RESEARCH ARTICLE

Evaluation of a novel point-of-care test kit, ABSOGEN™ PCT, in semi-quantitative measurement of procalcitonin in whole blood

Hi Jeong Kwon¹ | Jehoon Lee¹ | Hae-il Park¹ | Kyungja Han^{1,2}

¹Department of Laboratory Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea

²The Seoul St. Mary's Hospital IVD Medical Devices Development Center, Seoul, Korea

Correspondence

Kyungja Han, Department of Laboratory Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea.
Email: hankja@catholic.ac.kr

Funding information

The Korea Ministry of Trade, Industry & Energy, Grant/Award Number: 10049771

Background: In response to inflammation, procalcitonin plasma concentrations increase more rapidly than other acute-phase reactants and higher values are associated with severe disease. Procalcitonin measurements assist in determining whether antibiotic therapy should be used. Point-of-care testing (POCT) is performed for early decision making about additional testing or therapy. The ABSOGEN™ PCT (Bumyoungbio, Inc., Suwon, Korea) is a rapid novel semi-quantitative immunochromatographic PCT assay that analyses whole blood samples. We compared the patient quantitative test results to ABSOGEN™ PCT test results.

Methods: Whole blood was loaded onto an ABSOGEN™ PCT cartridge and incubated for 10 minutes. The color intensity of the band of the cartridge was measured using an accompanying device and with the naked eye. The results were graded as negative (<0.1 ng/mL), low (0.1 to <1.0 ng/mL), middle (1.0-2.0 ng/mL), and high (>2.0 ng/mL). A total of 158 specimens with procalcitonin levels measured from 0 to 18.96 ng/mL were used for comparison study.

Results: The concordance rate between ABSOGEN™ PCT using the reader and quantitative assay, between ABSOGEN™ PCT using naked eyes and quantitative assay, and between ABSOGEN™ PCT using the reader and naked eyes for the same category was 83.5% ($P=.040$), 78.5% ($P<.001$), and 82.3% ($P=.001$), respectively. The concordance rates for the ± 1 categories were all 100%.

Conclusion: ABSOGEN™ PCT is an accurate assay. It is easy to use, simple, fast, portable. The assay has potential value in clinical applications, especially in emergency care.

KEYWORDS

immunochromatographic, point-of-care testing, procalcitonin, semi-quantitative

1 | INTRODUCTION

When an infectious etiology is proven or strongly suspected and the response results in hypofunction of uninfected organs, the term sepsis (or severe sepsis) should be used. Severe sepsis includes acute organ dysfunction that can manifest in any organ and frequently manifests clinically as shock, respiratory failure, acute kidney injury, hematologic or metabolic disturbances, or neurologic decline. Septic shock

is a form of severe sepsis where the organ dysfunction involves the cardiovascular system. Sepsis results in a complex set of interactions between the inciting microbes and the host immune response, which triggers the inflammatory cascade and coagulation pathway. Microbial invasion of the bloodstream is not essential because local inflammation can also elicit distant organ dysfunction and hypotension. In patients whose blood cultures are negative, the etiologic agent is often established by culture or microscopic examination of infected material

from a local site. In several case series, the majority of patients with a clinical picture of severe sepsis or septic shock had no evidence of infection.^{1,2}

There is no specific diagnostic test for sepsis. Definitive etiologic diagnosis requires identification of the causative microorganism from blood or a local site of infection. Management of sepsis patients involves early infection recognition, source control, fluid therapy, antibiotics, and hemodynamic supportive care. Early treatment of sepsis is most effective and early confirmation of systemic inflammation and sepsis, as done by procalcitonin measurement, is most important.^{2,3}

Procalcitonin is a polypeptide that is the precursor for calcitonin in C cells of the thyroid. In response to inflammation, procalcitonin is synthesized by other tissues including those of the liver, kidney, and pancreas, and plasma concentrations increase more rapidly than other acute-phase reactants from a very low baseline concentration. Procalcitonin is used as a biomarker for the diagnosis of sepsis, severe sepsis, and septic shock. The higher values are associated with severe disease and procalcitonin measurements are used to guide antibiotic therapy. Using serially monitored procalcitonin levels, the duration and need of antibiotic therapy can be better adapted to the individual requirements of the patient.³⁻⁵

For rapid diagnosis, point-of-care test (POCT) is performed for early decision-making about additional testing or therapy. Despite being semi-quantitative, POCT results are helpful in situations when quantitative measurements are required quickly, such as within 1-3 hours. However, a semi-quantitative POCT should be sensitive enough to indicate or exclude systemic inflammation.³

ABSOGEN™ PCT (Bumyoungbio, Inc., Suwon, Korea), is a novel, rapid, and semi-quantitative immunochromatographic POCT assay that analyses whole blood. The present study compared patient quantitative test results to ABSOGEN™ PCT test results.

