



Saint Luke's Regional Laboratories Clinical Laboratory Letter

May 2012

Correction of INR with Plasma

In September 2004, Saint Luke's Regional Laboratories published guidelines for the correction of the INR with plasma infusion. At that time, our blood collection agencies supplied us with Fresh Frozen Plasma (FFP). This product was prepared by separating whole blood and freezing the plasma within 8 hours. Because of the logistical difficulties encountered with transporting and processing of blood from remote mobile collection sites, FFP has been replaced by plasma frozen within 24 hours (FP24). Compared to FFP, FP24 has approximately 20% less of the labile coagulation factors, V and VIII. Because of this major change, the laboratory has reevaluated the correction of prolonged INR's by FP24.

Often times, plasma is ordered prophylactically to rapidly correct an elevated INR in a patient receiving Coumadin therapy prior to an invasive procedure. The INR results of 227 nonbleeding patients, who were transfused with plasma only, were analyzed between Oct 25, 2011 and May 16, 2012.

Pre-transfusion INR	INR Correction per Plasma Unit
1.0 – 1.5	0 – 0.1
1.6 – 1.8	0 – 0.3
1.9 – 2.6	0.1 – 0.5
2.7 – 4.9	0.3 – 1.1
5.0 – 9.9	0.8 – 2.5
10.0 – 14.0	4.0 – 6.0
14.1 – 20.0	5.8 – 8.4

These results were almost identical to those obtained in 2004. The longer the pre-transfusion INR, the greater the correction achieved with a single unit of plasma. An INR of 12 can usually be corrected to an INR of 2 with only 2 bags of plasma. Whereas, as many as 4 bags of plasma

may be necessary to correct an INR of 1.8 to less than 1.5. When the INR is 1.8 or less, transfusion of plasma corrects INR an average of only 0.1 per unit transfused, largely because the INR of blood bank plasma itself ranges between 1.1 and 1.3. The difference in coagulation activity between donor plasma and patient plasma is so small that plasma transfusions produce minimal demonstrable effect on the patient's INR.

Physicians performing invasive procedures want to avoid hemorrhagic complications and often regard a mild elevation of a coagulation test result as an indication to order plasma. The decision to prophylactically transfuse plasma is based on two unproven assumptions:

1. Mild prolongation of PT/INR (defined as an INR <1.8) predicts bleeding from an invasive procedure
2. Prophylactic plasma transfusions result in fewer bleeding events

An analysis of the Vitamin K dependent coagulation factors at different INR values clearly contradicts the first assumption. As seen in the following table, vitamin K dependent coagulation factors still average 50% of normal at an INR of 1.8. Minimal hemostatic concentration (MHC) of each factor is not reached until the INR increases to 2.8.

INR	FII (%)	FVII (%)	FIX (%)	FX (%)
1.5	60	100	120	90
1.8	50	50	60	25
2.0	40	40	60	20
2.3	40	40	40	15
2.5	25	35	40	15
2.8	20	25	35	15
MHC	20-40	10-20	25-50	10-25

These results explain why a mildly elevated INR is not usually associated with spontaneous hemorrhage and does not increase the risk of bleeding during routine invasive procedures. Studies during the last 20 years in patients undergoing liver biopsies, bronchoscopic biopsies, renal biopsies, central line vein cannulation, thoracentesis and angiography have repeatedly demonstrated that INR and PTT are not predictive of hemorrhage. While a patient with an INR of 1.8 or less may bleed during an invasive procedure, the medical literature clearly demonstrates that the incidence of hemorrhage is not different from that of patients with a normal INR. However, it must be remembered that the risk of bleeding is greater if the platelet count is decreased, platelet function is abnormal, the patient has received antiplatelet medication, has experienced massive trauma or is undergoing extensive surgery.

In view of this information, the common practice of prescribing plasma to correct a mildly elevated INR prior to an invasive procedure needs to be reevaluated. It is usually not necessary or efficacious to correct an INR below 1.8 to achieve adequate hemostasis.

Absolute Neutrophil Count

The absolute neutrophil count (ANC) is equal to the product of the white blood cell count (WBC) and the fraction of polymorphonuclear cells (PMN) and band forms noted on the WBC differential analysis:

$$\text{ANC} = \text{WBC (cells/uL)} \times \%(\text{PMN} + \text{bands}) \div 100$$

Recurrent infections are the most significant consequence of neutropenia. The propensity to infection is related to the ANC level and the duration of neutropenia. Neutropenia is often categorized as mild, moderate or severe, based upon the level of ANC. Mild neutropenia corresponds to an absolute neutrophil count between 1000 and 1500/uL, moderate between 500 and 1000/uL, and severe with less than 500/uL. The risk of infection begins to increase at an ANC below 1000/uL.

Patients with an ANC <500/uL due to chemotherapy are at high risk for bacterial infection. This is particularly true in cancer patients with an ANC <100/microL for more than five days.

The most common bacteria that infect neutropenic patients are endogenous bacteria, including *Staphylococcus aureus* from the skin and Gram negative organisms from the gastrointestinal and urinary tracts. Patients receiving broad spectrum antibiotics for two weeks or more while neutropenic are more prone to infection with enteric bacteria and/or fungi, while patients with indwelling catheters or other foreign bodies are more likely to become infected with coagulase-negative staphylococci.

Common sites of infection include the oral cavity and mucous membranes, skin, perirectal and genital areas. The primary source of bacteremia is chemotherapy-induced mucositis and breaks in the gastrointestinal lining. Isolated neutropenia does not increase the susceptibility to viral or parasitic infection.

Airline Drinking Water Safety Alert!

In October 2011, an Aircraft Drinking Water Rule (ADWR) went into effect. This rule is a result of investigations beginning approximately 10 years ago that repeatedly showed contamination of domestic airline potable water systems with coliform bacteria. The coliform bacteria group includes *E. coli*, *Klebsiella*, *Enterobacter*, *Citrobacter*, *Hafnia* and *Serratia*. The presence of these bacteria indicates poor water quality and may indicate the presence of other enteric pathogens including *Salmonella*, *Shigella*, *Cryptosporidium* and *Giardia*.

The ADWR requires that every aircraft undergoes annual water testing that includes a minimum of two samples taken from both galley & lavatory sources. A positive test indicates that coliform bacteria, including potential pathogens are present. The safety of airline drinking water is currently monitored by no less than 3 Federal agencies, including the FAA, FDA, and EPA. Some have recommended that immunocompromised passengers should request only canned drinks or bottled water & avoid coffee or tea made with tap water. Of note, ice is usually supplied by a caterer and not made on the aircraft.