Lactic Acidosis in Patients With Cancer

Jeanne Held-Warmkessel, MSN, RN, ACNS-BC, AOCN®, and Deena Damsky Dell, MSN, RN-BC, AOCN®, LNC

Lactic acidosis is the most common metabolic acidosis in hospitalized patients—the result from an underlying pathogenic process. To successfully manage lactic acid production, its cause needs to be eliminated. Patients with cancer have many risk factors for developing lactic acidosis, including the cancer diagnosis itself. Patients with lactic acidosis are critically ill, requiring an intense level of nursing care with accompanying frequent cardiopulmonary and renal assessments. The mortality rate from lactic acidosis is high. Therefore, appropriate nursing interventions may include end-of-life and palliative care.

Lactate Metabolism

LA is constantly produced by the cytoplasm of almost all of the cells, particularly the red blood, brain, gut, and skin cells. LA is a normal end product of glucose metabolism via the anaerobic glycolytic pathway. When adequate oxygen and nutrition reach the cells, they obtain their needed energy from the glycolic production of pyruvate, the end product of glycolysis. The pyruvate is converted to acetyl coenzyme A (CoA) by the enzyme pyruvate dehydrogenase. Thiamine is needed as a cofactor for this reaction. The acetyl-CoA enters the cell’s mitochondria and joins in the tricarboxylic acid cycle (TAC), or Krebs cycle.

Thirty-six molecules of adenosine triphosphate (ATP) are produced from one molecule of glucose. If no oxygen is available, the TAC cycle does not proceed, and energy is obtained by converting pyruvate to LA by the enzyme lactate dehydrogenase in the presence of nicotinic acid dehydrogenase (NADH). That anaerobic process only produces four molecules of ATP per molecule of glucose, which dramatically decreases the amount of ATP available to cells (Brandis, n.d.; Emmett, 2013; Gunnerson, 2013; Nandwani, Saluja, Yats, & Mehta, 2010; Ruiz et al., 2011) (see Figure 1).

LA is transported by the blood, primarily to the liver (60%-90%) and kidneys (30%), as well as heart and other tissues, where it is metabolized back to glucose (gluconeogenesis) (Brandis, n.d.; Emmett, 2013; Ruiz, 2011). Two molecules of LA produce one molecule of glucose. This process is referred to as the Cori cycle, and normally results in a balance between the production and use of LA (Brandis, n.d.; Emmett, 2013; Nandwani, Saluja, Yats, & Mehta, 2010; Ruiz et al., 2011). The prevailing theory that explains this increase is referred to as the WARBURG effect, which states that cancer cells engage in anaerobic metabolism of glucose even when oxygen is present. The Warburg effect is most strongly associated with lymphoma and leukemia (Martinez-Outschoorn, 2013; Ruiz et al., 2011).

Other mechanisms that may contribute to the development of lactic acidosis in patients with cancer are decreased ability to clear lactate from the liver because of the presence of cancer, overproduction of lactate caused by thiamine and/or riboflavin deficiencies, and embolization of the microvasculature by malignant cells (Emmett, 2013; Ruiz et al., 2011). Patients with cancer also are prone to sepsis, which may cause impaired tissue perfusion with anaerobic metabolism (Blomkalsn, 2007; Dell, 2014).

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Lactic acidosis is the result of an underlying pathogenic process. Elimination of the etiology is necessary to successfully manage LA production (Wiederkehr & Emmett, 2014). When the stimulus prompting lactic acidosis is corrected or eliminated, lactate is oxidized, the bicarbonate level will increase, and the acidosis will be corrected (Wiederkehr & Emmett, 2014).

After diagnosis of lactic acidosis, the patient’s routine medication list needs to be examined. A large number of medications have the ability to cause lactic acidosis in patients (see Table 1). When a medication is implicated as a possible cause, the medication needs to be discontinued and/or not administered in the future (Liamis et al., 2010). If the patient is receiving total parenteral nutrition, the addition of thiamine will delivery of oxygen to the cells. This can result from overproduction of lactate, secondary to circulatory, pulmonary, or hemoglobin transfer illnesses. It can also result from decreased use of lactate (as in liver disease), inhibition of gluconeogenesis, or thiamine deficiency. In Type B lactic acidosis, impaired delivery of oxygen does not exist or cannot be established. Therefore, Type B lactic acidosis may be because of underlying disease (classified as Type B1), medications or toxins (classified as Type B2), or inborn errors of metabolism (classified as Type B3) (Cohen, 1976; Gunnerson, 2013; Nandwani et al., 2010).