2 | MATERIALS AND METHODS

2.1 | Characteristics of procalcitonin test using ABSOGEN™ PCT

ABSOGEN™ PCT is a one-step, lateral flow, immunochromatographic sandwich-type assay. The cassette consists of the sample application pad and the conjugate pad. Anti-procalcitonin antibody and goat anti-mouse IgG antibody were used. Whole blood (90 µL) or control fluid was dispensed into a sample well of the cartridge and incubated for 10 minutes. Procalcitonin in the samples bonds with the gold colloid monoclonal anti-procalcitonin antibody conjugate, and in turn bonds with the anti-procalcitonin antibody on the test line. The bonding is visually evident as a red band on the test line. The intensity of the test line is directly proportional to the concentration of procalcitonin. The red band develops on the test and control lines when the procalcitonin concentration is ≥ 0.1 ng/mL. The red line must develop on the control line; if not, the test is invalid (Figure 1). The results were graded as negative (<0.1 ng/mL), low (0.1 to <1.0 ng/mL), middle (1.0 - 2.0 ng/mL), and high (>2.0 ng/mL). The color intensity of the band was measured using an ABSOGEN READER (Bumyoungbio, Inc.) and with the naked eye.

FIGURE 1 The control line(C) and test line(T) of the semi-quantitative kit for the procalcitonin analysis. Negative (<0.1 ng/mL), low (0.1 to <1.0 ng/mL), middle (1.0 - 2.0 ng/mL), and high (>2.0 ng/mL)

2.2 | Method description

The study was approved by the Institutional Review Board of Seoul St. Mary's Hospital. ABSOGEN™ PCT was calibrated at the beginning of the study by the manufacturer. Data from the ABSOGEN™ PCT were compared with the results using the Modular E170 analyzer (Roche Diagnostics, Mannheim, Germany). Procalcitonin assay from patients admitted to Seoul St. Mary's Hospital from April 2015 to July 2015 were performed. A total of 158 specimens were evaluated. One hundred and fifteen specimens with procalcitonin levels ranging from 0 to 18.96 ng/mL were randomly selected for this study by the Modular E170 analyzer and 43 specimens were from health check-ups. Ages range from 15 to 90 years, with 51.7 ± 19.9 (age mean $\pm$ SD) for the 158 samples, 77 males (54.4 ± 19.9), and 81 females (49.1 ± 19.4).

ABSOGEN™ PCT Analysis was performed using fresh whole blood sample remnants collected in EDTA tubes for routine CBC assay. The specimens were sent to The Seoul St. Mary's Hospital IVD Medical Devices Development Center to be analyzed with ABSOGEN™ PCT methods. No samples were stored after completion of the study. All tests were finished within one working day. The method comparison study used EP12-A2.⁶ IBM SPSS Statistics Version 20 (IBM Corp., Armonk, NY, USA) was used for statistical analyses.

3 | RESULTS

3.1 | Comparison of the ABSOGEN™ PCT and the quantitative method

A procalcitonin level of 0.1 ng/mL determined by the quantitative method using the Modular E170 analyzer was used for comparison. Positive percent agreement by the reader was 83.9% (95% confidence interval [CI] 75.1%-90.0%). Negative percent agreement by the reader was 92.3% (95% CI 83.2%-96.7%). Overall percent agreement by the

TABLE 1 Positive percent agreement (PPA), negative percent agreement (NPA), and overall percent agreement (OPA) at 0.1 ng/mL procaltitonin level

Reader device			Naked eye		
PPA	NPA	OPA	PPA	NPA	OPA
83.9%	92.3%	87.3%	71.0%	98.5%	82.3%
95% CI, 75.1-90.0	95% CI, 83.2-96.7	95% CI, 81.3-91.6	95% CI, 61.1-79.2	95% CI, 91.8-99.7	95% CI, 78.5-84.5

TABLE 2 Comparison of ABSOGEN™ PCT using the reader and the quantitative method

	ng/mL	Quantitative method (E170)				Total
		<0.1	0.1 to <1.0	1.0 to 2.0	>2.0	
Reader	<0.1	60	15			75
	0.1 to <1.0	5	59	1		65
	1.0 to 2.0		2	7	3	12
	>2.0				6	6
	Total	65	76	8	9	158
Concordance		Main diagonal (bold) 83.5% Main+first lateral diagonal 100%				

McNemar's test $P=.040$.

