

Editorial

Mario Plebani* and Leonardo M. Fabbri

Procalcitonin-guided antibiotic therapy: a potentially effective and efficient strategy

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Antimicrobial resistance has emerged as a major issue affecting both patient outcomes and overall resources in healthcare systems. In addition, the evidence that antibiotic use causes resistance is increasingly recognized as a sound rationale to prevent their inappropriate prescription [1]. Respiratory tract infections contribute significantly to the problem of antibiotic misuse. Approximately 75% of all antibiotics prescribed in the ambulatory setting are for acute respiratory tract (ARI) infections, and albeit their use is associated with a significant symptomatic effect, their use is inappropriate because the vast majority of these infections are viral [2]. In addition, clinical and microbiological evaluations are neither sensitive nor specific to differentiate bacterial from viral respiratory tract infections [3], and thus of limited value for directing therapy.

Guidance for antibiotic treatment is increasingly requested and an interesting approach is to identify easily obtainable and non-invasive biomarkers, in addition to usual clinical and bacteriological indicators, to guide physicians. Potential advantages of such a strategy would be to personalize and individualize antibiotic initiation and duration according to the patient's response to antimicrobial treatment. Among the several biomarkers that have been identified and proposed, procalcitonin (PCT), a calcitonin precursor hormone, is probably the most promising one. Guidance about serum PCT concentration has substantially reduced antibiotic use in patients presenting at the emergency department (ED) or admitted to hospital for lower respiratory tract infections [2, 4, 5]. In a meta-analysis including 14 trials including 4221 patients, the use of PCT to guide initiation and duration of antibiotic treatment in patients with ARIs was found to be effective: antibiotic consumption was significantly reduced across different clinical settings and ARI diagnoses, while its use was not associated with higher mortality rates or treatment failure [6]. Same data were obtained in a multicenter, prospective, parallel-group, open-label trial called PRORATA trial: the PCT-guided strategy to treat suspected bacterial infections in non-surgical patients in intensive care units (ICU) was

found to be effective in reducing antibiotic exposure and selective pressure with no apparent adverse outcomes [7]. For patients in the PCT group, the absolute difference of 2.7 days between the mean number of days without antibiotics by day 28 corresponded to a 23% relative reduction in antibiotic exposure. The authors did not report any difference in the length of stay in ICU between groups, as well as no difference in mortality and adverse events [7]. In a recent study that we conducted in patients admitted to hospital for severe exacerbations of COPD associated with clinical signs of bacterial infections (increased and purulent sputum and/or respiratory failure), the PCT-guided reduction of duration of antibiotic treatment from 3 to 10 days was not associated with increased risk of exacerbations in the following 6 months [8].

Despite the evidence that PCT-guided care management results in reduction of antibiotic exposure and hospital length of stay while improving the timing of diagnosis and treatment, the existing economic literature on PCT is limited and presents several limitations [9, 10]. The paper by Phillip Schuetz and Colleagues, which is published in this issue of *Clinical Chemistry and Laboratory Medicine*, therefore, is very welcome as it adds further evidence of the substantial cost savings associated with PCT protocols of ARI in comparison to usual care [11]. The cost impact model built by the authors was evaluated in three US clinical settings: 1) Hospital Ward/ED, 2) Hospital ICU, and 3) Outpatient Clinic/ED. In all three settings, PCT-guided care was shown to be cost saving across all treatment settings and diagnoses, with saving ranging from \$5,329,824 in the outpatient clinic to nearly \$700,000 in the hospital ward/ED. In the ICU setting the net saving resulted to be of nearly \$700,000. The results are robust to changes in key parameters and variations in most parameters resulted in only small changes in total savings. The data of this study are particularly important as the cost savings associated with PCT-guided care is not associated with any meaningful differences in quality and treatment outcomes, while it reduces antibiotic exposure. In addition, the transferability of the data to other healthcare systems seems very sure.

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***Corresponding author: Mario Plebani**, *CCLM* Editor-in-Chief, Department of Laboratory Medicine, University-Hospital of Padua, Via Giustiniani 2, 35128, Padua, Italy, Phone: +39 0498212792, Fax: +39 049663240, E-mail: mario.plebani@unipd.it
Leonardo M. Fabbri: Department of Oncology Haematology and Respiratory Disease, University of Modena & Reggio Emilia, Modena, Italy