Author's response to reviews

Title: Prevalence of urinary colonization by Extended Spectrum-Beta-Lactamase Enterobacteriaceae among catheterised inpatients in Italian Long Term Care Facilities

Authors:

Luca Arnoldo (arnoldo.luca@libero.it)
Roberta Migliavacca (r.miglia@unipv.it)
Laura Regattin (laura.regattin@ass3.sanita.fvg.it)
Annibale Raglio (araglio@ospedaliriuniti.bergamo.it)
Elisabetta Nucleo (e.nucleo@unipv.it)
Melissa Spalla (melissa.spalla@unipv.it)
Francesca Vailati (fvailati@ospedaliriuniti.bergamo.it)
Laura Pagani (laura.pagani@unipv.it)
Silvio Brusaferro (brusaferro.silvio@aoud.sanita.fvg.it)

Version: 6 Date: 3 October 2012

Author's response to reviews: see over
Dear editor,
I would like to submit the following article “Prevalence of urinary colonization by Extended Spectrum-Beta-Lactamase Enterobacteriaceae among catheterised inpatients in Italian Long Term Care Facilities.”

Submitting this research article I warrant, on behalf of myself and my co-authors, that the article has not been formally published in any other peer-reviewed journal, is not under consideration by any other journal and does not infringe any existing copyright or any other third party rights. Moreover, no related papers have been published.

Besides no conflict of interest concern this study.

I would like to submit the answers to reviewers’ questions for the article:

Below I answered to reviewers' questions.

Kind regards
Reviewer’s report 1

Reviewer: Christopher Crnich

Major Compulsory Revisions

- A revised manuscript should include more detail on how facilities were selected for inclusion in this study

  We added it in the text:
  “Eight contact centres (CCs), that were located throughout the national territory (Figure 1), involved local LCTFs (on voluntary basis), they had to guarantee:
  - a minimum of 9 patients for CC
  - to fill-in a patient data form;
  - presence of laboratory with VITEK 2 technology;
  - possibility of the laboratory to isolate strain and freeze it for following use”.

- A revised manuscript should include more data on the source population in study facilities (overall number of residents, overall number of catheterized residents, proportion of eligible residents who participated in the study)

  According to this suggestion we added the total n. of residents (2258) while all residents with a Urinary catheter (>24 hrs) were enrolled.

- A revised manuscript should report if the study protocol was reviewed by an IRB and whether or not informed consent of subjects was performed as part of the study protocol.

  All patients joined in the study on a voluntary basis after signing an informed consent. Patients' data were used anonymously, under Italian law an ethic committee approval was not necessary at the time of the study for non experimental point prevalence studies.

- A revised manuscript should include data on length of residence in study facilities, length of catheterization prior to data collection, and a bivariate comparison of these characteristics and the ESBL colonization outcome.

  Data about length of resident were inserted in the logistic regression model.
  We also added data about length of catheterization

- A revised manuscript should include a multivariate logistic regression model of the risk factors associated with ESBL colonization (including methods for selection of candidate risk factors, methods for model building, and methods for assessing model fit).

  We specified in the text that the statistical analysis included a first bivariate analysis (results are reported) and than these variables were included in logistic regression model.

Minor Essential Revisions:
• I would like to see more detail on the rationale for selection of certain variables in a revised manuscript.

We reported in Methods that variables were selected according to risk factors reported in the literature for HAI in LTCFs.

• I would like to see data on recent (not current) antibiotic use in a revised manuscript. If this data is not available, this should be specified in a revised manuscript.

Because of the point prevalence study we collected only data on current antibiotic use.

• Figure 1 was not included in the draft I reviewed.

We included it on revised manuscript

• The grammar of the manuscript needs to be greatly improved before it can be published.

The article was revised by English professional language editing service

• I would like to see a much more conservative discussion section in the revised manuscript in which the authors devote more of the discussion to the internal validity of their study and much more focus on the external validity of their study

We modified the text in this way:

“Due to the sample dimension and to the patients selection criteria (we limited the study only to patients with urinary catheter) this study certainly cannot be considered completely representative of the Italian BLs situation, but it gives a first picture of the problem in a crucial healthcare sector as is LTCFs and shows the need for urgent investments both in monitoring and controlling antibiotic resistance in LTCFs”.