Main diagonal (boldface): Agreement within the same categories.

Main diagonal+first lateral diagonal: agreement within ± 1 categories.

TABLE 3 Comparison of ABSOGEN™ PCT using the naked eye and the quantitative method

	ng/mL	Quantitative method (E170)				Total
		<0.1	0.1 to <1.0	1.0 to 2.0	>2.0	
Naked Eyes	<0.1	64	27			91
	0.1 to <1.0	1	45			46
	1.0 to 2.0		4	8	2	14
	>2.0				7	7
	Total	65	76	8	9	158
Concordance		Main diagonal (bold) 78.5% Main+first lateral diagonal 100%				

McNemar's test P -value $<.001$.

Main diagonal (boldface): Agreement within the same categories.

reader was 87.3% (95% CI 81.3%-91.6%). The positive percent agreement, negative percent agreement, and overall percent agreement assessed with the naked eye was 71.0% (95% CI 61.1%-79.2%), 98.5% (95% CI 91.8%-99.7%), and 82.3% (95% CI 78.5%-84.5%), respectively (Table 1). The concordance rate between ABSOGEN™ PCT using the reader and quantitative assay, between ABSOGEN™ PCT using naked eyes and quantitative assay, and between ABSOGEN™ PCT using the reader and naked eyes for the same category was 83.5% ($P=.040$), 78.5% ($P<.001$), and 82.3% ($P=.001$), respectively. The concordance rates for the main plus first lateral diagonal categories were all 100% (Tables 2-4).

3.2 | Precision and linearity

To evaluate the assay's precision, low grade (0.06-0.09 ng/mL) and middle grade (1.53-1.89 ng/mL) sera were used. Low- and middle-grade positive controls were assayed in duplicate twice a day in an

analytical run on five working days. All test results for precision were in the expected grades. To evaluate the assay's linearity, four concentrations of sera (0.75, 1.5, 3.0, and 6.0 ng/mL) were used. The expected grade was low, middle, high, and high for each solution. Each concentration sample was assayed four times. All test results for linearity were in the expected grade, except for one that, at 3.0 ng/mL, was middle instead of high grade.

3.3 | Interference

Specimens from 0.1 ng/mL to 3.0 ng/mL were used for evaluation. Serum containing 0.01 ng/mL procaltitonin was prepared as a dilution serum, as were 10 whole blood and plasma specimens. Samples containing 30%, 45%, 55%, and 60% hematocrit were prepared by adding dilution serum or removing plasma. Samples containing 1000 mg/dL triglyceride or 15.8 mg/dL total bilirubin were prepared by adding a very high-level sample. Results with whole blood and plasma

	ng/mL	Reader				Total
		<0.1	0.1 to <1.0	1.0 to 2.0	>2.0	
Naked Eyes	<0.0	74	17			91
	0.1 to <1.0	1	43	2		46
	1.0 to 2.0		5	8	1	14
	>2.0			2	5	7
	Total	75	65	12	6	158
Concordance		Main diagonal (bold) 82.3% Main+first lateral diagonal 100%				

TABLE 4 Comparison of ABSOGEN™ PCT using the reader and the naked eye

McNemar's test P -value=.001.

Main diagonal (boldface): Agreement within the same categories.

displayed no differences in the 10 samples. Hematocrit 55%, triglyceride 1000 mg/dL, and bilirubin 15.8 mg/dL has no effect.

4 | DISCUSSION

Sepsis is a life-threatening condition and various biomarkers have been evaluated for its diagnosis, risk stratification, and prognosis. There is no single biomarker that provides sufficient diagnostic discrimination, either to diagnose or exclude sepsis, and a few biomarkers are worth discussing as a conceptual illustration or because of their purported clinical value.²

Procalcitonin is involved in the host inflammatory response. Multiple studies have been done looking at procalcitonin as a specific diagnostic and prognostic biomarker for sepsis. The United States Food and Drug Administration has approved the use of procalcitonin for risk assessment for day 1 of intensive care unit admission to determine the progression of severe sepsis and septic shock, designating <0.5 ng/mL and >2 ng/mL as low and high risk for illness severity, respectively. Procalcitonin has also been studied as a marker in a pilot antibiotic stewardship program. Although procalcitonin is the most promising sepsis biomarker to date, the assay availability and consensus on how the procalcitonin absolute values should be interpreted and used for clinical judgment is still undecided.²

There are pros and cons of using procalcitonin as a sepsis marker. Testing of procalcitonin is more expensive than white blood cell count, C-reactive protein testing, and determination of lactate level, with no superior outcomes.^{7,8} But, procalcitonin more specifically and cost-effectively indicates bacterial infections than other inflammatory biomarkers, and is the only widely available biomarker that improves choices about initiation and duration of antibiotic treatment.⁹ In addition to the quality of the test, sample volume, analysis time, the need for sample dilution, and cost are very important factors. When sepsis is diagnosed, starting antibiotics is urgent.

