

Taurolidine versus Heparin Lock to prevent Catheter-related Bloodstream Infections in Patients on Home Parenteral Nutrition



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Home parenteral nutrition

- Main therapy for chronic intestinal failure
- Venous access: central tunneled catheter / subcutaneous port
- Main problem: catheter-related bloodstream infections (CRBSI)
 - ✓ Effect on quality of life and healthcare costs
 - ✓ determine outcomes of HPN programs
 - ✓ mainly in subset of patients
 - ✓ growth of microbes in biofilm on inner catheter surface
 - ✓ resistance to antibiotics: no penetration into biofilm
 - ✓ repeated catheter removal compromises access

Catheter-related bloodstream infections ¹

- in HPN: 0.34 episodes / catheter year

- Measures to decrease CRBSI
 - ✓ training to perform aseptic techniques
 - ✓ antimicrobial filters
 - ✓ topical antimicrobial agents
 - ✓ fibrinolytic agents (alteplase)
 - ✓ systemic antibiotics:

No measure sufficiently effective to prevent CRBSI

Taurolidine

- potent antiseptic agent
- broad spectrum activity against all bacteria and yeasts ^{1;2}
non-toxic : end-products taurine, CO₂ and water
- mechanism: reaction with microbial cell wall
prevents bacterial adhesion to biological surfaces ^{3;4}
- no reported side effects or bacterial resistance to taurolidine ⁵
- efficacy against CRBSI in hemodialysis, chemotherapy ^{1,6}

