



Contents lists available at ScienceDirect

Pancreatology

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

Evaluation of local instillation of antibiotics in infected walled-off pancreatic necrosis

Mikkel Werge^{a,*}, Srdan Novovic^a, Stine Roug^b, Jenny Dahl Knudsen^c, Erik Feldager^a, Lise Lotte Gluud^a, Palle Nordblad Schmidt^a

^a Department of Gastroenterology and Gastrointestinal Surgery, Copenhagen University Hospital Hvidovre, Denmark

^b Digestive Disease Centre, Copenhagen University Hospital Bispebjerg, Denmark

^c Department of Clinical Microbiology, Copenhagen University Hospital Hvidovre, Denmark

ARTICLE INFO

Article history:

Received 7 February 2018

Received in revised form

31 May 2018

Accepted 19 June 2018

Available online xxx

Keywords:

Necrotizing pancreatitis

Infection

Pancreatic collection

Treatment

ABSTRACT

Background: Infected walled-off pancreatic necrosis (WON) is associated with increased morbidity and mortality. Systemic antibiotics are the main treatment, but are associated with adverse reactions and risk of superinfections. This study evaluates the efficacy of local instillation of antibiotics into WON.

Methods: We performed a retrospective cohort study of all consecutive patients with infected WON, who were treated with endoscopic transmural drainage and necrosectomy (ETDN) at a tertiary referral hospital between 2012 and 2016. A total of 91 patients were included. Patients often received concomitant intravenous and local antibiotics. Local antibiotics were added to the irrigation fluid depending on microbiological findings. A beneficial response was defined as the eradication of a microbe on subsequent culturing. Univariable and multivariable logistic regression analyses were used to evaluate antimicrobial efficacy.

Results: At the first drainage 81 (86%) patients had infected and 10 sterile WON. Among patients with bacterial infections, neither local nor systemic antibiotics were associated with the eradication of microbes between first and second culture. Between the second and third culture, the use of local antibiotics was associated with the eradication of microbes (OR, 2.54; 95% CI, 1.25–5.18; $p = 0.01$), but not systemic antibiotics (OR, 0.75; 95% CI, 0.38–1.38; $p = 0.33$). Twelve patients had fungal infections treated with local amphotericin B between first and second culture. The fungus was eradicated in all 12 patients.

Conclusion: Local instillation of antibiotics may be a promising supplement to systemic administration.

© 2018 IAP and EPC. Published by Elsevier B.V. All rights reserved.

1. Introduction

Infected walled-off pancreatic necrosis (WON) is associated with complications such as sepsis, septic shock, and multiple organ dysfunction. Most patients receive several systemic antibiotics. However, the administration of systemic antibiotics is often complicated by concomitant hepatic and renal insufficiency. In order to exert its antibacterial effect in WON, systemically administered antibiotics need to overcome a number of potentially limiting steps, i.e. to cross the capillary endothelium and the capsule surrounding the WON. The ability of the intravenously

administered antibiotics to penetrate into WON can be questioned. Studies on penetration of different antibiotics into the pancreatic necrosis are scarce and primarily involve few patients in the early phase of acute pancreatitis [1,2]. Studies in rats have investigated the penetrability of the antibiotics into experimental pancreatic necrosis [3]. However, besides physiological differences between animal and human species, the morphology of mature, human encapsulated necrosis at the time of detection and treatment is most certain to be more complex than that of experimental, standardized abscesses in animals [4].

Thus, the questionable penetration of antibiotics into an encapsulated collection and frequent association between infected WON and hepatic and/or renal insufficiency make safe and sufficient antibiotic treatment in patients with infected WON challenging.

Since 2009, we have routinely added antibiotics (either gentamicin, vancomycin, or amphotericin B) to the irrigation fluid for the

* Corresponding author. Copenhagen University Hospital Hvidovre, Department of Gastroenterology and Gastrointestinal Surgery, Kettegård allé 30, 2650, Hvidovre, Denmark.

E-mail address: mikkel.parsberg.werge@regionh.dk (M. Werge).

treatment of WON.

The aim of this study was to evaluate the efficacy of local instillation of antibiotics in the treatment of infected WON.

2. Methods

We evaluated 131 patients treated with endoscopic transmural drainage and necrosectomy (ETDN) in our centre between 2012 and 2016. All patients were registered prospectively, but data are analysed in a retrospective manner.

We included patients with a well-documented episode of acute pancreatitis based on the Atlanta criteria leading to WON [5], who received local and/or systemic antibiotic treatment and from whom we obtained at least one culturing sample. Only patients with confirmed infected WON at index endoscopy or patients developing infected WON confirmed at second endoscopy were included.

The indication for endoscopic intervention was persistently symptomatic collections despite either optimal conservative treatment, percutaneous drainage, or in few cases also surgical treatment. Symptoms included infection, pain, gastric outlet obstruction, bile duct obstruction, and leakage (e.g. ascites). The endoscopic procedure was performed as earlier described [6]. Endosonography-guided, transgastric or transduodenal drainage was performed using a curved linear array echoendoscope. Needle puncture was performed followed by fluid aspiration for microbiological testing. A guidewire was inserted through the needle and a knife incision was done over the wire. The tract was dilated with a dilation balloon up to 20 mm. Two double pigtail stents and a naso-cystic catheter were placed through the tract and into the cavity. Endoscopic necrosectomy was usually not performed during the index endoscopy.

