

Antibiotic prophylaxis of Diarrhoea in Athletes

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Abstract

With the improved fitness and conditioning of athletes, the most common reason for an athlete to miss training or competing whilst abroad is illness.

Traveller's diarrhoea (TD) is one of the most common illnesses with athletes potentially unable to compete at all and/or perform at sub-optimal level following infection for several days

One of the most effective antibiotic prophylaxis group for TD is the fluoroquinolones but due to the potential risk of tendon damage with long-term use of these, athletes have taken probiotics, bovine colostrum, and practiced avoidance measures such as alcohol hand gel, as well as good food hygiene, to pre-vent attacks of TD instead of a prophylactic antibiotic. Rifaxamin, due to its poor bioavailability (and thus non-systemic absorption) has been proposed as a prophylaxis for TD. This study examines the effectiveness of Rifaxamin in elite athletes travelling to areas of high risk for TD.

Statistics for TD were available in England Hockey athletes at The Hockey World Cup and The Commonwealth Games in 2010 in Delhi, India when athletes took no antibiotic prophylaxis but staff did. The same athlete group then travelled to South Africa and Malaysia, this time taking Rifaxamin as prophylaxis.

When no antibiotics were taken the incidence of TD was significantly higher in the group than when antibiotic prophylaxis was taken. Furthermore, there were no reported cases of tendon damage after taking *Rifaxamin*.

The results show that taking oral *Rifaxamin* as an antibiotic prophylaxis may be an effective addition in the prevention of TD in athletes.

INTRODUCTION

Travellers' diarrhoea (TD) is the most predictable travel-related illness ranging from 30-70%, depending on the destination. People can still contract TD despite reasonably good hygiene. Bacterial pathogens are the most common cause of TD (80-90%) with intestinal viruses accounting for 5-8% and Protozoa around 10%, but they manifest later.¹

Enterotoxigenic *E Coli* is the most common pathogen, followed by *Campylobacter jejuni*, *Shigella* and *Salmonella*. Of the viruses, Norovirus, rotavirus and astrovirus have been isolated. Giardia is the main protozoal pathogen. High-risk areas of TD include most of Asia, the Middle East, Africa, Mexico and Central and South America.

Bouts of TD do not prevent against future attacks and more than one episode of TD can occur in a single trip. Bacterial diarrhoea presents with the sudden onset of mild to moderate abdominal cramps, loose stools, fever, vomiting and possibly bloody diarrhoea. Untreated bacterial diarrhoea can last 3-5 days or longer (viral 2-3 days and protozoa weeks to months).

Several approaches can reduce (but not eliminate) TD:

- Food and beverage selection (avoid unwashed food, salads washed in nonpotable water, ice creams, undercooked meat, seafood and unpeeled fruit and vegetables)
- Drinking bottled water only
- Probiotics (*Lactobacillus* and *Saccharomyces boulardii*)
- Bovine colostrum (no good trial evidence)

Prophylactic antibiotics are effective and have been shown in controlled trials to reduce TD from 40% to 4%. However, resistance has occurred and so Trimethoprim-sulfamethoxazole and Doxycycline are no longer considered effective.¹

The fluoroquinolones (*Ciprofloxacin*) have been the most effective both for prophylaxis and treatment of TD (except *Campylobacter*)[1,3]. However, in the athletic population there is a *theoretical* risk of tendon rupture with this class of drug. As such, only non-athletes have used Ciprofloxacin as prophylaxis. The majority of tendon ruptures appear to take place in the

Achilles tendon (between 1991 and 2002 the 90-day

cumulative risk of Achilles tendon rupture was 17.7/100,000 in Ciprofloxacin users compared to 5/100,000 in the normal population).² The majority of patients were over 60 years old and either on corticosteroids or with renal or other chronic diseases. Even though the overall risk is very low, elite athletes have been reluctant to take *Ciprofloxacin* as a prophylactic drug although there have been no published cases of tendon rupture during or after taking oral *Ciprofloxacin* in elite athletes.

Rifaxamin has been proposed as a prophylaxis in elite athletes.^{3,4}

Rifaxamin is a semi-synthetic antibiotic based on *Rifamycin*. It has poor bioavailability and is therefore poorly systemically absorbed thus acting locally in the intestine. As such, it has few side effects and a very low risk of tendon rupture due to its non-systemic absorption. It has been licensed in the USA since 1998 for the treatment of TD and is has been licensed in the UK since 2011 for the same indication.