¹ Allon M, *Clin Infect Dis* 2003;36:1539

² Koldehoff M, *Int J Antimicrob Agents* 2004;24:491

³ Gorman SP, *J Appl Bacteriol* 1987;62:315

⁴ Erb F, *Eur J Drug Metab Pharmacokinet* 1983;8:163

⁵ Torres-Viera C, *Antimicrob Agents Chemother* 2000;44:1720

⁶ Yahav D, *Clin Infect Dis* 2008;47:83

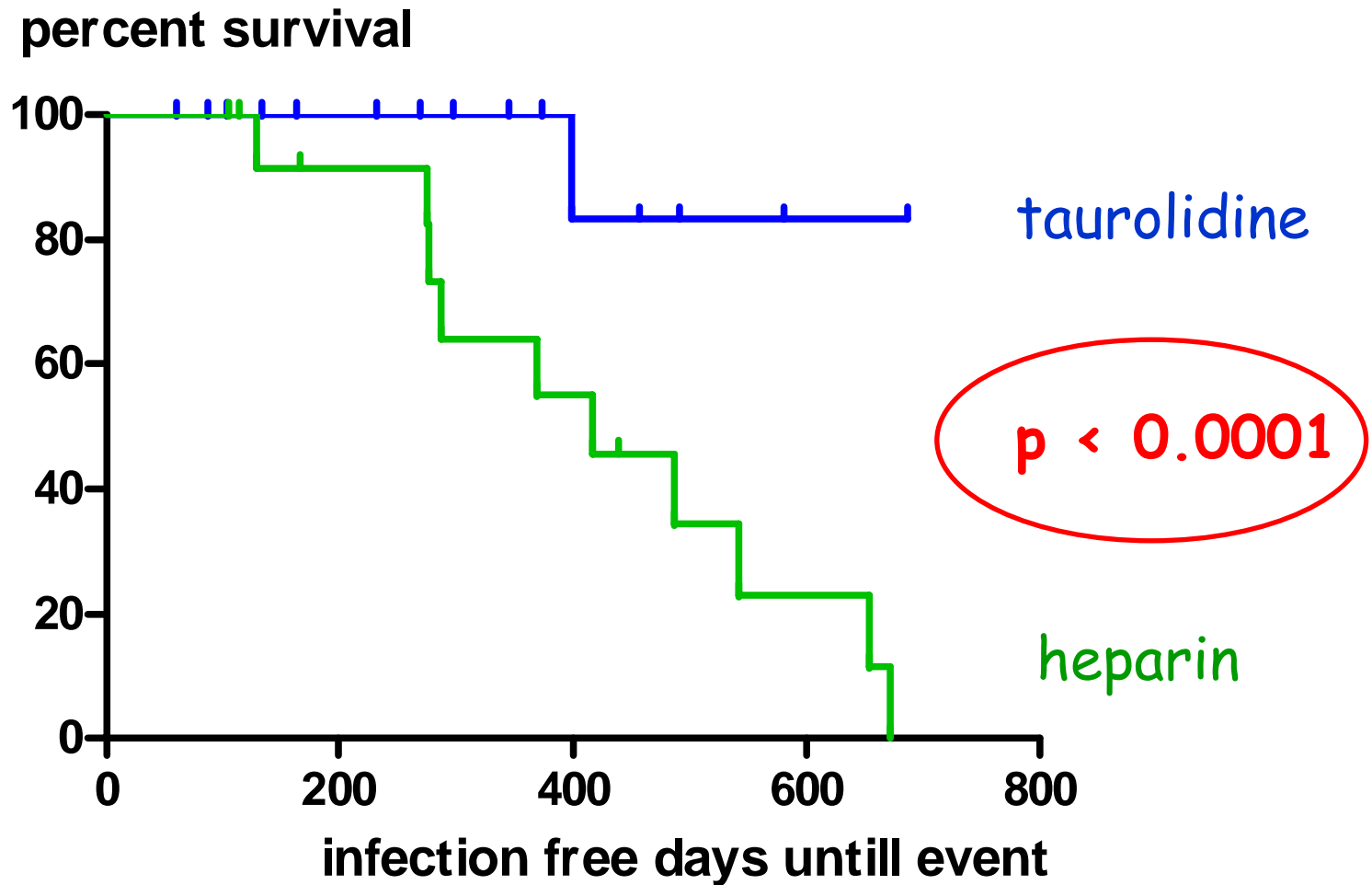
Aim

- first prospective trial in setting of HPN
- compare catheter lock therapy with taurolidine versus standard (heparin) for efficacy to prevent CRBSI
- in patients with recent episode of CRBSI
(i.e. proven susceptibility to infection)

