

5. Indications for the use of urokinase in peritoneal dialysis-associated peritonitis

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Guidelines

(Include recommendations based on level I or II evidence)

The use of antibiotics with catheter replacement is superior to antibiotics with urokinase to treat peritoneal dialysis-associated peritonitis. (Level II evidence)

Suggestions for clinical care

(Suggestions are based on Level III and IV evidence)

- **Urokinase may lyse some fibrin thrombi that obstruct catheters.**

7000 IU of urokinase infused into the obstructed PD catheters of 10 CAPD patients (4 of whom had peritonitis) restored flow without causing complications (Strippoli et al 1989).

Urokinase or streptokinase combined with antibiotic therapy succeeded in curing peritonitis in 8/16 patients but failed in another 8 patients treated with the same regimen (Murphy et al 1991).

Intraluminal urokinase treatment repeated daily for 3 days in conjunction with intensive antibiotic treatment cured peritonitis in 9 paediatric CAPD patients whereas relapses occurred in 75.8% of events in controls (Klaus et al 1992).

A literature review of largely anecdotal reports of streptokinase and urokinase treatment of PD peritonitis concluded that streptokinase had an unacceptably high adverse reaction rate and that catheter removal was a more effective therapy than thrombolysis. The authors proposed that clinicians should reserve urokinase treatment for antibiotic-compliant patients who develop two or more episodes of recurrent or persistent peritonitis and in whom dialysis catheter removal is contraindicated (Worland et al 1998).

Background

The use of urokinase seems logical, because of its potential to dissolve fibrin clots causing the obstruction of peritoneal dialysis (PD) catheters and to dissolve biofilm lining the inside of PD catheters, which harbour microorganisms in patients with peritonitis.

The purpose of this guideline is to identify the circumstances in which that procedure might be used.

Search strategy

Databases searched: MeSH terms and text words for peritoneal dialysis were combined using “and” with MeSH terms and text words for catheters. These were then combined using “and” with MeSH terms and text words for urokinase. The search was carried out in Medline (1966 – October Week 5 2002). The Cochrane Renal Group Trials Register was also searched for trials not indexed in Medline.

Date of searches: 26 November 2002.

What is the evidence?

Williams et al (1989) performed a randomised controlled trial in which 17 patients received intraperitoneal urokinase (5000 IU) on the second and fourth days of appropriate antibiotic treatment for CAPD peritonitis; 14 patients underwent catheter replacement. A further 6 patients who had a recurrence of peritonitis after urokinase treatment underwent catheter replacement. Peritonitis subsequently recurred in significantly more patients after urokinase treatment (41%) than after catheter replacement (5%).

In a randomised prospective trial, 24 patients with persistent or recurring CAPD peritonitis received treatment with antibiotics for 14 days; 12 also received intraperitoneal urokinase. Treatment succeeded in 8 patients who received urokinase compared with 1 who received antibiotics alone (Innes et al 1994).

A prospective randomised trial of 80 peritoneal dialysis patients (40 in each group) that compared treatment with antibiotics and intraperitoneal urokinase 5000 IU against treatment with antibiotics alone showed no statistically significant difference in outcomes between the two treatment groups. Outcomes included duration of peritonitis, severity of symptoms and signs of peritonitis, and peritonitis recurrence or relapse rate (Gadallah et al 2000).

Summary of the evidence

The evidence to date neither supports nor rejects the use of urokinase in PD-associated peritonitis.

What do the other guidelines say?

Kidney Disease Outcomes Quality Initiative: No recommendation.

British Renal Association: Refers to Gokal et al (1993): If outflow obstruction occurs shortly after catheter placement or after peritonitis, it may be due to a clot or fibrin. Flushing with streptokinase or urokinase and heparin may restore the flow immediately.

Canadian Society of Nephrology: No recommendation.

European Best Practice Guidelines: Refer to the International Guidelines.

International Guidelines: Adults: Re Outflow/Inflow Obstruction:

1. Conservative or non-invasive approaches such as body position change, walk on staircases, laxatives, flushing with heparinized saline (“push-and-suck” manoeuvre) should be undertaken. If these fail, then instillation of fibrinolytic agents (urokinase, streptokinase 10.000 U in 2 mL left in the catheter for 2 hours) may be tried (Gokal et al 1998).