To date, there have been very few studies on the prophylactic use of *Rifaxamin* to prevent TD. One study observed adult US travellers to Mexico and found a 58% protection against TD when taking oral *Rifaxamin* compared to placebo.⁵ There has also been one small study in elite athletes (USA athletes in Beijing 2008) taking oral *Rifaxamin* as prophylaxis, which had very encouraging results but the numbers were very small (106 patients received *Rifaximin*).⁵

Antibiotic Prophylaxis of TD in GB Hockey Athletes

With the improved fitness and conditioning of athletes, the most common reason for an athlete to miss training or competing, whilst abroad, is illness. Traveller's diarrhoea is the most common illness with an athlete potentially unable to compete for up to 3 days and after that not performing at optimum level for several more days.

Due to the potential risk of tendon damage with long-term use of *Ciprofloxacin*, athletes have taken probiotics, bovine colostrum and use alcohol hand gel, as well as employing good food hygiene to pre-vent attacks of TD. They do not take a prophylactic antibiotic.

METHODS

World Cup - Delhi 2010

In 2010, Delhi hosted the men's Hockey World Cup. The athletes were at risk of TD, not only from food but unclean water in the showers and on the pitch (which was watered with unclean water). As the players regularly dive on the pitch they were at risk of ingesting the water.

The athletes used the following to reduce the risk of TD:

- Bottled water to drink and brush teeth
- Alcohol hand gel to use before and after meals and after training/playing
- Washing of gum shields with bottled water prior to insertion into the mouth
- Good food hygiene (avoidance of unwashed and unpeeled fruit and vegetables, salads, ice cream and ice for drinks, as well as only eating in hotels and "safe"/clean restaurants)
- Daily probiotic capsule

Of the 18 athletes, none took a prophylactic antibiotic. Seven members of staff received a daily dose of 250 mg *Ciprofloxacin* as prophylaxis.

If anyone (athlete or staff) had symptoms and signs of TD, they were isolated and treated with 500 mg *Ciprofloxacin* twice daily for 2 days and fluid support with Dioralyte.

RESULTS (TABLE 1)

Over a 3 week period in Delhi, eight athletes contracted TD, missing an average of 2 days from training or competing. All were treated with oral *Ciprofloxacin* for 2 days and recovered well with no side effects from the medication (including tendon damage either immediately or weeks later).

Of the seven staff, all took prophylactic antibiotics and only one contracted TD.

Commonwealth Games - Delhi 2010

The Games were held in the same venue as the men's World Cup although the athletes and staff stayed in the athletes' village for the majority of the time rather than in a hotel. A total of 38 athletes and 14 members of staff applied the same preventative measures. All staff were offered a daily antibiotic prophylaxis with a daily dose of 250 mg *Ciprofloxacin*. All the female staff took a daily antibiotic. However two of the male members of staff declined.

RESULTS (TABLE 1)

Over a 3 week period, amongst the 20 male athletes there were ten cases of TD and two cases in 18 female athletes. An average of 2 days were missed from training or competing.

Amongst the 14 members of staff, 12 were taking *Ciprofloxacin* prophylaxis. Of these, three developed TD (two on no prophylaxis and one taking *Ciprofloxacin*).

TABLE 1

Venue			Number	No taking <i>Ciprofloxacin</i> Prophylaxis	No of TD Cases	Av Days missed from Training
World Cup. Delhi	Athletes	Male	18	0	(44%)	2
	Staff		7	7	(14%)	n/a
Commonwealth Games, Delhi	Athletes	Male	20	0	10 (50%)	2
		Female	18	0	(11%)	2
	Staff	Male team	7	5	(43%)	n/a
		Female team	7	7	100%	n/a

DISCUSSION

The results from the Commonwealth Games and World Cup clearly demonstrate that *Ciprofloxacin* is a good prophylaxis against TD but due to the risk of tendon damage, athletes are unwilling to take it. It could be speculated that women might have better hand hygiene than men and therefore have less risk of TD due to less risk of contamination with pathogens. The female athletes arrived in India 5 days later than the males and did not stay in a hotel prior to going to the athletes' village. Additionally, females dive on the pitch less than males and so are less likely to ingest contaminated water, which increases the risk of developing TD.

Future Study

As mentioned, there has been one small study on the use of *Rifaxamin* in athletes.⁴ Due to its non-systemic absorption, it is considered safe for athletes to take and therefore further studies were conducted with the same group of male athletes that participated in the Hockey World Cup and Commonwealth Games.

Background

The men's Champions Trophy competition was due to be held in the same venue as the previous tournaments. Unfortunately, due to political reasons, the venue was changed to New Zealand, which was not considered to be a high-risk area for TD. However, the men's squad travelled to Malaysia for 2 weeks and South Africa for 3 weeks. Both of these venues have had high numbers of TD recorded on previous trips, leading to prolonged player and staff absence at times of competition. Therefore, it was decided to use these venues to study the effectiveness of *Rifaxamin* in the prophylaxis of TD.

