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## Fresh Frozen Plasma

Fresh frozen plasma (FFP) is one of the time honored products maintained within our blood banks. Traditionally, it has been used to correct deficiencies of serum procoagulants, associated with abnormal bleeding. Now, we are faced with an additional choice. Many large, blood collection centers are suggesting substituting a new product, frozen plasma collected within 24 hours (FP24), for our old familiar standby FFP. Review of available information will hopefully shed light on this option.

The new plasma product FP24, gives blood collection centers 24 hours to freeze collected donor plasma, as opposed to an 8 hour freezing requirement for traditional FFP. This in turn, allows these facilities more flexibility in managing plasma inventories; a situation recently made more difficult by the desire to avoid multiparous, female plasma donors in an attempt to reduce the incidence of transfusion-related acute lung injury (TRALI). It also allows more FP24 to be made available for all potential recipients. Thus, advantages should theoretically ensue to all our medical communities with the replacement of FFP by FP24.

Many recent studies in the medical literature have shown that FP24 and FFP have similar levels of coagulation factors and clinically relevant plasma proteins with the exception of F VIII, which is characteristically about 25% lower in FP24 than in FFP. These lower levels of F VIII found within FP24 are felt adequate to treat multiple coagulation factor deficiencies as seen in DIC and liver disease, as 20% levels of FVIII are considered hemostatic in these patients. F VIII levels in these plasma products are not clinically relevant in patients with isolated F VIII deficiency (hemophilia A); because currently, virally inactivated, recombinant clot-

ting factor concentrates are readily available for F VIII. Neither FFP or FP24 are indicated for use in hemophilia A, and these two products (FFP and FP24) are thus virtually interchangeable therapeutically. These indications are summarized below:

- 1) Correction of multiple coagulation factor deficiencies as seen in:
  - Severe liver disease.
  - Disseminated intravascular coagulation (DIC).
  - Dilutional coagulopathy associated with massive transfusion.
  - Vitamin K / Coumadin reversal.
  - Neonates / Children (reconstitution for whole blood exchange)
- 2) Replacement of select coagulation factor deficiencies in which specific concentrates are not available.
- 3) Replacement of plasma protein deficiencies (AT III, Protein C, Protein S) in which specific concentrates are not available.
- 4) Plasma infusion in Thrombotic Thrombocytopenia Purpura (TTP) or Hemolytic Uremia Syndrome (HUS).

Clinicians will soon begin seeing some units of FP24 when ordering FFP. Based on the above medical data, our hospital blood banks will handle these products as being interchangeable.

#### References:

Katz L., Kiss J. Plasma for transfusion in the era of transfusion – related acute lung injury mitigation. *Transfusion* 2008; 48: 393-397.

-J.S.

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Pathology Associates of the Roaring Fork Valley is pleased to announce that we are now participating with Blue Cross Blue Shield of Colorado. Effective July 1, 2009, we are able to accept BCBS members.

# Laboratory Detection of Date Rape Drug

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Questions have recently arisen concerning laboratory testing for the “date rape drugs”. The most common of these is flunitrazepam / Rohypnol, an ultra short acting benzodiazepine. Although this drug is available in Europe and Asia, where it is sometimes used for recalcitrant insomnia, it has not been approved by the FDA, and is thus considered to be an illegal drug in the US.

The prevalence of the date rape drugs is very difficult to ascertain. Many anecdotal reports suggest their infrequent use, but difficulties in laboratory identification of flunitrazepam make these data less than robust. A British study found no instances of flunitrazepam in 75 patients who reported spiked drinks. They felt alcohol abuse was much more problematic in this patient population. Toxicology fellows at the Rocky Mountain Poison and Drug Center in Denver echoed the UK data, saying that in Colorado nearly all cases of alleged “spiked drinks” are found to be associated with very high alcohol levels, in patient blood, without flunitrazepam detected.

The laboratory identification of flunitrazepam / Rohypnol is difficult. The drug is naturally present in the serum in very low levels. It is largely metabolized to 7-amino flunitrazepam, which is generally present in urine for approximately 72 hours after ingestion, an often small time window in these emotionally difficult cases. Adding to the problems in detection of these drugs are the antibody based (immunoassay) urine drug tests routinely used by our hospital laboratories. These all test for several classes of drugs, such as benzodiazepines, based on a monoclonal antibody, generally raised against the most prominent drug of the class, i.e. diazepam. Obviously as the drug of interest deviates from the parent compound, the affinity of our identifying antibody to the drug in question decreases, and detection of the drug is consequently impaired.

The pharmacokinetics of Rohypnol result in the following scenario: A typical 1 or 2 mg dose is rapidly absorbed orally, resulting in a typical

serum level of 5-10 ng/ml. Stated sensitivity of urine testing for one of our commonly used laboratory methods is 350 ng/ml for a positive result, with an even higher detection limit for the metabolite. This level of urine sensitivity makes detection unlikely.

With the above considerations in mind, how should we proceed in our own medical community?

- 1) Consider the possibility of flunitrazepam / Rohypnol in alleged cases of date rape. Unfortunately its use may also be increasing among high school and college students. It is also used by heroin and cocaine devotees.
- 2) Obtain blood and urine samples from the patient ASAP. Flunitrazepam is generally reported to be detectable in urine for 72 hours after ingestion. A recent report notes its possible presence for up to 5 days.
- 3) Consider that a negative benzodiazepine screen at any of our hospital laboratories, by standard methods, does not exclude the presence of flunitrazepam / Rohypnol. Also consider that, although Rohypnol is the most common, it is not the only, date rape drug.
- 4) Whenever clinical considerations suggest the possibility of flunitrazepam / Rohypnol use, laboratory testing, specific for the drug must be obtained.
- 5) Reference laboratories which perform gas chromatography methods are able to identify much lower levels of the drug than can our hospital based toxicology screening methods. And, as an illegal drug in the US the mere presence of flunitrazepam / Rohypnol is of great significance for our patients without need for further quantitation.
- 6) In alleged cases of date rape, the Denver based Rocky Mountain Poison and Drug Center recommends that the Colorado State Crime lab be enlisted for aid in identifying these drugs.

—J.S.