

## Influence of Etamsylate on Centrifugation Process: A Clinical Laboratory Case Series

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**Abstract:** Centrifugation is a routine process performed in the clinical laboratory to separate serum and plasma from whole blood for analyte testing. Drug interaction in laboratory testing is a frequently observed problem. In this study, we have noticed a hemostatic drug, Etamsylate which influences in centrifugation process. In our case series we have elaborated on the difficulty in separation of serum after centrifugation which we noticed in our clinical laboratory in patients who had a positive history of intake of drug Etamsylate for various reasons. We correlated the improvement of serum separation with the levels of Etamsylate in plasma in these patients and have presented our findings in the form of case series report in this study.

**Keywords:** Etamsylate, Centrifugation, serum, plasma

### INTRODUCTION

Centrifugation is the process which uses centrifugal force to separate particles suspended in the liquid medium. The suspension to be centrifuged is placed in centrifuge tube, then it kept in a rotor and rotates at a definitive speed [1]. The type of instrument used for centrifugation is known as centrifuge. There are different types of centrifuges are available. In most of the clinical laboratories including ours, horizontal head swinging bucket rotor centrifuge is commonly used for separating serum or plasma from whole blood. Centrifugation is a routine process performed in the clinical laboratory to separate serum and plasma from whole blood for analyte testing.

The collected sample is allowed to stand at room temperature without disturbing for 15-30 mins to enable clotting. The clot is removed by centrifugation at 2500 revolutions per minute (rpm) for 15 minutes. The liquid portion of whole blood obtained after clotting is known as serum.

Etamsylate, a drug commonly used in clinical practice for hemostatis. It is indicated in certain clinical conditions like menorrhagia, postpartum hemorrhage, hematemeses, melena, hemoptysis and minor surgical procedures such as tooth extraction, abortion. It has an antihyaluronidase and proaggregant action. It increases thrombopoiesis and activates the formation of thromboplastin from the damaged blood vessels. It reduces the synthesis of prostacyclin I<sub>2</sub> (P<sub>g</sub>I<sub>2</sub>). It also facilitates aggregation and adhesion of platelets, thereby reduces the hemorrhage [2,3]. A study done by Alvarez-Gurrere M et al. suggest that Etamsylate increases the expression of P-Selectin, a cell adhesion molecule in human platelets and endothelial cell membranes, thereby improves platelet adhesiveness and restores capillary resistance [4]. In clinical laboratory, analyte testing process is influenced by many factors. One among them is drug interaction in analyte testing [5]. In

our case series we have elaborated on the difficulty in separation of serum after centrifugation which we noticed in our clinical laboratory in patients who had a positive history of intake of drug Etamsylate for various reasons. We correlated the improvement of serum separation with the levels of Etamsylate in plasma in these patients and have presented our findings in the form of case series report in this study.

### CASE SERIES

This study was conducted at Sree Balaji Medical College & Hospital, Chennai from June 2017 to August 2017. These findings were noted in our daily routine in the department of biochemistry central laboratory.

Our laboratory protocol involves the collection of whole blood by phlebotomists in plain vacutainers and then post transport to our department they are allowed to clot at room temperature for 15 minutes following which we centrifuge the samples at 2500rpm for 15 minutes. The separated serum is utilized for routine analysis.

In the following cases also the same protocol was followed. But even after repeated centrifugation and repeat sample request the centrifugation process failed to yield separated serum. The cases were recalled for full detailed history analysis and the following was found.

**Case 1**

A 45 year old female came to our hospital for master health check up. Blood was collected and centrifuged at 2500 rpm for 15 minutes. Serum was not separated. Again we centrifuged the sample at 2500 rpm for another 5minutes. Again serum was not separated. Repeat sample was collected from the patient. Again serum was not separated after centrifugation. Detailed history was collected from the patient, she revealed that she had a history of menorrhagia for 2 days. For which she had come to the hospital where she received Tab. Etamsylate 500mg stat dose. She has given blood sample within half an hour of taking the tablet.

