

Does Visual Turbidity Correlate With Serum Triglyceride Levels in Babies on Total Parenteral Nutrition?

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Abstract

Introduction: Intravenous lipid is commonly used as part of total parenteral nutrition (TPN) in premature babies. The gold standard of measuring lipid tolerance involves measuring serum triglyceride levels. Many hospitals in Asia do not have this facility and rely on visual turbidity to titrate the rate of lipid infusion. The aim of this study was to determine if visual turbidity correlates with serum triglyceride levels. **Materials and Methods:** Twenty-seven samples were taken from 8 babies on intravenous (IV) lipid infusion for the analysis of serum triglyceride levels and visual turbidity (assessed by 2 senior neonatologists independently). Serum turbidity was classified either as clear or turbid. Lipid intolerance was defined as triglyceride levels greater than 200 mg/dL (2.25 mmol/L). **Results:** Both neonatologists similarly classified 20 out of 27 specimens. Serum triglyceride levels for clear samples (n = 10) were significantly lower than those for turbid samples (n = 10) ($P < 0.01$). The clear specimens all had normal serum triglyceride levels (mean, 1.16 mmol/L; range, 0.43 to 1.96). Not all turbid specimens had unacceptable serum triglyceride levels (mean, 2.37 mmol/L; range, 1.37 to 5.75). In the remaining 7 specimens, there was a difference in opinion regarding serum turbidity. The triglyceride levels for these 7 samples were all normal (mean, 1.17 mmol/L; range, 0.66 to 1.72). **Conclusion:** Serum turbidity may be used as a screening tool in assessing lipid tolerance in babies on TPN as all clear samples had acceptable serum triglyceride level if we set the maximum cutoff at 2.25mmol/L. Patients with turbid samples should ideally have their serum triglyceride taken to confirm lipid intolerance before altering their lipid infusion rate as they may have acceptable triglyceride levels.

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Introduction

Intravenous lipid infusion is commonly used as part of total parenteral nutrition (TPN) in newborn babies. Upon infusion, it forms an emulsion that resembles endogenously produced chylomicrons. These chylomicrons are large lipoproteins (80 to 500 nm) consisting mainly of triglycerides that are hydrolysed by the enzyme lipoprotein lipase. Lipid intolerance occurs when the rate of lipid infusion overwhelms this enzyme's activity. This results in an increased level of circulating chylomicrons, which is believed to increase serum turbidity.

Ideally, the serum triglyceride levels of babies on intravenous lipid infusion should be monitored, and infusion rates adjusted to maintain a maximum triglyceride levels between 150 and 200 mg/dL (1.7 to 2.25 mmol/L).¹

However, not all centres may have the advantage of this facility. As such, simpler and less costly alternative tracking tools when using intravenous lipids should be made available for such centres, as it would be necessary to avoid hyperlipidaemia.

Numerous studies have shown that severe hyperlipidaemia has detrimental effects on these growing babies.² The aim of this study was to assess the validity of using visual turbidity to screen for lipid intolerance in babies on intravenous lipid infusion.

Materials and Methods

All babies on TPN with intravenous (IV) lipid infusion admitted to the Singapore General Hospital Neonatal Department from 1 February 2004 to 31 March 2004 were

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recruited. The intravenous (IV) lipid infusion comprised continuous intravenous 20% medium-chain triglyceride/long-chain triglyceride infusion (lipofundin 20% MCT/LCT) over a minimum of 12 hours before blood samples were taken (this is to mimic the current practice of nurseries that uses visual turbidity as a measurement of lipid tolerance). Blood samples were taken and sent for an analysis of their serum triglyceride levels. A concurrent capillary tube was taken from the same blood specimen, centrifuged for 1 minute and given to 2 senior neonatologists (at least 5 years experience) to independently assess turbidity visually. Both neonatologists were blinded to the babies' identities, serum triglyceride levels and rate of lipid infusion, and to each other's assessment.

Samples were labelled "clear" if the samples appeared clear to both the naked eye and against a lighted background. Samples were labelled "turbid" if they appeared turbid to both the naked eye and against a lighted background. The samples were labeled "disputed" if there was a difference in opinion between the 2 neonatologists.