Methodology

The first trip was to South Africa with 27 athletes and 10 staff for 3 weeks. All individuals were asked to give informed consent to taking the medication (daily dose of 200 mg *Rifaxamin*) - see Appendix 1. Athletes and staff followed normal non-medication preventative advice.

In Malaysia, there were 18 athletes and 10 staff. Again, all athletes gave informed consent to take the antibiotic.

RESULTS (TABLE 2)

South Africa

All 27 athletes and staff took *Rifaxamin* 200 mg daily for the duration of the trip. Two members of staff stopped taking it due to side effects. One stopped after one dose due to nausea and one stopped after

four doses due to multiple side effects, including nausea, vomiting, dizziness and abdominal pain, which all resolved after cessation of medication.

There were no recorded cases of TD through the whole duration in either staff or athletes. There were also no recorded side effects amongst the athletes during the trip. There were also no recorded cases of tendon damage or rupture 6 months after stopping the medication.

Malaysia

All 18 athletes took a daily dose of *Rifaxamin*. Of the ten staff members, six took prophylaxis. The two members of staff who suffered side effects in South Africa declined and two new members of staff declined to take prophylaxis. One of those chose to administer a daily probiotic instead.

Amongst the athletes, there was one episode of TD (treated with oral Azithromycin and fluid management) and amongst the staff, there were no recorded cases of TD. After 4 months, there were

TABLE 2

Venue			Number	Number taking prophylactic Rifaxamin	Number withdrawn due to side effects	TD Cases	Av days missed training	Cases of Tendon Rupture
Malaysia	Athletes	Male	27	27	0	0	0	0
	Staff		10	10	2	0	0	0
South Africa	Athletes	Male	18	18	0	1	2	0
	Staff		10	6	0	0	n/a	0

no cases of tendon rupture or damage amongst athletes or staff.

Discussion

Whilst in Delhi, both for the Hockey World Cup and Commonwealth Games, there were a significant number of cases of TD, amongst players and staff, which had an impact on player numbers both in training and competition. Although it would have been a better control to have gone back to the same venue, it is clear from the results that the introduction of prophylactic *Rifaxamin* has helped produce a significant reduction in the number of cases of TD when visiting areas which historically have had a significant number of cases of TD. The antibiotic was generally well tolerated (with only two individuals suffering enough side effects to stop taking it) and, to date, there have been no cases of tendon rupture, which has been the worry when taking oral *Ciprofloxacin*.

CONCLUSION

Although, the results would have been validated by the withdrawal of probiotics taken by some athletes at the same time and by visiting the same venue, the results still suggest that oral *Rifaxamin* should be considered as a useful prophylaxis against TD for elite athletes visiting high risk areas and therefore reduce the crucial number of days missed for training or competing. However, other non-antibiotic measures should still be used in conjunction, including good food and water hygiene and alcohol hand gels. The use of oral probiotics and bovine colostrum still needs further evaluation.

What Are The New Findings?

- Illness, rather than injury, is now the most common reason for Hockey athletes to miss training and/or competing
- *Rifaxamin* may be a safe antibiotic prophylaxis for athletes in the prevention of TD
- *Ciprofloxacin*, as an antibiotic prophylaxis for TD, is still declined by athletes due to the very small risk of tendon rupture

How might it impact on clinical practice in the near future?

- When travelling abroad with athletes to countries of high risk of TD, *Rifaxamin* is a useful addition as prophylaxis
- *Rifaxamin* should be taken with other measures to prevent TD

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Competing Interests

The supplies of *Rifaximin* were provided by NORGINE Pharmaceuticals Limited.

References:

- 1 Connor B A. Yellow Book CDC.Travellers' Diarrhoea. Chapter 2: The Pre-travel consultation, Self-Treatable conditions: 2012: <http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-2-the-pre-travel-consultation/travelers-diarrhea.htm>
- 2 Sode J, Obel N, Hallas J et al. Use of fluroquinolones and risk of Achilles tendon rupture: a population-based cohort study. *Eur J Clin Pharmacol* 2007; **63(5)**: 499-503.
- 3 Tillet E, Loosemoore M. Setting standards for the prevention and management of travellers' diarrhoea in elite athletes: an audit of one team during the Youth Commonwealth Games in India. *Br J Sports Med* 2009; **43(13)**: 1045-1048
- 4 Khan K. E-letter: Rifaximin for the Prevention of Travellers' Diarrhoea in Elite Athletes <http://blogs.bmj.com/bjbm/2010/03/11/e-letter-rifaximin-for-the-prevention-of-travellers-diarrhoea-in-elite-athletes/> Accessed 18 December 2012.
- 5 Matinez-Sandoval F et al. Prevention of travelers' diarrhoea in US Travellers to Mexico. *J Travel Med* 2010; **17(2)**: 111-117.