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Taurolidine lock in the treatment of colonization and infection of totally implanted venous access devices in cancer patients

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Abstract

Background: Taurolidine lock is known to be effective in preventing catheter-related infections in a variety of venous access devices, including long term venous access devices for chemotherapy. Though, literature about the use of taurolidine for treating catheter colonization or catheter-related blood stream infection is scarce.

Method: We have retrospectively reviewed the safety and efficacy of 2% taurolidine lock for treatment of catheter-colonization and of catheter-related bloodstream infection in cancer patients with totally implanted venous access devices. Diagnosis of colonization or catheter-related infection was based on paired peripheral and central blood cultures, according to the method of Delayed Time to Positivity.

Results: We recorded 24 cases of catheter-related infection and two cases of colonization. Taurolidine lock—associated with systemic antibiotic therapy—was successful in treating all cases of catheter-related infection, with disappearance of clinical symptoms, normalization of laboratory values, and eventually negative blood cultures. Taurolidine lock was also safe and effective in treating device colonization. No adverse effect was reported.

Conclusion: In our retrospective analysis, 2% taurolidine lock was completely safe and highly effective in the treatment of both catheter-colonization and catheter-related bloodstream infection in cancer patients with totally implanted venous access devices.

Keywords

Oncology access, techniques and procedures, catheter-related bloodstream infection, catheter-colonization, taurolidine lock

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Introduction

An adequate and reliable venous access device (VAD) is integral part of the management of cancer patients. In this population, the VAD is used not only for the administration of chemotherapy but also for other purposes (supportive treatments, parenteral nutrition, hydration, or blood sampling). Therefore, current guidelines strongly recommend inserting a proper central VAD (a tunneled or non-tunneled catheter, or a totally implanted venous device) in every cancer patient undergoing treatment, with the aim of minimizing the interruption of the therapy, preserving peripheral veins, and reducing the risk of extravasation.[1,2]

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All VADs, including totally implanted devices (ports), are at risk of infection. Both catheter-colonization (CC) and catheter-related bloodstream infection (CRBSI) of VADs have a great clinical and economic impact on the management of the cancer patient, as they increase the rate of morbidity, prolong hospital stay, and increase medical costs.[3]

Colonization is the first step toward infection, and it may occur via the extraluminal or the intra-luminal route.[2] For long term devices, contaminated hubs along the infusion line are the most common source of entrance of microorganisms, by migration via the internal surface of the catheter resulting in an intra-luminal colonization.[4–6] Overgrowth of colonizing bacteria, or the selection of particularly aggressive strains, or the decrease in the immune defenses of the host, are all potential causes of a shift from colonization to infection.

Bacteria and fungi colonise the internal surface of the catheter creating a biofilm. A microbial biofilm is a structured consortium of microbial cells surrounded by a self-produced polymer matrix that includes also components from the host (fibrin, platelets, immune-globulins, etc.) and can be mono- or poly-microbial.[7–10]

Biofilm protects bacteria from the exposure to antibiotic drugs, so that the infection may persist despite adequate therapy; infections resistant to treatment and/or recurrent infections are typical indications for VAD removal.[2,11] Though, insertion of a new VAD may be sometimes difficult in patients with limited availability of veins and may be associated with transient interruption or delay of treatment.[12,13]

Antibiotic lock technique is an effective strategy for attempting to save an infected VAD. It consists in locking the catheter with a high concentration of antibiotics while it is not in use, leaving the antibiotic solution inside the lumen for an appropriate period of time. Antibiotic lock is always coupled with systemic antibiotic administration.[2] The antibiotic lock technique is recommended by current guidelines as a part of management of catheter-related infections in a few well-defined circumstances (not complicated and non-metastatic infections, when the salvage of catheter is highly required).[11] In recent times, it has been postulated to use a therapeutic lock not using an antibiotic drug, but a non-antibiotic antimicrobial agent such as taurolidine or ethanol or chelating compounds (sodium citrate, tetra-sodium-EDTA).

Taurolidine is an antimicrobial agent with a broad-spectrum activity against bacteria and fungi. It is a derivative of the aminoacid taurine and it interacts with component of the wall of the bacteria cell causing an irreversible injury. Resistance to taurolidine has never been reported at this time.[14] Many studies have documented the efficacy of taurolidine in the prevention of CRBSI[14–17] and a meta-analysis has confirmed a greater efficacy of taurolidine in the prevention of CRBSI compared with other lock solutions, even in high-risk patients, without any adverse effect.[18] Though, data about taurolidine as therapeutic lock are still scarce.