Analysis of results were done using SPSS for Windows version 9. Serum levels were expressed as means $\pm$ standard deviation. Comparison of continuous data was done using unpaired Student's *t*-test. Using the results of this study, 4 statistical models were generated to analyse the probability of serum triglyceride values being higher than 2.25 mmol/L (the upper limit used by most neonatal nurseries) or 1.7 mmol/L (the upper limit used by conservative nurseries).

The working hypothesis for both Model I and Model II was that "observing a turbid specimen suggests an elevated triglyceride level above the acceptable normal upper limit of 1.7 to 2.25 mmol/L (150 to 200 mg/dL)". Model I analysed only specimens determined as turbid by both neonatologists. Model II used a conservative approach and included the disputed samples as turbid samples for analysis purposes.

The working hypothesis for both Models III and IV was "observing a clear specimen suggests an elevated triglyceride level above the acceptable normal upper limit of 1.7 to 2.25 mmol/L (150 to 200 mg/dL)". Model III analysed only specimens determined as clear by both neonatologists. Model IV used a conservative approach and included disputed samples as clear for analysis purpose.

Results

A total of 27 blood samples were taken from 8 babies who were on continuous intravenous lipid (lipofundin 20% LCT/MCT) infusion. The mean gestational age at the time of inclusion of study was 30 ± 3.5 weeks (range, 29 to 35). The mean birth weight of these babies was 1277 ± 635 g (range, 415 to 2530). They were receiving between 1 g/kg over 24 hours and 3.2 g/kg over 24 hours of intravenous lipids.

Both neonatologists similarly classified 20 out of 27 specimens as clear ($n = 10$) and turbid ($n = 10$). In the remaining specimens, the neonatologists could not agree as to whether they were clear or mildly turbid. These specimens were labelled as disputed cases.

All the clear specimens had normal serum triglyceride levels (mean, 1.16 ± 0.50 mmol/L; range, 0.43 to 1.96). Not all turbid specimens had unacceptable serum triglyceride levels (mean, 2.37 ± 1.25 mmol/L; range, 1.37 to 5.75). All the disputed cases had normal serum triglyceride levels (mean, 1.17 ± 0.33 ; range, 0.66 to 1.72) (Table 1).

Triglyceride levels from the clear samples were significantly lower when compared with the turbid samples ($P < 0.01$) (Fig. 1), and when compared with the combined turbid and disputed samples ($P < 0.05$) (Fig. 2).

Results from Model I and Model II (conservative) suggest that a turbid specimen did not necessarily mean that the patient had lipid intolerance. Both models showed that observing a turbid specimen did not mean patients had a serum triglyceride level greater than 2.25 mmol/L. If a conservative level for serum triglyceride of 1.7 mmol/L was used, Model I showed some correlation with visual turbidity ($P = 0.06$). However, this observation was lost in Model II.

Interestingly, results from Model III and Model IV (conservative) suggest that a clear sample meant it was highly unlikely that the patient had lipid intolerance. In both models, observing a clear sample meant it was highly unlikely that the serum triglyceride levels were above 1.7 mmol/L.

Discussion

Many hospitals in Asia continue to use visual serum turbidity to titrate the rate of lipid infusion in babies on TPN, either because they are unable to measure serum triglyceride levels, or due to the high cost of performing this test routinely.

There have been very few studies done to review this practice of using visual turbidity to assess lipid intolerance since Schreiner et al,³ in 1979, concluded that visual estimate is an unreliable method to grade turbidity in babies on intravenous lipid infusion. Twomey and colleagues,⁴ in

Table 1. Turbidity versus Serum Triglyceride (mmol/L) Levels

Turbidity	No of patients	Mean (mmol/L)	Standard deviation	Minimum (mmol/L)	Maximum (mmol/L)
Clear	10	1.160	0.502	0.43	1.96
Turbid	10	2.377	1.251	1.37	5.75
Disputed	7	1.165	0.331	0.66	1.72

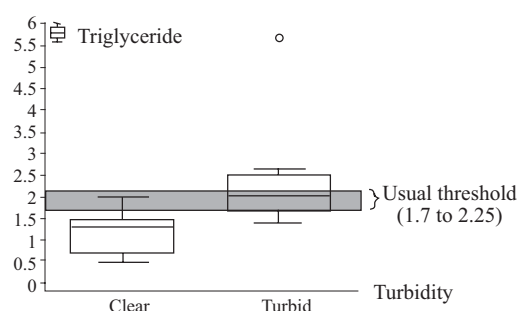


Fig. 1. Forrest plot of serum triglyceride (mmol/L) vs visual turbidity in clear vs turbid specimens.

