Food Control 24 (2012) 6–14

Contents lists available at SciVerse ScienceDirect

Food Control

journal homepage: www.elsevier.com/locate/foodcont

Review

Alternative strategies to use antibiotics or chemical products for controlling *Campylobacter* in the food chain

M. Ganan[b], J.M. Silván[a], A.V. Carrascosa[a], A.J. Martínez-Rodríguez[a,*]

[a] Instituto de Investigación en Ciencias de la Alimentación (CIAL), CSIC-UAM, Nicolás Cabrera, 9 - Campus de la Universidad Autónoma de Madrid, 28049 Madrid, Spain
[b] Instituto de Fermentaciones Industriales (CSIC), Juan de la Cierva, 3, 28006 Madrid, Spain

ARTICLE INFO

Article history:
Received 27 January 2011
Received in revised form
26 May 2011
Accepted 19 September 2011

Keywords:
Campylobacter
Food safety
Food control
Natural compounds
Chicken

ABSTRACT

Campylobacteriosis is considered the most frequent zoonosis in humans, and the handling and/or consumption of poultry meat is considered the main source for human infection. The reduction of the rates of infection in chickens should make an effective contribution to substantially controlling the illness in humans. However, the increase of the general concern about the spreading of antibiotic resistance in humans has determined the elimination of antibiotics as growth promoters in livestock. At this point, it is essential to search for new, natural and sustainable strategies to reduce the incidence of this bacterium in the food chain, especially in its main host. The objective of this review is to revise the different strategies, designed to reduce the presence or to eradicate *Campylobacter* from the human food chain.

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1. Introduction

Campylobacter is considered to be the most important causal pathogen of food-borne gastrointestinal illnesses worldwide, with poultry, and especially chicken, being the main source of infection in humans (Lee & Newell, 2006). Since a large proportion of the European Union (EU) chicken production is contaminated with the pathogen (EFSA, 2010a) and given the recent ban by the European Union on the use of antibiotics in animal feed to promote growth (European Commission, 2003), it is essential to search for new, natural and sustainable strategies to reduce the incidence of his bacteria in the food chain, especially in its main host.

Colonisation of chicken's gastrointestinal tract by *Campylobacter* first entails its adherence to the mucous membrane lining the intestine, followed by adherence to the intestinal epithelial cells. After this specific and irreversible adherence, in the final step the bacteria invade the cells. Consequently, the use of agents that can prevent the adherence and/or invasion of the pathogen in the host could be a useful approach in the struggle against *Campylobacter*. Another alternative strategy could be to introduce probiotic bacteria in the diet, which would compete for nutrients and sites of adherence to the mucous membrane and cells, produce substances

* Corresponding author. Tel.: +34910017964; fax: +34910017905.
E-mail address: adolfo.martinez@csic.es (A.J. Martínez-Rodríguez).

0956-7135/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.foodcont.2011.09.027

harmful to the pathogen and/or modulate the animal's immune response. The addition of antimicrobial compounds of natural origin to chicken feed could be another possible way to tackle this problem. In this paper, after describing the main characteristics of *Campylobacter* (Section 2) and the clinical spectrum of human campylobacteriosis (Section 3), we review the main aspects of *Campylobacter* transmission and epidemiology (Section 4) and the role of chicken as the main reservoir of *Campylobacter* (Section 5). Adherence to and invasion of intestinal epithelial cells by *Campylobacter* is discussed (Section 6), pointing out alternative strategies to use antibiotics or chemical products for controlling *Campylobacter* in the food chain (Section 7).

2. General characteristics of *Campylobacter*

C*ampylobacter* is currently considered to be the main cause of bacterial diarrhoeic food-borne illnesses (Levin, 2007), and in many regions the number of cases reported are higher than those recorded for other food-pathogens, such as *Salmonella*, *Shigella* and *Escherichia coli* O157:H7. It is believed to be responsible for 400 to 500 million cases of gastroenteritis worldwide per year (Olson, Ethelberg, van Pelt, & Tauxe, 2008).

The *Campylobacter* genus has 17 species, 14 of which have been associated with human illnesses, and of these, *Campylobacter jejuni* and *Campylobacter coli* cause more than 95% of the infections attributed to this genus (Park, 2002). Members of the *Campylobacter* genus are gram-negative bacilli, with a curved spiral shape and one or two polar flagella. *Campylobacter* has a characteristic corkscrew-like movement which, in contrast to other mobile bacilli, permits it to penetrate the mucous membrane lining the walls of the gastrointestinal tract (Shigematsu, Umeda, Fujimoto, & Amako, 1998).

