

## Catheter-Related Infection (CRI) Treatment with Taurolidine - Citrate Lock Solution in Patients Undergoing Total Parenteral Nutrition

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### ABSTRACT

The use of central venous catheter (CVC) is associated with risk of catheter-related infection (CRI). They have a huge impact on healthcare costs. One of the prevention strategies of CRI is the administration of non-antibiotic lock solutions such as taurolidine. Taurolidine has been proposed as a lock therapy in CVC because of its antimicrobial effect against a broad range of microorganisms. Some authors suggest a beneficial role of taurolidine lock solution application not only for prevention of CRI but for CRI therapy too. In this paper we report six cases of patient undergoing TPN with CRI treated with taurolidine 1.35 % - citrate 4% (TC), implanted in Department of Pain Therapy - Vascular Access Device Ambulatory, (Monaldi Hospital, Naples - Italy). Patients were in Total Parenteral Nutrition (TPN) and received central (CBC) and peripheral blood culture (PBC), clinical evaluation, white blood cell (WBC) count. Patients with positive blood culture received TC every 48 hours throughout vascular access. Parenteral nutrition was suspended only during the day of TC infusion. The drug was administered until the patients didn't show no fever. In our experience, TC eradicated CRI in all six patients in a six-days therapy, interrupting the TPN only for three days. No side effects occurred. The efficacy of TC in this series of case reports has made possible to resolve all CRI with simple outpatient treatments and therefore could be a further task in the management of infective TPN complication.

**Keywords:** CVC Related Infections, Taurolidine, Parenteral Nutrition, Lock Solution

### Introduction

The use of central venous catheter (CVC) is associated with risk of colonization and infection (Mermel *et al.*, 2009); regardless of clinical implications, catheter-related infection (CRI) have a huge impact of healthcare costs (Hollenbeak, 2011). The pathophysiological mechanism of the CRI is due to the formation of a biofilm of microbial cells associated with the CVC internal lumen surface and clothed in an extracellular envelope that increase the capacity of the biofilm cells to survive (Lebeaux *et al.*, 2014a).

Therefore one of the prevention strategies of CRI is the administration of antibiotic lock solution into CVC lumen. This highly concentrated antibiotic solution dwells in the CVC not using the device, eradicating any bacteria in the lumen and preventing from spreading them into the blood stream (Lebeaux *et al.*, 2014b).

Non-antibiotic lock solutions are available such as ethanol or taurolidine. Taurolidine, a derivative of the aminoacid taurine, has been proposed as a lock therapy in CVC because of its antimicrobial effect against a broad range of microorganisms (Bradshaw and Puntis, 2008; Johnston *et al.*, 1993). Some authors suggest a beneficial role of taurolidine lock solution application not only for prevention of CRI but for CRI therapy in oncology too (Joshi and Mahajan, 2003). In this paper we report six cases of patient undergoing TPN with CRI successfully treated with taurolidine 1.35% - citrate 4% (TC).

## Materials and Methods

Six patients that received Total Parenteral Nutrition (TPN) with amino glicidic and lipidic solution were investigated for CRI. For all central (CBC) and peripheral blood culture (PBC), clinical evaluation, white blood cell count (WBC) were provided.

After CRI diagnosis TC had been administered every 48 h in the vascular access at volume of the vascular access device plus 20% (Table 1). Parenteral nutrition was suspended only for the day of TC infusion. The drug was administered up to no fever recurrence. No patients required systemic antibiotic therapy or had Metastasis or local septic complications.

**Table 1:** Device type, blood culture and taurolidine volume for every case

Case	CVC Device	Reason for nutritional support	Blood Culture		Taurolidine	
			Central	Peripheral	Volume (ml)	Nr of administrations
1	Port-a-cath	Short bowel syndrome	S. Epidermidis	S. Epidermidis	3	3
2	PICC	Bowel subocclusion	G. Adiacens	G. Adiacens	2.5	3
3	PICC	Enteral nutrition failure post sepsis Syndrome	S. Hominis	S. Hominis	2.5	3
4	Hickmann line	Short bowel syndrome	S. Epidermidis	S. Epidermidis	4	3
5	PICC	Fasting after complicated pancreasectomy	S. Epidermidis	S. Epidermidis	2.5	3
6	PICC	Short bowel syndrome	S. Epidermidis	S. Epidermidis	2.5	3

### Case 1

80 y-old, female, BMI 26 with a short bowel syndrome developed fever during TPN infusion after 10 months of Port-a-cath implant. CBC and PBC revealed the presence of S. Epidermidis. After 3 administration of TC 3 ml there were no clinical signs of CRI, and CBC and PBC negativization.

## Case 2

48 y-old, male, BMI 18. Bowel subocclusion after emicolectomy. He implanted a PICC to start HTPN. He reported fever during nutritional infusion 8 weeks from surgery. CBC and PBC reported the presence of *Granulicatella Adiacens*. After 3 administration of TC 2.5 ml there were no clinical signs of CRI, and CBC and PBC were negative.

## Case 3

78 y-old, male, BMI 29. This patient underwent emergency abdominal aortic aneurysm repair. Once moved to sub-ICU a PICC was placed to start TPN and after 10 weeks fever had been recorded. CBC and PBC showed the presence of *Staphilococcus Hominis* and 2.5 ml of TC were administered. After 3 ml there were no clinical signs of CRI, and CBC and PBC negativization.

## Case 4

46 y-old, female, BMI 17. After ileum and colon resection for Chron's disease, she was affected by short bowel syndrome. She already replaced 6 Hickmann lines used for HTPN. 12 weeks after the last Hickmann implant, she developed fever during nutritional infusion. CBC and PBC revealed the presence of *Staphilococcus Epidermidis*. 4 ml of TC were administered. After 3 administration there were no clinical sign of CRI and CBC and PBC were negative.