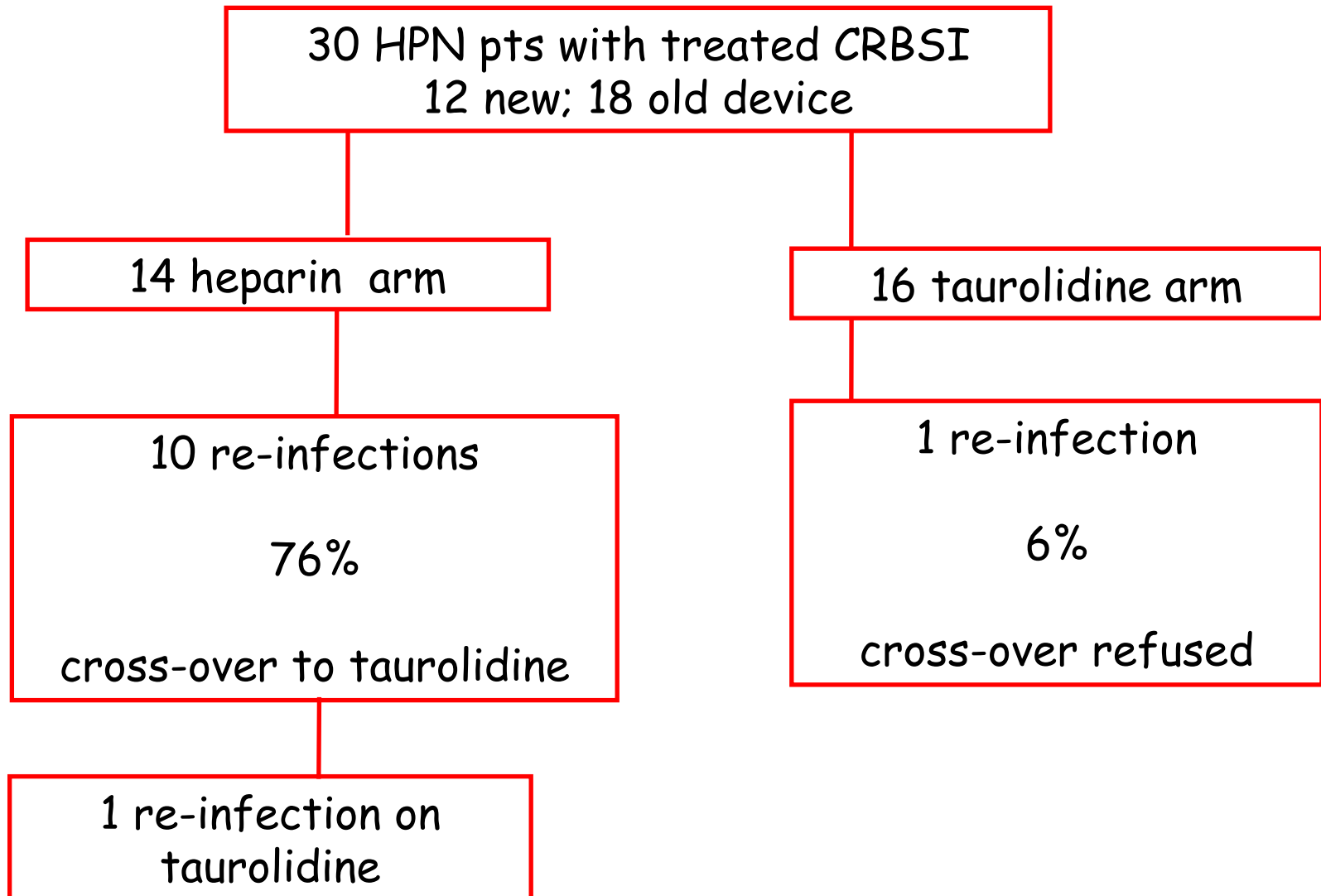
Methods

- ✓ study population: largest Dutch HPN centre
60 with Hickman or Porth - a- cath (20 arteriovenous fistula)
- ✓ patients developing CRBSI: clinical signs AND positive blood cultures
no other focus
- ✓ infection treatment, with new or old new access device
randomize: continue HPN using as catheter lock
heparin (5 mL, 150 U/mL) or taurolidine (5 mL, 2% solution)
- ✓ primary end-point: new episode of CRBSI
- ✓ therapy failure: cross-over to other arm

Kaplan Meier analysis: infection-free survival



Results: trial profile



Main Results

- 30 patients included with CRBSI between 2006⁴ and 2008³

	Heparin	Taurolidine
catheter days	4939	5370
infection-free survival (d)	176 ± 46	641 ± 44

- no side effects in either group
- no catheter occlusions in either group

Results: demographics

		Heparin	Taurolidin P	
Female (n)		10 (71%)	12 (75%)	n.s.
Age (yrs ±SD)		49 ± 16	55 ± 13	n.s.
Cause of IF	Motility disorder	5 (36%)	5 (31%)	n.s.
	High output stoma	1 (7%)	1 (6%)	n.s.
	Short bowel syndrome	5 (36%)	6 (38%)	n.s.
	Other	3 (21%)	4(25%)	n.s.
Type of access	Hickman	8 (57%)	11 (69%)	n.s.
	Port-a-cath	6 (43%)	5 (31%)	n.s.
New device pre-study		6 (43%)	6 (38%)	n.s.

Results: culture at inclusion

	Heparin	Taurolidine	P
Staphylococcus sp.	7 (50%)	9 (56%)	n.s.
epidermidis	5 (36%)	7 (44%)	n.s.
lugdunensis	1 (7%)	1 (6%)	n.s.
aureus	1 (7%)	1 (6%)	n.s.
Other Gram +	4 (29%)	2 (13%)	n.s.
Gram -	3 (21%)	4 (25%)	n.s.
Other	0	1 (6%)	n.s.

Results

	Heparin	Taurolidine	P
Infections/1000 catheter days before inclusion (n)	2,33	2,36	n.s.
Infections/1000 catheter days after inclusion (n)	2.02	0.19	0.008
Culture at end-point			
Staph	5	0	
Other Gram +	2	0	
Gram -	3	0	
fungi	0	1	

Conclusions

- ✓ Strong evidence for protective effect of taurolidine in prevention of CRBSI in the first RCT in HPN vs heparin in patients with proven susceptibility to these infections
- ✓ No evidence for side effects or catheter occlusions
- ✓ Taurolidine has changed our perspective on line sepsis

Discussion

- ✓ based on small non-controlled study by Jurewitsch & Jeejeebhoy
(Clin Nutr 2005;24:462)
- ✓ strength: single centre: same protocol
individuals with proven susceptibility to infections
similar effect after crossing over
- ✓ weakness: single centre / study size due to restrictions: open-label
- ✓ will resistance develop?

Confirmation in large multicenter / multinational trial

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