Can procalcitonin testing reduce antibiotic prescribing for respiratory infections?

SIR—Christ-Crain and colleagues have recently reported that procalcitonin (PCT) testing can reduce significantly antibiotic prescribing (from 83% in the control group down to 44% with PCT-guided treatment) in patients admitted with a lower respiratory tract infection (LRTI) [1]. Clearly, achieving such a large reduction in antibiotic prescribing, and with no deleterious effect on clinical outcomes as in this study, would be extremely desirable in all health care settings. In the UK, both methicillin-resistant Staphylococcus aureus (MRSA) and Clostridium difficile are important nosocomial infections, which recently have attracted much attention by both the media and the Department of Health. Antibiotic usage in hospitals has been shown to be a risk factor for both C. difficile [2] and MRSA [3, 4], as well as for antibiotic resistance in other bacterial species. Because of the common risk factors, the same preventative strategies, including control of antibiotic usage, can reduce both MRSA and C. difficile [5]. Recently, there have been reports of both increasing numbers of C. difficile and an increasing case-fatality ratio [6, 7].

Inflammatory markers may help to identify patients who require antibiotics, and PCT may be preferable to C-reactive protein (CRP) testing. The main advantage of PCT is its faster response to inflammatory insults such as bacterial sepsis: as a result, PCT is both more sensitive and more specific than CRP in the diagnosis of bacterial infection [8]. We decided to conduct an assessment of whether the excellent results by Christ-Crain could be obtained in routine use, that is, outside the randomised trial settings typically associated with high level of enthusiasm and commitment. As our assessment was not a randomised trial, we primarily aimed at auditing the proportion of patients receiving antibiotics despite a low PCT test result, using as standard the low antibiotic usage (10.4%) achieved by Christ-Crain et al. [1] for this category of patients in their randomised trial.

Methods

The Microbiology Department took a Kryptor analyser on a temporary loan for over a period of 2 months (February and March 2005) and conducted 188 tests for care of the elderly patients (aged 70 years and above) and 31 for chest medicine patients. Before the testing started, a protocol had been distributed and meetings had been arranged with the physicians in these two units. All physicians in these two units were encouraged to utilise the PCT result, as well as the clinical and radiology findings, as the basis for their antibiotic decision. All PCT test results had comments added by the medical microbiologists to encourage an appropriate response in line with the findings in the report by Christ-Crain and colleagues [1]: thus, antibiotic use was discouraged, but not completely banned, if the PCT test result was <0.25 μg/l. During the study conducted by Christ-Crain, PCT testing was always done soon after admission, presumably involving the out-of-hours service in Clinical Chemistry, whereas we accepted we did not have the resources to offer anything more than one daily run of PCT tests, which guaranteed a result within 24 h of the specimen collection. We thought that this delay in testing would not necessarily be a major disadvantage, because the admitting staff may have more confidence in a low PCT result excluding bacterial infection after chest X-rays and other tests had also been done. Unlike Christ-Crain et al. [1], we included patients with both community-acquired and hospital-acquired LRTIs but excluded LRTIs in the intensive care unit.

Results

The key findings of our assessment are summarised in Table 1. The directly verifiable savings, from patients whose antibiotics were stopped, were estimated to be about £1,306: this was much less than the overall cost for the PCT tests (£6,570).

Conclusions

PCT testing did allow a reduction in antibiotic usage but not to the same extent as in the previously published randomised trial: 34.7% of our evaluable patients whose PCT was <0.25 μg/l were continued on antibiotics, as opposed to only 10.4% in the study by Christ-Crain. Our failure to match the standard set by Christ-Crain in their study could be because of differences in the settings or, perhaps, of the greater difficulty in enlisting support and collaboration in routine use as opposed to during a clinical trial.

The overall measurable savings as a result of antibiotic discontinuation did not match what would have been the overall cost of the PCT tests: one of the reasons for this was that the antibiotics discontinued in our hospital after the PCT test result were mainly inexpensive oral antibiotics (such as doxycycline and amoxicillin). Another explanation for the limited directly verifiable drug budget savings is that 37% of our patients with a low PCT were not on antibiotics at the time of the test: the low PCT result is likely to have influenced the decision of not starting antibiotics afterwards, but these savings cannot be measured or verified in a non-trial situation without a comparison group.

Apart from the savings in the drug budget, it is likely that other benefits may be derived from PCT testing, but, again, these cannot be measured outside clinical trial settings. These further likely benefits may include a reduction in the side-effects associated with antibiotics or the use of IV lines, a reduction in C. difficile and a reduction in MRSA. Wilcox in 1996 estimated that preventing one single case of C. difficile would save an excess of £4,000, with a reduction in the length of stay accounting for most of the extra cost [9].
Research letters

Table 1. The key findings of our assessment of procalcitonin (PCT) testing in patients presenting or developing a lower respiratory tract infection.

- The PCT test result was <0.25 μg/l in 131 of the 219 tests: this indicated that a bacterial LRTI was unlikely in these 131 patients.
- Analysis of the 121 evaluable patients whose PCT was <0.25 μg/l showed that:
  - 42 patients (34.7%) were on antibiotics despite the low PCT: this compares with the lower figure of 10.4% in the Lancet study [1].
  - 45 patients (37%) were not on antibiotics, and the low PCT result may have helped not to start them afterwards.
  - 34 patients (28%) were on antibiotics and had their antibiotics stopped after the low PCT test: as a result, the direct financial savings in the drug budget was estimated to be £1,306.
- The cost of the procalcitonin test was estimated to be £30 per test (including reagents—rental, labour and overheads): thus the total cost for 219 tests would have been £6,570.
- There was a significant amount of inappropriate requesting for the PCT test and this could escalate if the PCT test became part of the routine repertoire: any increase in inappropriate testing would affect the cost–benefit balance.

Our conclusion is that the introduction of routine PCT testing in our hospital can help to reduce antibiotic prescribing in patients presenting with LRTIs, but not to the same extent as in the study by Christ-Crain et al. [1]. We have also highlighted how the directly verifiable savings, based on antibiotic discontinuations in patients with low PCT, may not match the cost of PCT testing and cannot be used as the sole justification for this rather expensive test. We hope that in future, increased competition between manufacturers may reduce the price of PCT testing. Ideally, PCT testing should be available on the same platform used for the common biochemistry tests done on admission, and not on a separate dedicated analyser, so that there would be negligible extra labour costs and the test could be more easily made available out-of-hours.

Key points

- We audited the introduction of PCT testing for patients presenting with lower respiratory tract infections: 34.7% of patients with a low PCT were continued on antibiotics as opposed to 10.7% in the recently published randomised trial.
- The overall cost of PCT testing (about £30 per test) did exceed the directly verifiable savings in the drug budget, but the full extent of the savings and the impact of the other potential benefits can only be measured in a clinical trial.
- A cheaper PCT test available on the same platform used for the common biochemistry tests conducted on admission, and not on a separate dedicated analyser, could be of significant interest.

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Conflicts of interest

None.

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