In this study on cancer patients, we have reviewed our experience with 2% taurolidine as therapeutic lock in totally implanted VADs with documented CC or CRBSI.

Patients and methods

This is a retrospective cohort study conducted in the Unit of Anesthesia, Intensive Care Medicine, and Vascular Access Team of CRO National Cancer Institute, a Clinical and Research Cancer Institute located in Aviano (PN), Italy.

This study received approval from regional ethical committee.

Intra-procedural and routine follow-up information of these cases were derived from clinical charts for all the patients who had previously given their consent to the use of clinical data for research purposes.

Twenty-six consecutive patients (14 males and 12 females) with proven CC or CR-BSI related to totally implanted VADs (ports) were found in our review.

Patients were affected by solid tumors ($n=18$), non-Hodgkin lymphoma (NHL) ($n=5$), multiple myeloma ($n=2$), and chronic lymphocytic leukemia (CLL) ($n=1$).

CR-BSI was clinically suspected on the basis of clinical signs of infection, temperature $>38°C$, chills, arterial hypotension, and/or alterations of laboratory tests as abnormal peripheral white blood count (WBC) or high procalcitonin (PCT) levels.

In patients with clinically suspected CR-BSI, peripheral blood and catheter blood samples were simultaneously collected for culture. The method of differential time to positivity (DTP) was adopted to differentiate between CC, CRBSI and bloodstream infections not related to the VAD. DTP was defined as the difference in the time it took for a blood culture drawn through the central venous catheter and a culture drawn from a peripheral vein to become positive. A catheter blood culture becoming positive at least 2 h earlier than the peripheral blood culture (same micro-organism) allows an accurate diagnosis of CRBSI.[19] When the catheter blood culture is positive, but the peripheral blood culture is negative, the diagnosis of CC is established.

In patients with documented CRBSI, the choice between conservative treatment and VAD removal was made by the medical staff, evaluating each individual case on the basis of the clinical condition, the type of germs, the presence of local signs of inflammation, the absence of metastatic or local septic complications, as well as the need of preserving the port for further chemotherapy. VAD removal was performed in all patients with pocket infection and in all patients with fungal infection.

In patients who were candidate to conservative treatment, either with proven CC or with proven CR-BSI, the

same management was adopted, that is, 2% taurolidine lock plus systemic antibiotic administration guided by the antibiogram. The therapeutic lock consisted in 3 ml of 2% taurolidine inserted into the port and left in place for 24 h; the lock solution was aspirated at the end of 24-h period before proceeding with the new taurolidine lock. This procedure was repeated for five consecutive days. On the sixth day, the device was flushed with 10 ml of normal saline and on the seventh day, a paired culture of peripheral blood and catheter blood was performed.

All patients had given informed consent for the treatment with 2% taurolidine lock.

During the week of treatment, the port was not used. A temporary central or peripheral VAD was inserted for systemic antibiotic administration and supportive treatments.

Results

We collected data from 24 patients with CRBSI documented by DTP, as well as from two patients with documented CC, all treated without VAD removal. As from the chart we reviewed, all 26 patients received the same protocol of treatment described above.

Microbial isolates from blood cultures included Escherichia coli ($n=10$), Staphylococcus epidermidis ($n=6$), Staphylococcus aureus ($n=2$), Staphylococcus haemolyticus and Staphylococcus hominis ($n=2$), Escherichia coli and Staphylococcus epidermidis ($n=1$), Clostridium perfringens ($n=1$), Staphylococcus hominis subsp. Hominis ($n=1$), Enterobacter cloacae complex ($n=1$). Microbial isolates from the blood of patients with bacterial colonization of the catheter included Staphylococcus epidermidis ($n=1$) and Pseudomonas aeruginosa ($n=1$).

The treatment protocol described above (2% taurolidine lock + systemic antibiotic therapy) was clinically effective in all cases of CRBSI or CC. Antibiotic therapy was suspended at the end of taurolidine lock treatment in all patients with regression of clinical symptoms and normalization of laboratory values, regardless of the type of germ and with documented negative blood cultures.

All patients recovered completely, with disappearance of clinical symptoms, normalization of laboratory values and eventually negative blood cultures on the seventh day. In most cases, the VAD was also subsequently used for chemotherapy, infusions and blood samples without further problems and for a variable period of time (Table 1).