## Case 5

65 y-old, male, BMI 23. Patient underwent partial pancreatectomy and needed HTPN for two months. 6 weeks after PICC placement, he developed fever during nutritional infusion. CBC and PBC showed the presence of *Stafilococcus Epidermidis*. After 3 administration of TC 2.5 ml there were no clinical sign of CRI and CBC and PBC were negative

## Case 6

43 y-old, female, BMI 22. She was affected by Chron's disease and underwent emergency surgery for total colectomy due to several bowel obstructions. She was referred to our center to position a PICC and to start HTPN. After 4 months she referred fever. CBC and PBC revealed the presence of *Staphilococcus Epidermidis*. After 3 administration of TC 2.5 ml there were no clinical sign of CRI and CBC and PBC were negative.

## Results

All the patients were in HTPN, just the third one started TPN during hospital stay. The request for nutritional support were : short bowel syndrome (n=3), bowel subocclusion (n=1), enteral nutrition failure in post sepsis syndrome (n=1), fasting after complicated pancreasectomy (n=1).

The device used were : port a cath (n=1), PICC (n=4) and Hickmann line (n=1). Infection reported

from BCB and PBC were: Staphilococcus Epidermidis (n=4), Granulicatella Adiacens (n=1), Staphilococcus Hominis (n=1), TC was administered as reported in Table 1.

Fever was no more reported during nutritional solution infusion after the second TC administration in the 33% of the patients and after the third one in 100% of the patients. WBC count decreased as TC was administered. The percentage of WBC mean reduction was 5% after the first administration, 17% after the second one and 27% after the third one (Table 2).

**Table 2:** WBC reduction and temperature trend

Case nr.	Before I Administration		24 H From I Administration			24 H From II Administration			24 H From III Administration		
	WBC	Fever	WBC	Fever	% WBC reduction	WBC	Fever	% WBC reduction	WBC	Fever	% WBC reduction
1	9852	Yes	8450	Yes	-14%	7187	Yes	-27%	6722	No	-32%
2	13075	Yes	11094	Yes	-15%	9027	No	-31%	5779	No	-56%
3	14101	Yes	14386	Yes	2%	12432	Yes	-12%	11000	No	-22%
4	7568	Yes	7831	Yes	3%	7955	Yes	5%	7430	No	-2%
5	9783	Yes	9876	Yes	1%	8020	Yes	-18%	7896	No	-19%
6	13842	Yes	12791	Yes	-7%	10766	No	-22%	9380	No	-32%

Regardless of the number of administrations, none of patients reported hypersensitivity reactions, haematological manifestations or other side effects from TC.

## Conclusions

The use of CVC is associated with a risk of colonization and subsequent infection, in an European Review, bloodstream infections are the fourth case of hospital-acquired infections and the 33% of them were related to CVC (Mermel *et al.*, 2009).

Patients in TPN, especially the ones in ICU, are particularly at risk of CRI, probably due to continuous alterations in glycaemic levels with higher frequency of sustained hyperglycemia and consequent insulin use (Joshi and Mahajan, 2003). Beghetto *et al* reported TPN as independent risk factor for CVC-related infection, involving malnutrition, hyperglycemia, and severity of clinical status (Van Den Berghe *et al.*, 2001). Ball, *et al.* (2001) consider the TPN formula composition itself as a risk factor for CRI because of the contamination of particulates such as trace elements, not detected by routine microbiological methods (Ball *et al.*, 2001). Finally, the long time CVC usage for TPN counters the antimicrobial activity of chlorhexidine/silver sulfadiazine or minocycline/rifampicin catheters (Centers for Disease Control and Prevention, 2002).

Systematic administering of antibiotic lock solution into the CVC lumen to prevent CRI could increase antibiotic resistance. Guidelines recommend that the use of preventive antibiotic lock therapy should be restricted to patients with long-term intravascular catheters with multiple catheter-related

blood stream infections despite optimum aseptic techniques.

Taurolidine, a derivative of the aminoacid taurine, has been proposed as a lock therapy because of its antimicrobial effect against a broad range of microorganisms. Studies about patients receiving haemodialysis are encouraging, and data supporting its use as a lock in CVC are increasing over the time (Bradshaw and Puntis, 2008; Johnston *et al.*, 1993). Some authors suggests a beneficial role of taurolidine lock solution application too for CRI therapy spreading trough bloodstream in oncologic patients synergistically with systemic antibiotic chemotherapy, resulting in a high rate of complete recovery without replacement of the device (Joshi and Mahajan, 2003).

In our experience, TC eradicated the CRI in all six patients in a six days therapy, interrupting TPN just for three days. No side effects occurred. The lack of consensus on proper TC posology for therapeutical purpose forced us to evaluate after each administration the clinical impact of therapy. In two patients (case 2 and 6) the fever didn't occur just after two taurolidine administrations but the marked decline in WBC, still in pathologic range, suggested us to keep on a third administration.

Our usual treatment before TC would have requested the vascular device removal and, after seven days, implanting another one. Patient should have undergone two surgical procedures in few days, stop TPN for at least 6 days, and new costs for hospital personal and device.

The efficacy of TC in this case reports has made possible to treat CRI with simple outpatient treatments and therefore could be a further task in the management of infective TPN complication. The possibility of minimizing the withdrawal times of TPN is a really important advantage in these patients, although a few cases reported in our experience does not allow to reach definitive conclusions. Further studies on the routine application of TC in CRI are still needed.

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