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LETTER TO THE EDITOR Open Access

Analysis of blood culture in a rat model of cecal ligation and puncture induced sepsis

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To the Editor,

Sepsis shows a high incidence and is associated with a high mortality [1, 2], and experimental studies are useful for a better understanding of sepsis and for identifying new therapies [3].

The cecal ligation and puncture (CLP) model is considered as the gold standard experiment for studying sepsis in animals. Recent guidelines recommend resuscitating animals after performing CLP including administration of fluid and chosen antimicrobials based on known pathogens. However, microbial identification is not a common practice in pre-clinical models of sepsis.

The aims of this original study were:

- To assess microbial situation in CLP-induced sepsis in the recent literature
- To document microbiology of blood cultures in rat CLP-induced sepsis performed in our lab.

Keyword-based review

The review was performed on PubMed using "CLP" and "rat" keywords for English-written papers in 2018 and 2019 and also for "mouse" and "CLP." Bacteriological documentation and antimicrobial therapy were collected.

CLP model in rats

Sixteen Wistar male rats, from 9 to 12 weeks of age weighing 350 to 450 g were obtained from Janvier (St. Berthevin, France). CLP model was performed as previously described [4, 5]. Septic shock was reached 16 h after induction by CLP, and blood samples were collected by jugular withdrawn. Culture and bacteriological analysis were done as previously described [6, 7].

Keyword-based review revealed a few administrations of antibiotics in CLP models

Our keyword-based review performed on PubMed resulted in 176 publications between 2018 and 2019 for rats. Among them, 22 (12.5%) were excluded for a different

Table 1 Blood culture analysis of 16 rats 16 h after CLP

	rat n°																N° of occurrences
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
Escherichia coli																	14
Enterococcus faecalis																	13
Enterobacter cloacae																	12
Staphylococcus aureus																	2
Streptococcus oralis																	1
Lactobacillus gasseri																	1
Lactobacillus murinus																	1

meaning of CLP acronym. In only 15% (23/154), antimicrobial therapy has been used, mostly (57%) the third generation cephalosporin (ceftriaxone) (Table S1).

For mice, 59 (14.6%) of 405 studies were excluded. In 18% (62/346), antibiotics have been administered, mostly (47/62, 76%) the carbapenem (imipenem/ertapenem) (Table S2).

However, none of the studies performed microbiological documentation before treatment.

Blood culture analysis 16 h after sepsis induction

In 16 CLP rats, *Escherichia coli* 88% (14/16), *Enterococcus faecalis* 81% (13/16), and *Enterobacter cloacae* 75% (12/16) were the main pathogens found in blood cultures (Table 1). All bacteria exhibit a wild-type phenotype for antimicrobial agent susceptibility.

Our literature review about CLP-induced sepsis showed that antibiotherapy and bacteriological documentation was not reported in experimental models.

Blood cultures in our CLP model frequently identified 3 bacteria, in accordance with common polymicrobial infections in stercoral peritonitis in humans. Further, similar microbial profile (*Enterobacteriaceae* and *Enterococci)* was also found between our CLP model and human peritonitis [8].

By analyzing antimicrobial susceptibility testing, all bacteria exhibit a wild-type phenotype. Carbapenems definitely proved to be the most congruent antibiotics in our model. However, antimicrobial narrow spectrum therapy, including cotrimoxazole, seemed appropriate (Table 2).

To conclude, our literature search shows that antimicrobial therapy is not daily used in the treatment of CLP-induced sepsis, and when used, no bacterial identification is performed. Our data indicates that blood culture is readily available and may give a correct indication on which antimicrobial therapy to use in CLP-induced sepsis.

Table 2 In vitro susceptibility (minimal inhibitory concentration (μg/mL)) of the organisms identified in the blood culture in our CLP rats ($n = 16$) to antimicrobial drugs

	E. coli	*E. cloacae*	*E. faecalis*
Imipenem	0.38	0.38	1
Tazocillin	2	2	2
Cotrimoxazole	0.6	0.125	0.016
Levofloxacin	0.06	0.06	1

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s40635-020-00310-6.

Additional file 1: Figure S1. Peritoneal fluid culture analysis of 16 rats 16 hours after CLP

Additional file 2: Table S1. Probabilistic antimicrobial therapy used in rat CLP models in the literature published in 2018 and 2019

Additional file 3: Table S2. Probabilistic antimicrobial therapy used in mouse CLP models in the literature published in 2018 and 2019

Abbreviation

CLP: Cecal ligation and puncture

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Authors' contributions

PVA and AB designed the experiments. PVA and BD performed the experiments and collected the blood samples. PVA and HJ performed the bacteriological analysis. All authors discussed the data, drafted or revised critically the manuscript for important intellectual content, and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

All experiments using laboratory animals were conducted in our lab in accordance with the National and European Institutes of Health guidelines and were approved by the local animal research ethics committee (Lariboisière-Villemin, Paris, France) (APAFIS#9385-2016113016181432 v4).

Consent for publication

Not applicable

Competing interests

All other authors declare that they have no competing interests.

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