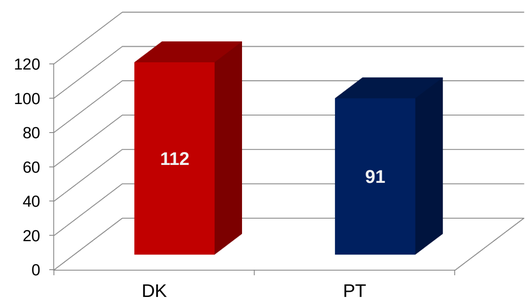
Denmark	Portugal
V-Penincilin	Amoxicilin-clavulanic acid
Roxithromycin	Azithromicin
Amoxicillin-clavulanic acid	Levofloxacin

Table 1 – Top 3 antibiotics used in the study. Denmark *vs* Portugal

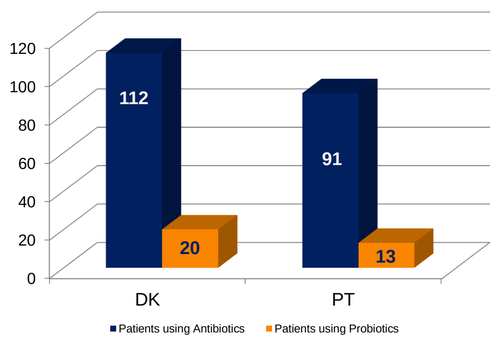
RESULTS

A total of 91 antibiotics consumers were surveyed, from February to March 2015 in PT and in DK, 121 consumers were surveyed from January to March 2014. In PT, 19,2% and in DK, 11,5% of respondents had experienced AAD during the treatment and the use of probiotics in Portugal (16,7%) and in and Denmark (15,7%). Most used antibiotics were amoxicilin-clavulanic acid, azithromicin and levofloxacin (PT) and v-penincilin, roxithromycin and amoxicillin-clavulanic acid (DK). In 91% of cases of patients who took probiotics did not occur diarrhea.

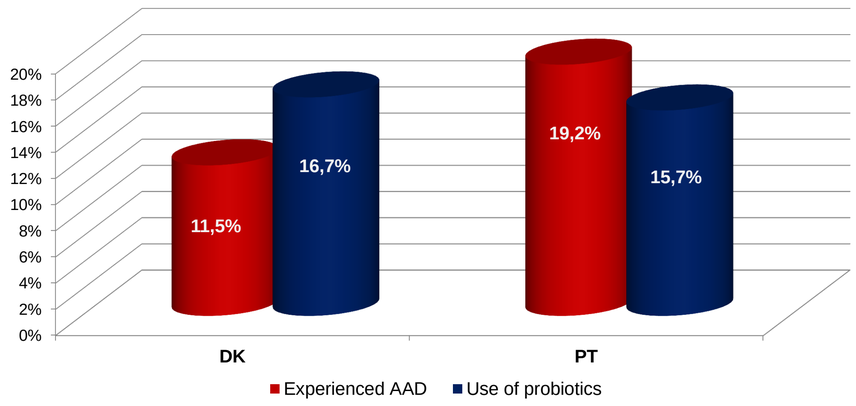
Graphic 1 – Sample size – patients usin antibiotics



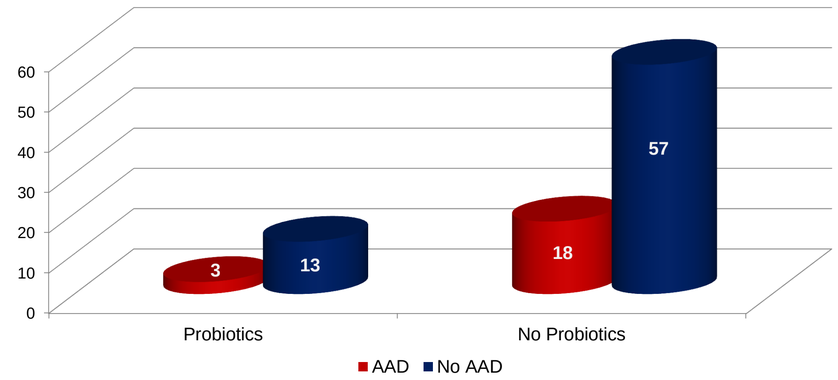
Graphic 2 – Consumption of ATB and Probiotcis



Graphic 3 – Experience AAD vs Use of probiotics



Graphic 4 – Relation between the consumption of the probiotics and incicence of diarrhea



DISCUSSION

Through the descriptive analysis it was found that the incidence of diarrhea was higher in the group that did not take probiotic than the one that took it. From the obtained results, it is clear that probiotics have a positive influence in the expression of AAD, and prevented the onset of AAD: only 5 out of 40 patients (12,5%) who took probiotic expressed diarrhea during antibiotic treatment and none showed diarrhea after treatment. Those not taking probiotic had a higher incidence of AAD during treatment (16,6%, n=27) and were the only ones who expressed diarrhea after treatment.
In both populations the incidence of diarrhea decreases with the probiotic usage. The incidence of the diarrhea is ore evident when broad spectrum antibiotics were used. All cases of the concomitant diarrhea with the usage of probiotic were mentioned by patients using broad spectrum of antibiotics.
Due to the small number of questionnaires that have been achieved and the lack of homogeneity of the sample, with more people who not took the probiotic than those who take, was not possible to make statistical analysis tests. As far as we know, this is the first study regarding the influence of probiotics in AAD at a community level, while most studies are performed in hospital setting or a study every strain is done individually. There is not much knowledge about probiotics and studies of marketed formulations are important for excipients that can influence the action of probiotic.

CONCLUSION

In general, the objectives were fulfilled and it was concluded that probiotics prevent AAD when administered during antibiotic therapy in any age group, and reduces the incidence and severity of diarrhea. Diarrhea had a higher prevalence among respondents who did not take probiotics during treatment, and after treatment did not occur in those taking probiotics. Gender was shown to have some influence on the incidence of diarrhea. It was found that knowledge about probiotics is very little and that may have influence on the adherence to its use. Uncertain factors remains as the term "loose stool" that can be perceived differently by patients. In order to make the results statistically significant, it is necessary to conduct a new study, or a continuation of the same, for a longer period of collection. It is also necessary that the number of respondents who take probiotic is equivalent to those who not take it.

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