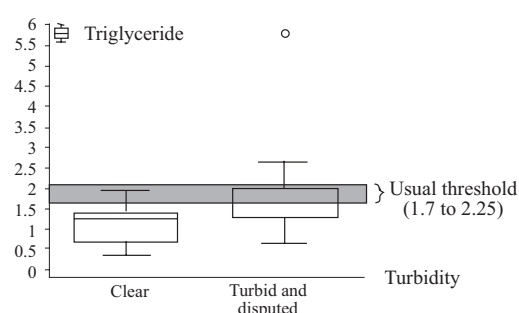


Fig. 2. Forrest plot of serum triglyceride (mmol/L) vs visual turbidity in clear vs turbid and disputed specimens.

their study, measured serum turbidity objectively using the lipaemic index. They showed good correlation of the lipaemic index and serum triglyceride levels using pooled serum specimen mixed with different concentrations of intravenous lipid infusion. This observation was lost when they attempted to correlate the lipaemic index of visually turbid specimens with serum triglyceride levels.

In our study, observing a turbid specimen did not correlate with lipid intolerance in both models (Table 2) for serum triglyceride levels above 1.7 mmol/L and 2.25 mmol/L. We concluded from this result that visual turbidity was a poor method of detecting lipid intolerance in babies on intravenous TPN as a turbid sample did not necessarily mean that the patient had significant hypertriglyceridaemia.

Interestingly, in our study, observing a clear specimen meant it was highly unlikely that the serum triglyceride level was above 1.7 mmol/L and 2.25 mmol/L in both models (Table 3). This suggest that visual turbidity may be used as a screening tool to determine which babies are at high risk of lipid intolerance. However, due to the small sample size, this observation needs to be confirmed with a larger clinical trial.

The main limitations of this study were its small sample size and lower inter-rater reliability [7/27 (26%) specimens were classified differently].

Conclusion

Serum triglyceride levels remain the gold standard of determining lipid intolerance in babies on intravenous lipid

Table 2. Observing a Turbid Specimen Did Not Mean Patient had Lipid Intolerance

	Model I	Model II (Conservative)
Hypothesis tested	Only included cases identified as "turbid" (n = 10; mean, 2.34)	Included disputed cases as "turbid" (n = 17; mean, 1.87)
Mean triglyceride >2.25 mmol/L	t = 0.321 P = 0.3778 not statistically significant	t = -1.34 P = 0.9013 not statistically significant
Mean triglyceride >1.7 mmol/L	t = 1.71 P = 0.06	t = 0.645 P = 0.264 not statistically significant

Table 3. Patients Whose Samples Were Observed to be Clear Were Unlikely to Have Lipid Intolerance

	Model III	Model IV (Conservative)
Hypothesis tested	Only included case identified as clear (n = 10; mean, 1.160)	Included disputed cases as clear (n = 17; mean, 1.162)
Mean triglyceride >2.25 mmol/L	t = -6.86 P = 1.000	t = -10.47 P = 1.000
Mean triglyceride >1.7 mmol/L	t = -3.39 P = 0.9960	t = -5.18 P = 1.000

infusion and should be used to titrate intravenous lipid infusion rates. In places where this is not available, our results suggest that serum turbidity may be used as a screening tool in assessing lipid tolerance as all clear samples had acceptable serum triglyceride level. However, this observation needs to be confirmed with a larger clinical trial. Patients with turbid samples should ideally have their serum triglyceride taken to confirm lipid intolerance before altering their lipid infusion rate as they may have acceptable triglyceride levels.

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