Only in one case, 25 days after the treatment of an episode of CRBSI due to Escherichia coli, with eventual documented negative blood cultures, the patient had recurrent clinical symptoms of infection. Blood cultures from peripheral and central blood documented a new episode of CR-BSI from the same germ. Treatment with taurolidine lock and systemic antibiotics was repeated, with clinical success: symptoms disappeared, and blood cultures became negative. Since this episode, the VAD has been used regularly for over 4 months without any further problems.

No patient had any hypersensitivity reactions, or hematological side effects, or any organ toxicity potentially associated with the use of taurolidine. No adverse effect was reported, not event in the patient who repeated the treatment twice.

Discussion

Antibiotic lock is recommended by current guidelines as a part of management of catheter-related infections in a few well-defined circumstances.[11] As suggested by SEIMC guidelines in 2018,[20] a possible alternative to antibiotic lock is a lock with non-antibiotic antimicrobial agents, such as taurolidine.

Our experience suggests the clinical efficacy of 2% taurolidine lock for treating CC and CR-BSI of totally implanted devices in cancer patients. The synergistic action with an appropriate systemic antibiotic therapy guided by the antibiogram was associated with a high rate of complete recovery, avoiding VAD removal. Our protocol (3 ml of 2% taurolidine inside the device every 24 h for 5 days) was associated with a successful treatment of the bacterial colonization of the catheter and of the CR-BSI, as documented in the blood cultures performed 48 h after the last administration of taurolidine.

Among all cases successfully treated with our treatment protocol, there were also two patients with CRBSI caused by Staphylococcus aureus. In recent guidelines, CRBSI caused by Staphylococcus aureus is among the indications for VAD removal because antibiotic lock is expected to be ineffective.[20] In our experience, albeit limited to two cases only, 2% taurolidine lock—associated with systemic antibiotic administration—was clinically effective in the conservative treatment of CRBSI caused by Staphylococcus aureus, with disappearance of clinical symptoms, normalization of laboratory values and eventually negative blood cultures.

Taurolidine is characterized by an extraordinary broad antimicrobial activity associated with excellent tolerability in the absence of side effects and drug interactions. The absence of toxicity and drug interactions suggests the possibility of a wide use of taurolidine for treating colonization of central VADs and CR-BSIs, especially for infections by germs with marked resistance to antibiotics.

Limitations

Our study has some limitations. The first major limitation is that it is a single center experience, with a retrospective design and a small sample size. Furthermore, the study does not include a direct comparison with other possible conservative treatments (antibiotic lock or lock with other non-antibiotic agents).

Table 1. Patients with catheter colonization or CR-BSI related to totally implantable venous devices treated with taurolidine.

