Editorial

Clostridium difficile infection: should it be notifiable?

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Clostridium difficile is a frequent cause of colitis associated with the use of antibiotics but it had been described well before their generalized use.[1] The cases initially described were blamed on clindamycin. However, the growing use of penicillin and cephalosporin has enabled to verify that any other antibiotic, including vancomycin and metronidazole, usually used to treat such infection, could be responsible for it. Consequently, the number of cases has been increasing and at the beginning of the 2000 decade it was seen that infections by *Clostridium difficile* were also more serious, more refractory to the usual therapy and with a higher number of recurrences.[1] Such higher severity of the disease is due to the acquisition of the mutation (NAP1/BI/027) enabling the agent to produce more toxins. Directly related with the emergence of strains in this mutation is the widespread use of quinolones.[2] This very same mutation was described in hospital outbursts, first in Canada, and later in United States of America and in Europe. New mutations have emerged, in the meanwhile, conditioning also an increase on the general severity of the disease. Curiously, mutations were also detected preventing the formation of the toxins, making strains harmless.

In this new issue of the journal it is presented an article on a series of cases of *Clostridium difficile* causing diarrhoea in a service of Internal Medicine in a Greater Lisbon hospital.

It is estimated that 20 to 50% patients admitted and residing in institutions are asymptomatic carriers of *Clostridium difficile*.[3] Although asymptomatic, such patients are a source of contamination (faecal-oral transmission of *Clostridium difficile* and spores) for all the other inpatients. Curiously, asymptomatic carriers, in general remain without any evidence of the infection for the first stages of the hospitalization and are patients acquiring this agent again who evolve to the most serious forms of infection. Such protection seems to be related with the previous colonization with non-toxicogenic strains, as well as the presence of antitoxin IgG in higher levels also verified in asymptomatic carriers.[4] An aspect worth mentioning is the fact of newborns being in great number asymptomatic carriers of this agent (up to 50%), and it is not yet clear the motive, but it seems to be related with the absence of toxin receptors in the intestinal mucosa until around two years of age, and from that moment onwards the number of antibodies is enough for protection until adult age.

Risk factors for is this infection are known, besides the antibiotic use, and as such noted in the published article, the previous hospitalization (64% of the presented patient), advanced age and the presence of serious comorbidities. Other possible factors, although controversial, are therapies with gastric acid suppressive drugs also mentioned in this article and present in a considerable number of patients.

Also controversial is the acquired infection in the community (defined also as the absence of hospitalization in the previous year to infection, not only in the article presented referring only the absence of hospitalization in the previous month to the infection). Diarrhoea by *Clostridium difficile* has been seen in low risk populations, namely healthy individuals and without the use of antibiotics. In such cases the considered potential sources of transmission are foods mainly of animal origin.

The diagnosis of such infection is made based in the clinical assessment, additionally to a diagnostic laboratory test or an endoscopic evaluation demonstrating the existence of pseudomembranes in the colon. Also here it is not clear which is the ideal laboratorial test. The most used and the quickest one is based on toxin detection. The quickest tests are less sensitive, needing a higher quantity of toxin for the results to be positive. To carry out up to three researches in the same patients increases the diagnostic sensitivity at the expense of additional costs.[5]

The therapy must be started as soon as possible. Metronidazole is considered the first line antibiotic to treat a non-serious disease and vancomycin in its

serious form (definition which is not also consensual but in general is based in the presence of a higher leukocytosis than 15.000/µL or acute kidney failure).[1] The great advantage of oral vancomycin is because it is not absorbed therefore higher concentrations are achieved within the colon, different from metronidazole with a faecal concentration reducing as the mucosa inflammation subsides.[4] It seems reasonable the use of two antibiotics in fulminant cases or those extremely serious cases (oral vancomycin and endovenous metronidazole), and it should also be considered a sub-total colectomy. Several alternative or adjuvant therapies have been described and are being studied, namely the use of probiotics, use of new antibiotics and endovenous immunoglobulin.[6]

Infections do recur and can be related with spore resistance to antibiotherapy. The recommendations for the choice of antibiotics in recurrences are based once again in the severity of the infection, and it might be of some interest to extend the therapy.[6] The effective control of such infection goes also through the prevention of new colonization and the emergence of the disease in patients previously colonized.

An example of this are the implementation of special measures in the contact with infected patients, including gloves and an apron, which should kept while the diarrhoea lasts. Hands hygiene has here a fundamental role, and should be made with water and soap due to the spore resistance to alcoholic solutions. The restriction of use of particular antibiotic has demonstrated to ease the control of some outbursts. Such recommendations include the restriction of using cephalosporin, quinolones and clindamycin.

Several areas are under investigation namely, and once again, the use of probiotics and vaccines.

The treatment of asymptomatic carriers is not recommended, although with scarce studies and being questionable in cases of hospital outbursts, whether it makes sense to treat them in order to stop the chain of transmission.

As we can verify, doubts are also in higher number than certainties. Such infection has become a problem of public health. The number of asymptomatic carriers, as well as its true importance transmitting *Clostridium difficile* is not yet totally clarified. Also fundamental seems to be the early detection of new cases as well as the quick onset of therapy and the adoption of measures preventing its transmission to close relatives, also disrupting the transmission chain.

Is it not the time to include *Clostridium difficile* infection in the group of notifiable diseases? ■

References

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