Reviewer’s report 2

Reviewer: Yeongseon Lee

Minor revisions

- The abbreviations follow the full names.
  
  We modify the title:
  “Prevalence of urinary colonization by extended spectrum beta lactamase Enterobacteriaceae among catheterised inpatient in Italian long term care facilities”.

- We integrated in the text all your suggestions

- P value is not calculated but for decubitus in Table 3. The rest of the blanks is required to fill in-

  We complete the table 4 (because table 3 in the revised manuscript became table 4).
Reviewer’s report 3
Reviewer: Elisabeth Meyer

- Table 2: Is there a statistical significant difference in the prevalence of ESBL producers between LTCF in the North versus LTCF in the South? If so, please discuss why there could be regional differences.

There was not statistical significance in prevalence of resistance between north and centre-south LTCFs. We add in the article:
“there was not statistical significance (chi square test) in prevalence resistance between north and centre-south LTCFs”

- Table 4: It will easier to understand if data are presented in a bar chart instead of a table.

We divided the table in: one new table (number 3) and a new figure (number 2). The table 3 summarize PCRs sequences; the figure 2 is the bar chart with ESBL and resistant strain prevalence.
Reviewer’s report 4
Reviewer: Beatriz M Moreira
Major Compulsory Revisions

- Title should not contain abbreviation.

  We removed all abbreviation from title:
  “Prevalence of urinary colonization by extended spectrum beta lactamase Enterobacteriaceae among catheterised inpatient in Italian long term care facilities”.

- Study objective must be described clearly. Methods: We carried out a prevalence point study in…should say “a point prevalence study”. Describe here the specimen source screened. Define suspect AmpC hyperproducers.

  We changed a prevalence point study in “a point prevalence study”
  And we add in the text:
  “AmpC hyperproducers on the basis of cephemycin resistance”

  A multiplex-PCR protocol was used for identifying family-specific AmpC genes responsible for AmpC BL expression in organisms with or without a chromosomal AmpC BL gene

- ESBLs producers were screened for resistance genes by PCR assay: t is usually not possible to define ESBL genes just by PCR. Abstract must state other experiments done to characterize beta-lactamases.

  We added in the text
  “Finally ESBLs producers were screened for bla resistance genes by PCR assay”

  The microorganisms ESBL producing, screened by Vitek-2 System, were subjected to both the double-disk-synergy test and combo confirmatory test according to CLSI criteria.

- Results – 185 of 221 patients showed positive samples – please specify: 221 patients refer to the total screened? Total number of patients in 23 LTCFs?? The numbers presented in this section are very confusing. It is hard to follow the totals for each of the percentages

  We modified the text in this way:
  “211 patients with catheter were screened, 185 out of 211 patients showed positive samples for the presence of Enterobacteriaceae, 114 of these 185 were colonized by extended spectrum cephalosporins resistant microorganisms”.

- Manuscript must be thoroughly reviewed and rewritten

  The article was revised by English professional language editing service
• Background. Authors must describe the importance of performing a colonization survey. Why would this be important for antimicrobial use practices? For infection control? The different beta-lactamases are widespread in many different Enterobacterial species

We add in the text:
“Point prevalence surveys are useful tools to study initially the spread of resistant microorganisms in a population at risk such as the elderly, to understand the burden of the problem and to make a benchmark of resistance genes to control their development”.

• Methods. Was the study approved by an Ethics Committee

All patients joined in the study on a voluntary basis after signing an informed consent. Patients' data were used anonymously, under Italian law an ethic committee approval was not necessary at the time of the study for non experimental point prevalence studies.

• Formatting of tables must be reviewed

We changed tables format in the text.

• Table 3. Which are the comparison groups for statistical analysis

Table 3 (in the revised article it became table 4) the comparison is between patients that have at least one resistant sample and other patients (with no resistant samples and without any microorganisms)

• Are there any statistical significant differences for the prevalence of the different beta-lactamases according to geographic region?

We modified the text:
“The latter microorganism also showed geographical differences, that were statistically significant (p<0.05), in the expression of TEM-types gene, with TEM-92 present in 90.0% (18/20) of the strains in northern Italy and 52.9% (9/17) of TEM-92 in centre-south where the remaining ones were TEM-4 or TEM-24”.