Terlipressin Continuous Infusion: Please Mind the Solvent!

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Sir,

Terlipressin (TP) could be an alternative treatment in refractory septic shock [1]. This drug has been used in intravenous bolus, but concerns arise about its side effects, mainly vasoconstriction [2]. Also, bolus may need to be repeated every 4-6 hours and at least one paper indicated a rebound of effects and non-stable clinical situation that might be related with intermitent doses [3].

Although current clinical data are limited and dose ranging studies have not been conducted, continuous TP infusion could be a desirable method of administration in order to titrate effects (both positive and deletereous) [1,4,5].

For continuous TP infusion, the dilution of one vial (1 mg) in 50 ml sterile saline has been recommended. The resultant siringe thus contains 0.02 mg/ml TP and an infusion rate of 1 ml/h represents 0.02 mg/h [1].

This dilution method is simple and similar to the dilution of most of our intensive care drugs but it may not be ideal for TP.

TP is stable only at a narrow pH range (3-4) (manufacturer information). This is not a problem when TP is administered by rapid bolus, but if we make up a dilution with a final pH significantly higher than 4, drug activity may be severely afected.

In order to know what the best dilution for TP is we have measured final pH when different volumes of normal saline vs. 5% glucose are added to prepare a syringe for continuous infusion therapy. The results (Table **1**) show that dilutions with normal saline are out of the desired pH range of solution. On the other hand, a simple dilution with 5% glucose maintains the final solution in the optimal pH range.

We consider that this simple but important point must be considered when TP continuous infusion is indicated and prepared. It is possible that published effects of TP continuous infusion are biased by this disturbing factor. Also, this factor should be considered when treatment protocols and clinical trials are designed.

Table 1. Resultant Solution pH after Dilution of One Reconstituted TP Vial in Two Different Solvents

Solution	pH (x + SD)*
Vial *per se*	3.03 + 0.02
5% glucose (up to 10 ml)	3.24 + 0.01
Normal saline (up to 10 ml)	4.88 + 0.03
5% glucose (up to 50 ml)	3.62 + 0.02
Normal saline (up to 50 ml)	5.50 + 0.01

* The test has been repeated 5 times.

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