Patient	Sex (M/F)	Diagnosis	Days of permanence before infection	Clinical signs				Microbial isolates				Treatment	Blood culture 48 h after treatment	Days of permanence and use after taurolidine
				Fever	Chills	PCT (ng/ml)	WBC ($\times 10^9$/L)	Catheter	Time (h)	Peripheral blood	Time (h)			
1	F	Ovarian cancer	16	Yes	Yes	1.19	7.93	Staphylococcus aureus	15	Staphylococcus aureus	17	3 ml of taurolidine every 24 h for 5 days	Negative	227
2	M	NHL	863	Yes	Yes	6.49	8.64	Escherichia coli	3	Escherichia coli	9	3 ml of taurolidine every 24 h for 5 days	Negative	264
3	F	Uterine cancer	1323	Yes	No	0.60	8.80	Escherichia coli	2.8	Escherichia coli	15	3 ml of taurolidine every 24 h for 5 days	Negative	121
4	M	NHL	895	Yes	Yes	1.2	7.48	Escherichia coli	6.8	Escherichia coli	21	3 ml of taurolidine every 24 h for 5 days	Negative	232
5	M	Lung adenocarcinoma	20	Yes	Yes	0.94	28.74	Pseudomonas aeruginosa	34.4	Negative		3 ml of taurolidine every 24 h for 5 days	Negative	80
6	F	Follicular NHL + breast cancer	121	Yes	Yes	0.22	6.09	Staphylococcus epidermidis	2.8	Staphylococcus epidermidis	41.9	3 ml of taurolidine every 24 h for 5 days	Negative	150
7	F	Ovarian cancer	1367	Yes	No	0.24	4.22	Staphylococcus haemolyticus Staphylococcus hominis	9.3	Staphylococcus haemolyticus Staphylococcus hominis	15.6	3 ml of taurolidine every 24 h for 5 days	Negative	66
8	M	Multiple myeloma	410	Yes	No	0.11	0.09	Escherichia coli Staphylococcus epidermidis	7	Escherichia coli Staphylococcus epidermidis	16.3	3 ml of taurolidine every 24 h for 5 days	Negative	120
9	F	Pancreas adenocarcinoma	1155	Yes	No	16.56	7.01	Clostridium perfringens	8	Clostridium perfringens	10.6	3 ml of taurolidine every 24 h for 5 days	Negative	197
10	M	NHL	1477	Yes	Yes	0.20	13.55	Escherichia coli	7.3	Escherichia coli	15.7	3 ml of taurolidine every 24 h for 5 days	Negative	90
11	M	Testicular seminoma	150	Yes	Yes	0.19	0.64	Escherichia coli	1.3	Escherichia coli	15.6	3 ml of taurolidine every 24 h for 5 days	Negative	136
12	M	Lung adenocarcinoma	99	Yes	No	0.69	14.35	Staphylococcus hominis ss. Hominis	6.4	Staphylococcus hominis ss. hominis	13.1	3 ml of taurolidine every 24 h for 5 days	Negative	96
13	M	NHL + colon cancer	45	Yes	Yes	8.02	0.04	Staphylococcus epidermidis	18.4	Negative		3 ml of taurolidine every 24 h for 5 days	Negative	43
14	F	Nasopharyngeal carcinoma	86	Yes	Yes	20.43	1.17	Enterobacter cloacae complex	1.2	Enterobacter cloacae complex	4	3 ml of taurolidine every 24 h for 5 days	Negative	30
15	F	Breast cancer	1889	Yes	No	8.02	14.10	Escherichia coli	10.8	Escherichia coli	22.1	3 ml of taurolidine every 24 h for 5 days	Negative	30
16	F	Colon cancer + pancreas adenocarcinoma	222	Yes	Yes	1.85	14.05	Staphylococcus epidermidis	6	Staphylococcus epidermidis	15.4	3 ml of taurolidine every 24 h for 5 days	Negative	158
17	M	Multiple myeloma	1382	Yes	Yes	1.35	3.47	Staphylococcus epidermidis	5.4	Staphylococcus epidermidis	13.6	3 ml of taurolidine every 24 h for 5 days	Negative	50
18	M	Colon cancer	286	Yes	No	4.03	11.2	Escherichia coli	3.4	Escherichia coli	9.0	3 ml of taurolidine every 24 h for 5 days	Negative	187
19	F	Ovarian cancer	148	Yes	No	2.52	9.34	Staphylococcus aureus	5.4	Staphylococcus aureus	13.6	3 ml of taurolidine every 24 h for 5 days	Negative	245
20	F	Breast cancer	57	Yes	Yes	7.31	18.23	Escherichia coli	2.2	Escherichia coli	7.2	3 ml of taurolidine every 24 h for 5 days	Negative	198
21	M	Lung adenocarcinoma	124	Yes	No	3.43	6.45	Staphylococcus epidermidis	4.3	Staphylococcus epidermidis	14.2	3 ml of taurolidine every 24 h for 5 days	Negative	78
22	F	Breast cancer	58	Yes	Yes	1.51	9.23	Escherichia coli	3.2	Escherichia coli	12.3	3 ml of taurolidine every 24 h for 5 days	Negative	187
23	F	Rectal cancer	760	Yes	No	3.88	0.50	Staphylococcus hominis ss. Hominis	2.1	Staphylococcus hominis ss. Hominis	6.3	3 ml of taurolidine every 24 h for 5 days	Negative	30
24	M	NHL	73	Yes	Yes	1.93	0.36	Staphylococcus epidermidis	6,3	Staphylococcus epidermidis	11.2	3 ml of taurolidine every 24 h for 5 days	Negative	25
25	M	LLC	180	Yes	No	5.45	2.21	Escherichia coli	2.7	Escherichia coli	18.9	3 ml of taurolidine every 24 h for 5 days	Negative	145
26	M	Gastric cancer	120	Yes	Yes	8.85	3.52	Staphylococcus epidermidis	9,1	Staphylococcus epidermidis	12.2	3 ml of taurolidine every 24 h for 5 days	Negative	25

Conclusion

In cancer patients, a reliable venous access is integral part of the management. Infectious complications are not infrequent in patients undergoing chemotherapy, who may have abnormalities of the immune system. Furthermore, infection may imply VAD removal with risk of interruption or delay of the chemotherapy and with associated increase in management costs.

In our experience, 2% taurolidine lock—in association with systemic antibiotic administration—was consistently safe and effective in the treatment of CC and CR-BSI.

Declaration of conflicting interests

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