Implementation and audit

Document the outcome of urokinase-treated PD patients.

Suggestions for future research

Establish a registry of urokinase-treated PD patients and their outcomes.

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References

Gadallah MF, Tamayo A, Sandborn M et al. 2000. Role of intraperitoneal urokinase in acute peritonitis and prevention of catheter loss in peritoneal dialysis patients. *Adv Perit Dial* 16: 233-36.

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Innes A, Burden RP, Finch RG et al. 1994. Treatment of resistant peritonitis in continuous ambulatory peritoneal dialysis with intraperitoneal urokinase: a double-blind clinical trial. *Nephrol Dial Transplant* 9(7): 797-99.

Klaus G, Schafer F, Querfeld U et al. 1992. Treatment of relapsing peritonitis in pediatric patients on peritoneal dialysis. *Adv Perit Dial* 8: 302-05.

Murphy G, Tzamaloukas AH, Eisenberg B et al. 1991. Intraperitoneal thrombolytic agents in relapsing or persistent peritonitis of patients on continuous ambulatory peritoneal dialysis. *Int J Artif Organs* 14(2): 87-91.

Strippoli P, Pilolli D, Mingrone G et al. 1989. A hemostasis study in CAPD patients during fibrinolytic intraperitoneal therapy with urokinase (UK). *Adv Perit Dial* 5: 97-99.

Williams AJ, Boletis J, Johnson BF et al. 1989. Tenckhoff catheter replacement or intraperitoneal urokinase: a randomised trial in the management of recurrent continuous ambulatory peritoneal dialysis (CAPD) peritonitis. *Perit Dial Int* 9(1): 65-67.

Worland MA, Radabaugh RS, Mueller BA. 1998. Intraperitoneal thrombolytic therapy for peritoneal dialysis-associated peritonitis. *Ann Pharmacother* 32(11): 1216-20.

Appendix

Table 1 Characteristics of randomised controlled trial evidence

Study ID (author, year)	N	Study Design	Setting	Participants	Intervention (experimental group)	Intervention (control group)	Follow up (months)	Comments
Gadallah et al 2000	80	Randomised controlled clinical trial	University	PD patients who developed a first episode of peritonitis; 32.5% diabetic	Intraperitoneal urokinase (5000 IU) on first day of diagnosis	No urokinase	36	None
Innes et al 1994	24	Randomised controlled clinical trial	Teaching hospital	CAPD patients with resistant peritonitis (persistent or recurrent infection)	Urokinase 5000 Ploug units in 5 ml of 0.9 saline at onset of 3 rd peritonitis episode within 6 months (recurrent infection) or after 4 days of antibiotic treatment with no resolution (persistent infection); antibiotic treatment continued for 14 days	Placebo plus antibiotic (same as for experimental intervention)	Unclear	None
Williams et al 1989	37	Randomised controlled clinical trial	Teaching hospital	CAPD patients with peritonitis	Intraperitoneal urokinase (5000 IU) intravenous plus antibiotic	One stage removal and re-insertion of Tenckhoff catheter plus antibiotic	3-12 months	None

Table 2 Quality of randomised trials

Study ID (author, year)	Method of allocation concealment	Blinding			Intention-to-treat analysis	Loss to follow up (%)
		(participants)	(investigators)	(outcome assessors)		
Gadallah et al 2000	Unclear	No	No	No	Unclear	0
Innes et al 1994	Unclear	Yes	Not stated	Not stated	Yes	0
Williams et al 1989	Unclear	No	No	No	No	Unclear

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Table 3 Results for dichotomous outcomes

Study ID (author, year)	Outcomes	Intervention group (number of patients with events/number of patients exposed)	Control group (number of patients with events/number of patients not exposed)	Relative risk (RR) [95% CI]	Risk difference (RD) [95% CI]
Gadallah et al 2000	Catheter loss	3/40	6/40	0.50 (0.13 to 1.86)	-0.08 (-0.21 to 0.06)
Innes et al 1994	Failure of treatment of peritonitis	4/12	11/12	0.36 (0.16 to 0.82)	-0.58 (-0.89 to -0.27)
Williams et al 1989	Recurrent peritonitis at < 1 month	7/17	1/20	9.24 (1.12 to 60.43)	0.36 (0.11 to 0.61)

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