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WHITE PAPER

LEUKO EZ VUE®

The *LEUKO EZ VUE* test for elevated fecal lactoferrin is simpler and more sensitive than microscopy for fecal leukocytes.

Acute infectious diarrheal diseases represent one of the primary causes of morbidity throughout the world. Inflammatory infections like toxigenic *C. difficile*, *Salmonella*, *Shigella*, *E. histolytica* and *Campylobacter* often involve tissue damage, requiring immediate medical attention.[1] Noninflammatory cases are typically mild and do not cause mucosal damage, as with giardiasis, cryptosporidiosis, infections by rotavirus and norovirus, and functional disorders like lactose intolerance and irritable bowel syndrome.[1,2] The fecal biomarker, lactoferrin, is a stable glycoprotein that is expressed by activated neutrophils, a primary cell-type of leukocytes. During intestinal inflammation, the infiltration of activated neutrophils into the intestine increases fecal lactoferrin.[3-9] Multiple studies have linked elevated fecal lactoferrin to intestinal inflammation.[6-9]

The *LEUKO EZ VUE* test is an immunochromatographic test for the qualitative detection of elevated fecal lactoferrin as a marker of fecal leukocytes and an indicator of intestinal inflammation. The *LEUKO EZ VUE* test overcomes the problems of microscopy by utilizing immunochromatography technology and provides results in 10 minutes. The assay detects elevated levels of lactoferrin in fecal samples. Lactoferrin is very stable and is not degraded during infections by the toxins of pathogens such as *C. difficile*. The assay can be used with liquid, semisolid, and solid fecal specimens, and detects elevated levels of lactoferrin not degraded in the bowel.

The performance of the *LEUKO EZ VUE* test has been evaluated in a number of studies. In a mid-western hospital, a study involving 42 specimens was performed comparing fecal WBC smears, the *LEUKO EZ VUE* test, and a lactoferrin assay at a reference laboratory.[10] The results demonstrated that the *LEUKO EZ VUE* assay detected a higher number of positive results that compared identically with the reference method, indicating increased performance of fecal lactoferrin detection over microscopic examination for fecal leukocytes.

The *LEUKO EZ VUE* test offers more flexibility for specimen handling when compared to microscopy. In a study done at the Mayo Clinic by May *et al*,[11] 168 fresh patient stool specimens were tested by the *LEUKO EZ VUE* test and by microscopy for fecal leukocytes. Of these, 30 were positive for elevated fecal lactoferrin, 12 by both lactoferrin and microscopy and 1 by microscopy only. The authors concluded that the discrepant 18 lactoferrin-positive microscopy-negative were likely a result of lysed and degraded cells. Detecting elevated lactoferrin offers an advantage over microscopy as it does not require intact cells, allowing for longer specimen storage time prior to testing. Specimens being tested for lactoferrin may be stored for up to 2 weeks at room temperature.

The potential for false-negative results by microscopy has been reported by other groups. In a study by Granville *et al.*,[12] 205 stool specimens from adult inpatients were submitted for microscopy for fecal leukocytes. Discharge codes were retrieved and patients were divided into 2 groups. Group 1 included inflammatory gastrointestinal (GI) diseases (enteric infections, intestinal inflammation, bloody stool and acute vascular insufficiency, etc.) and group 2 included noninflammatory cases (no lower GI disease, impaction, IBS, constipation, etc.). Fecal specimens were examined within 1 hour of being received into the lab using microscopy and methylene blue stain for counting neutrophils. Using a cut-off of 1 cell per high-power field (HPF), only 32% of patients with infectious gastroenteritis were positive. In addition, patients with intestinal inflammation confirmed by endoscopy had undetectable neutrophils by microscopy. Reasons considered for this poor performance included degeneration of cells during transit and distribution of cells within the stool specimen. The authors concluded that microscopy for fecal leukocytes using a cut-off of 1 cell/HPF was about 20% better than a coin toss for detecting inflamed mucosa. Based on increased sensitivity and ease of use, the *LEUKO EZ VUE* test offers an improved method for detecting fecal leukocytes.

In a study from Lima, Peru, fecal leukocytes and fecal lactoferrin were evaluated as markers of inflammatory responses in children infected with different pathotypes of diarrhea-causing *Escherichia coli*.[13] The study was performed to learn more about the inflammatory response elicited by *E. coli* in symptomatic children compared to children who carried these pathotypes asymptomatically. Fecal smears stained with methylene blue were evaluated by skilled technicians for the presence of leukocytes. The *LEUKO EZ VUE* test was used to detect elevated fecal lactoferrin. There were 626 diarrhea episodes, with 72.7% considered mild, 25.6% considered moderate, and 1.8% considered severe. In 99 selected samples analyzed for fecal lactoferrin, 11 samples had high numbers of fecal leukocytes and all were lactoferrin positive. There were 88 samples with lower levels of leukocytes and 83 of these were positive for elevated lactoferrin. The presence of inflammation, as noted by fecal leukocytes and fecal lactoferrin, was associated with enterotoxigenic *E. coli*, indicating that this pathogen was associated with more inflammation than previously recognized.

A study performed at a medical center in Seoul, South Korea evaluated the utility of fecal lactoferrin and multiplex PCR in patients with moderate to severe diarrhea.[14] A total of 54 patients were included in the study. The results showed that fecal lactoferrin was more accurate than microscopy for detecting fecal leukocytes. This conclusion was based on the positive association of fecal lactoferrin with moderate to severe dehydration and the detection of bacterial pathogens by multiplex PCR. These observations corroborate those of Chen *et al.*[16] who showed that fecal lactoferrin correlated with bacterial infection and greater disease severity in children. The authors noted also that these results extend the utility of fecal lactoferrin testing beyond the scope of differentiation of inflammatory bowel disease from irritable bowel syndrome, to utility as a marker for severe dehydration and acute diarrhea associated with *C. difficile, Salmonella, Campylobacter,* and other bacteria that cause intestinal inflammation. This utility can be particularly useful in helping determine the etiology of infectious diarrhea when using multiplex molecular panels which report positive results for multiple pathogens up to 40% of the time.[16]

KEY POINTS

- The *LEUKO EZ VUE* test offers an easier method for detecting fecal leukocytes compared to microscopy
- The *LEUKO EZ VUE* test is not affected by lysed and degraded leukocytes, making it more accurate
- Specimens being tested for elevated lactoferrin may be stored at room temperature for 2 weeks before testing[17]

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17. LEUKO EZ VUE® Package Insert

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