As a part of the endoscopic treatment, fluid from the collection was aspirated for culturing before further endoscopic intervention. The samples were investigated with Gram stain and microscopy and cultured aerobic and anaerobic on various media. All findings were subsequently diagnosed using traditional microbiological tests and MALDI-TOF. Susceptibility tests were performed using Vitek II, E-tests and EUCAST methodology. The same methods for microbiological testing were used throughout the study period.

Irrigation of the necroses through naso-cystic catheter was initiated at the index endoscopy and was done 3–6 times a day (Supplementary Fig. 1). Empiric local antibiotic treatment was initiated with gentamycin early in the study period and later with vancomycin on the index endoscopy, as culturing results showed increased occurrence of Gram positive cocci, especially *Enterococcus faecium* [7]. The subsequent local antibiotic treatment was adjusted according to the susceptibility pattern. The irrigation volume depended on the size of the collection, but usually 100–250 mL per procedure. The dosing regimens are shown in Supplementary Table 1.

Our primary outcome was efficacy defined as the rate of eradication of isolates in cultures. The secondary outcome was mortality.

2.1. Statistics

The analyses were performed with STATA version 14 and Graphpad 7.0. Continuous data were expressed as medians with range and binary data as proportions.

The effects of antibiotics were assessed based on repeated cultures. A beneficial response was defined as the eradication of an isolate on subsequent culturing. In order, to assess the efficacy of local and systemic antibiotics Wilcoxon rank sum test and uni- and multivariate logistic regression were used, with isolates labelled as sensitive or not sensitive/antibiotics not given based on the

susceptibility testing.

Uni- and multivariate logistic regression analyses were also performed to assess possible predictors of mortality.

For each patient, the following data at the time of index endoscopy were registered: Age, gender, body mass index (BMI), aetiology, smoking status, Charlson comorbidity index (CCI), the dates for i) first onset of symptoms, ii) index endoscopy. We also recorded the microbial culturing results from the first, second, and third culturing from the collection, local and systemic antibiotics administered between first and second and second and third culturing, admission to intensive care unit (ICU), and mortality.

3. Results

Of 131 patients who underwent ETDN during the inclusion period, 26 had only one culturing performed during the admission, 7 patients had culturing performed from different collections, 7 had negative culturing, thus leaving 91 patients for present analysis.

The median age was 59 years (Table 1). The most common aetiology for acute necrotizing pancreatitis was biliary. At the first drainage 81 (86%) patients had infected and 10 sterile WON. A total of 139 isolates were found at the first drainage. Most patients were infected with enterococci (44%) or other Gram positive cocci. More than a quarter of the infected patients had fungal species cultured. The infected patients often had polymicrobial infections (56%). At the second culture 152 isolates were found. The microbial findings are presented in Table 2.

Between first and second culturing, most patients were treated with both systemic (91%) and local (98%) antibiotics (Table 3).

The microbial eradication rate according to susceptibility to the antibiotics and modality of administration can be seen in Fig. 1. The association between microbial eradication and the susceptibility to the administered antibiotics was assessed with uni- and multivariate regression analysis. The crude odds ratio (OR) for eradication for local antibiotics was 1.52 (95% CI, 0.73–3.17; $p = 0.26$) and systemic antibiotics 1.28 (95% CI, 0.64–2.59; $p = 0.49$) between the first and second cultures, the results were confirmed by multivariate regression (Table 4). Between second and third culture the use of local antibiotics was associated with the eradication of microbes (OR, 2.54; 95% CI, 1.25–5.18; $p = 0.01$), but not the use of systemic antibiotics (OR, 0.72; 95% CI, 0.38–1.38; $p = 0.33$).

Subgroup/sensitivity analyses showed that particularly the use of local amphotericin B was effective in the eradication of fungal species, as 12 fungal isolates treated with local amphotericin B between first and second culture were all eradicated. Due to the nature/distribution of data was it not possible to evaluate the efficacy of fungal eradication between first and second culture with logistic regression analyses. However, in Wilcoxon test local amphotericin B was associated with fungal eradication ($p = 0.001$) while systemic antifungals were not ($p = 0.43$). Between second and third culturing, local amphotericin B was associated with fungal eradication in both Wilcoxon test ($p = 0.011$), univariate ($p = 0.014$), and multivariate analysis ($p = 0.013$). This was not the case for systemic antifungals ($p = 0.55$, $p = 0.38$, and $p = 0.36$, respectively).

In subanalysis excluding the fungal infection, the effect of local antibiotics between the first and second culture is further reduced (univariate: (OR, 1.00; 95% CI, 0.42–2.34; $p = 0.99$); multivariate: (OR, 1.01; 95% CI, 0.43–2.40; $p = 0.97$)). However, between second and third culturing episode an effect is still observed (univariate: (OR, 2.25; 95% CI, 0.97–5.21; $p = 0.058$); multivariate: (OR, 2.38; 95% CI, 1.01–5.57; $p = 0.047$)).

Twelve patients (13%) died during admission. In univariate analysis, infection with enterococci was associated with death (OR, 5.77; 95% CI, 1.44–23.12; $p = 0.013$). After adjusting for age, gender,

Download English Version:

<https://daneshyari.com/en/article/8951967>

Download Persian Version:

<https://daneshyari.com/article/8951967>

[Daneshyari.com](https://daneshyari.com)