### Diagnostic Laboratory Testing
Lactic acidosis is diagnosed by an elevated LA level in the serum. A common cause of lactic acidosis is the result of an underlying pathogenic process. Elimination of the etiology is necessary to successfully manage LA production (Wiederkehr & Emmett, 2014). When the stimulus prompting lactic acidosis is corrected or eliminated, lactate is oxidized, the bicarbonate level will increase, and the acidosis will be corrected (Wiederkehr & Emmett, 2014). After diagnosis of lactic acidosis, the patient’s routine medication list needs to be examined. A large number of medications have the ability to cause lactic acidosis in patients (see Table 1). When a medication is implicated as a possible cause, the medication needs to be discontinued and/or not administered in the future (Liamis et al., 2010). If the patient is receiving total parenteral nutrition, the addition of thiamine will delivery of oxygen to the cells. This can result from overproduction of lactate, secondary to circulatory, pulmonary, or hemoglobin transfer illnesses. It can also result from decreased use of lactate (as in liver disease), inhibition of gluconeogenesis, or thiamine deficiency. In Type B lactic acidosis, impaired delivery of oxygen does not exist or cannot be established. Therefore, Type B lactic acidosis may be because of underlying disease (classified as Type B1), medications or toxins (classified as Type B2), or inborn errors of metabolism (classified as Type B3) (Cohen, 1976; Gunnerson, 2013; Nandwani et al., 2010).

### Pathogenesis
Excess lactate can result from increased production or decreased metabolism. This can occur from excess pyruvate formation, decreased entry of the pyruvate into the mitochondria, or an increase in NADH production, which increases the ratio of lactate to pyruvate (Emmett, 2013). In an otherwise healthy person, the rate of lactate use increases to counterbalance the lactate production imbalance that could be caused by vigorous exercise or a grand mal seizure. However, when lactate increases because of catecholamines-stimulating glycolysis—as in septic shock—mechanisms, such as impaired hepatic clearance, decrease the use of LA and lactic acidosis occurs (Emmett, 2013).

### Classifications
Lactic acidosis is classified as Type A or Type B. Type A occurs when reduced tissue perfusion results in impaired delivery of oxygen to the cells. This can result from overproduction of lactate, secondary to circulatory, pulmonary, or hemoglobin transfer illnesses. It can also result from decreased use of lactate (as in liver disease), inhibition of gluconeogenesis, or thiamine deficiency. In Type B lactic acidosis, impaired delivery of oxygen does not exist or cannot be established. Therefore, Type B lactic acidosis may be because of underlying disease (classified as Type B1), medications or toxins (classified as Type B2), or inborn errors of metabolism (classified as Type B3) (Cohen, 1976; Gunnerson, 2013; Nandwani et al., 2010).

### Table 1. Common Causes of Lactic Acidosis in Patients With Cancer

<table>
<thead>
<tr>
<th>Type</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Tissue hypoxia, Severe anemia</td>
</tr>
<tr>
<td></td>
<td>Tissue hypoperfusion, Cardiogenic, hemorrhagic, or septic shock; hypotension; heart failure; regional hypoperfusion (e.g., limb or mesenteric ischemia); cardiopulmonary arrest</td>
</tr>
<tr>
<td>B1</td>
<td>Type B1, Ketoacidosis; leukemia; lymphoma; AIDS; chronic severe alcoholism; thiamine deficiency; hepatic or renal dysfunction; pheochromocytoma; seizures</td>
</tr>
<tr>
<td>B2</td>
<td>Type B2, Acetaminophen; antiretrovirals; beta-antagonists (e.g., epinephrine, terbutaline); biquanides (e.g., phenformin, metformin); cyanide-containing drugs (e.g., nitroprusside); 5-fluorouracil; propofol; salicylates; sulfasalazine; valproic acid</td>
</tr>
<tr>
<td>B3</td>
<td>Type B3, Congenital inborn errors in metabolism (e.g., pyruvate dehydrogenase orpyruvate carboxylase deficiency)</td>
</tr>
</tbody>
</table>

*Note. Based on information from Brandis, n.d.; Emmett, 2013; Gunnerson, 2013; Nandwani et al., 2010.*
reduce the risk of lactic acidosis (Nandwani et al., 2010).

When lactic acidosis is caused by low circulating blood volume or is cardiac related, hydration and restoration of cardiac output with improving oxygen delivery to the tissues will reduce acidosis (Nandwani et al., 2010). Infectious causes also are treated with antibiotics (Nandwani et al., 2010). If vasopressors are required to treat hypovolemia, hydrate the patient before his or her initiation because vasopressors exacerbate acidosis (Nandwani et al., 2010).

Conflicting evidence exists related to sodium bicarbonate therapy as treatment of lactic acidosis because few clinical trials demonstrate safety and efficacy (Nandwani et al., 2010). Mortality may be increased by the use of sodium bicarbonate (Kim, Son, & An, 2013). Therefore, sodium bicarbonate therapy should be used judiciously in patients with lactic acidosis because it may actually increase LA production and make the acidosis worse (Wiederkehr & Emmett, 2014) (see Figure 2). Occasionally, fluid volume excess or renal impairment can be managed by dialysis (Nandwani et al., 2010). Other methods to manage lactic acidosis—such as other buffers—have not been established.

Implications for Nursing and Conclusion

Patients with lactic acidosis are critically ill and require an intensive care unit-level of nursing care. Frequent cardiopulmonary and renal assessments are required. Signs of lactic acidosis include tachycardia, tachypnea, and dyspnea (Liamis et al., 2010). Patient management includes maintaining blood pressure, cardiac output, renal function, and ventilation. Interventions include hydration, vasopressors, and intubation with ventilation. To manage sepsis, healthcare providers should order antibiotic therapy. The mortality rate from lactic acidosis is high. Therefore, initiating end-of-life and palliative care may be appropriate because many patients may not survive this metabolic derangement.

References


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