One common characteristic of food-borne pathogens is that they tend to be highly adaptive microorganisms, owing to the need to survive adverse conditions imposed by food-processing and the use of preservatives. By contrast, *Campylobacter* has numerous growth requirements and is unusually sensitive to environmental stress. Paradoxically, in spite of being the most frequent bacterial food pathogen, *Campylobacter* seems to lack many of the adaptive responses associated with resistance to stress presented by most of the others (Park, 2002). Different adaptive strategies have been described in the last years concerning to stress resistance in *Campylobacter* (Martínez-Rodríguez, Kelly, Park, & Mackey, 2004; Martínez-Rodríguez & Mackey, 2005; Murphy, Carroll, & Jordan, 2006; Sagarzazu, Cebrian, Condon, Mackey, & Manas, 2010).

Its most distinguishing growth requirement is the fact that it is a microaerophile, and presents optimum growth in atmospheres with 5% O_2, 85% N_2 and 10% CO_2 (Altekruse, Stern, Fields, & Swerdlow, 1999). Also, in spite of being thermophilic, with optimum growth temperatures between 37 °C and 42 °C, it is sensitive to high temperatures and can not survive pasteurisation or most culinary treatments (Jacobs-Reitsma, Lyhs, & Wagenaar, 2008). *Campylobacter* is also highly sensitive to desiccation, osmotic stress, and aeration, and does not survive sodium chloride concentrations above 2% (Park, 2002). It is precisely these characteristics which restrict the ability of these microorganisms to multiply outside the animal host and, in contrast to most food-pathogens, they can not multiply in foods during processing or storage.

3. Human disease and treatment

The clinical spectrum of enteric disease caused by *Campylobacter,* mainly by *C. jejuni* and *C. coli,* ranges from severe inflammatory to moderate non-inflammatory diarrhoea. The severity of symptoms depends on the contaminant strain and also on the physical condition of the host (Blaser & Engberg, 2008).

In spite of most cases being self-limiting, in a small percentage of cases, long-term and potentially serious complications can arise. Sequelae derived from infection by this pathogen can include clinical entities such as Guillain-Barre syndrome (Rabinstein, 2007), Reiter's syndrome or reactive arthritis (Pope, Krizova, Garg, Thiessen-Philbrook, & Ouimet, 2007; Townes, 2010).

Treatment with antibiotics for uncomplicated *Campylobacter* infection is rarely indicated. Antimicrobial treatment is usually required in patients with severe or prolonged enteritis, especially in infants or the elderly, immunocompromised individuals and in cases of extra-intestinal manifestations. The pharmaceuticals most used are macrolides and fluoroquinolones. Increases in the incidence of infection caused by antibiotic-resistant strains of *Campylobacter* make these illnesses increasingly difficult to treat (Zhang & Plummer, 2008).

4. Transmission and epidemiology

Infections by *Campylobacter* in humans are generally caused by consuming contaminated foods of animal origin, with poultry, especially chicken being the main reservoir, although it has also been found in other types of poultry, cattle, swine and sheep, in wild birds and in pets (Lee & Newell, 2006).

A large proportion of the world's chicken production is contaminated with *Campylobacter*. Some studies show that more than 98% of products derived from raw chicken in shops could be contaminated with this bacterium (Jacobs-Reitsma et al., 2008; Pearson et al., 2000). Recently, it has been demonstrated that around 80% of chicken carcasses on the EU market are contaminated with *Campylobacter*, according to a region-wide baseline survey by the European Food Safety Authority (EFSA) (EFSA, 2010a). Prevalence of *Campylobacter* varied hugely among member states, ranging from a minimum of 5% in Estonia to a maximum of 100% in Luxembourg (Fig. 1). There appears to be consistently reported lower prevalence of positive flocks in the north of the continent, but the reason for this has not yet been established (Newell & Fearnley, 2003). Cross-contamination from inadequate handling of food in the home is an important source of infection (Mattick et al., 2003). In spite of the fact that freezing contaminated meats significantly reduces the survival of *Campylobacter*, this pathogen has been isolated from previously frozen products (El-Shibiny, Connerton, & Connerton, 2009).

Most illnesses caused by *Campylobacter* in humans correspond to isolated cases, and epidemic outbreaks are rare and usually associated with the consumption of unpasteurised milk or contaminated water (Kalman et al., 2000; Richardson et al., 2007). It is believed that only a small fraction of cases of campylobacteriosis worldwide are in fact reported. Moreover, this is exacerbated by the difficult diagnosis of *Campylobacter* and the fact that its symptoms are often mild, not requiring medical intervention.

According to the EFSA, campylobacteriosis is the most frequent illness of animal origin to attack Europeans, followed by salmonellosis and listeriosis. According to their last report, 190,566 cases were confirmed in Europe in 2008 (EFSA, 2010b), and significant different were found between countries (Fig. 2). In Spain, 11.4 confirmed cases per 100,000 inhabitants were reported, the same value notified in 2007 (EFSA, 2010b). For other European countries, such as United Kingdom, Czech Republic and Germany, the number of confirmed cases decreased in 2008 compared to 2007, but no statistically significant differences were observed in the analysis of reported cases between 2004 and 2008. In the US, *Campylobacter* has been detected more frequently than both *Salmonella* and *Shigella* together. In 2009, according to the Foodborne Diseases