**Case 2**

A 37 years male patient had come to the casualty department with complaints of pain abdomen for three days and one episode of hemoptysis in the morning. Blood sample sent from the casualty for routine blood investigations. When the patient sample was centrifuged, serum was not separated. On detailed patient history, he revealed the history of intake of

Etamsylate 500mg tablet stat.and he has given sample within two hours of stat dose.

**Case 3**

A 25 year old male had come with history of dental caries, tooth extraction was done to the patient. Blood was sent to the laboratory for routine blood investigations. Again serum sample was not separated after centrifugation. On detailed patient analysis, he has given the history of taking tablet Etamsylate 500 mg stat dose before the procedure.

These patients when they had taken a stat dosage of 500mg Etamsylate on another occasion 2 venous samples were collected at half an hour post stat dose [1] then after 5 hours [2] and then after 24 hours(3) and finally after 48 hours(4). The samples collected were one in plain tube and another in heparinized tubes. Plain tubes (A1,2,3,4) were allowed to clot according to protocol and then centrifuged at 2500rpm for 15 mins. The other heparinized tubes (B1,2,3,4) were centrifuged at 3000rpm for 10 mins and plasma separated.

The separated plasma was used to estimate Etamsylate using high performance liquid chromatography method. And the findings of serum separation were correlated with plasma levels and post elimination of the drug.

**Table-1: Correlation between Plasma Levels of Etamsylate and Serum Separation**

S.NO.	TIME OF SAMPLING AFTER STAT DOSE	DRUG CONCENTRATION	SERUM SEPERATION
1	30 mins	2 µg/mL	No separation A1
2	5 hours	9 µg/mL	No separation A2
3	24 hours	3 µg/mL	Partial separation A3
4	48 hours	Nil	Full separation A4



**Image-1: No serum separation**



**Image-2: Serum separation after 48 hours**

## DISCUSSION

Etamsylate, an angioprotective and antihemorrhagic drug, which acts in the initial step of hemostasis (platelet – endothelium interaction). By enhancing the expression of a cell adhesion molecule, P-Selectin in platelets and endothelial cells, it improves the platelet adhesion and restores capillary resistance. This results in decreased bleeding time and blood loss. It is one of the most commonest drug prescribed in clinical practice for several medical conditions [6]. It is completely absorbed from the gastrointestinal tract, reaches peak concentration within 4 hours of ingestion and 70% of the drug is excreted in 24hrs and 100% of the drug is completely excreted in urine within 48 hours. The binding rate of plasma proteins is 95% [7,8].

In clinical laboratory processes, drug interference on analyte testing is common. Several studies also reported some of the drugs interfere in the testing of particular analyte [5]. To best of our knowledge, no study reported about a drug which interferes in centrifugation process itself. This is the first study to report about the drug Etamsylate interfering in serum separation. We found that in all the above mentioned cases, the serum of the patient was not separated while centrifugation. When we enquired with the patient, we found that all the 3 patients was taken Tab etamsylate 500 mg stat dose and given sample. We also found that this patient was not having any type of coagulopathies. No other medical illness was also present at the time of sample collection and also no other drugs were taken, the only drug they have taken before sample collection is Etamsylate. Hence we have decided to find out the correlation between the plasma concentration of etamsylate and serum separation time by High performance liquid chromatography. After 24 hours of the stat dose, we collected new sample from the patient and processed. Surprisingly there was minimal separation of serum. After 48 hours, serum was separated normally during centrifugation. This also correlated well with the pharmacokinetics of the drug with proper serum separation after complete elimination of the drug from the system. But the exact mechanism behind etamsylate and its influence on serum separation is not known.

## CONCLUSION

Our study concluded that Etamsylate is influencing in serum separation. Drug history is a main factor to be rule out during blood collection. Because it can affect even in centrifugation process. These drug interferences can be minimised with help of using serum separator gel tubes instead of using plain tubes. Future large scale studies are needed to prove the mechanism behind the influence of etamsylate on serum separation.

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