Since high procalcitonin levels indicate the immediate need for sepsis therapy, a bedside test that yields results quickly can be critically important. In this situation, the present novel POCT could be useful. The ABSOGEN™ PCT blood procalcitonin test is a very simple and rapid test. The turnaround time is rapid because it uses whole blood; centrifugation is not required and the reaction is rapid. Serum

or plasma also can be used. Sample volume for the test is small and no need for dilution. Even though the reaction band is narrow and faint, there is no difficulty in differentiating positive and negative, but some effort is needed to differentiate the grades using the naked eye. We recommend using the reader. This POCT utilizes a simple and crude grading. With low-grade positive, repeated testing after 6-24 hours or waiting for the results from the main analyzer is preferred. If sepsis is clinically suspected, antibiotics should be initiated. Medium- and high-grade positive are indications for antibiotic use. Once antibiotic therapy has begun the decision of continuing or stopping becomes less urgent. Reduction from high to low grade during antibiotic therapy is a sign that antibiotic use should be continued, whereas antibiotic change is absolutely necessary upon grade increase from negative or low grade to medium or high grade.

To conclude, ABSOGEN™ PCT is easy, rapid, and simple to use, and is portable. It appears to be useful for clinical applications, especially emergency care in cases of sepsis.

ACKNOWLEDGMENTS

This work was supported by the Technology Innovation Program (No: 10049771, Development of Highly-Specialized Platform for IVD Medical Devices) funded by The Korea Ministry of Trade, Industry & Energy. All test kits were kindly provided by Bumyoungbio, Inc., Suwon, Korea. The funding organization played no role in the study design; collection, analysis, and interpretation of data.

REFERENCES

1. Munford RS. Severe sepsis and septic shock. In: Kasper D, Fauci A, Hauser S, Longo D, Larry Jameson J, Loscalzo J, eds. *Harrison's Principles of Internal Medicine*, 19th edn. New York: McGraw-Hill; 2015: <http://accessmedicine.mhmedical.com.proxy.cuk.ac.kr:8080/book.aspx?bookid=1130>. [Internet] Accessed June 10, 2016.
2. Han J, Cribbs SK, Martin GS. Sepsis, severe sepsis, and septic shock. In: Hall JB, Schmidt GA, Kress JP, eds. *Principles of Critical Care*, 4th edn. New York: McGraw-Hill; 2015: <http://accessmedicine.mhmedical.com.proxy.cuk.ac.kr:8080/content.aspx?bookid=1340§ionid=80033910>. [Internet] Accessed June 10, 2016.
3. Meisner M. Update on procalcitonin measurements. *Ann Lab Med*. 2014;34:263-273.
4. Hortin GL. Amino acids, peptides, and proteins. In: Burtis CA, Ashwood ER, Bruns DE, eds. *Tietz Textbook of Clinical Chemistry and Molecular*

- Diagnostics*, 5th edn. St. Louis, MO: Elsevier Saunders Publishing; 2012:523–524.
5. Bouadma L, Luyt CE, Tubach F, et al. Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomised controlled trial. *Lancet*. 2010;375:463–474.
 6. CLSI. *User Protocol for Evaluation of Qualitative Test Performance; Approved Guideline-Second Edition*. CLSI Document EP12-A2. Wayne, PA: CLSI; 2008.
 7. Schuetz P, Mueller B. Procalcitonin as a sepsis biomarker: Procalcitonin: an effective screening tool and safe therapeutic decisionmaking aid for emergency department patients with suspected sepsis. *Ann Emerg Med*. 2015;66:318–319.
 8. Talan DA. Procalcitonin as a sepsis biomarker: procalcitonin is not a useful biomarker of sepsis. *Ann Emerg Med*. 2015;66:318–319.
 9. Pecoraro V, Germagnoli L, Banfi G. Point-of-care testing: where is the evidence? A systematic survey. *Clin Chem Lab Med*. 2014;52:313–324.

How to cite this article: Kwon HJ, Lee J, Park H-I, Han K. Evaluation of a novel point-of-care test kit, ABSOGEN™ PCT, in semi-quantitative measurement of procalcitonin in whole blood. *J Clin Lab Anal*. 2017;31:e22111. <https://doi.org/10.1002/jcla.22111>