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The use of Nitrofurantoin in Renal Impairment in Primary Care - A Pilot Study

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Can nitrofurantoin be effectively used in patients with impaired renal function?

- The BNF advises that nitrofurantoin should avoided if eGFR less than 60 mL/minute/1.73 m^2, however the Renal Drug Handbook advises use above 20ml/min
- This pilot showed that the BNF guidance should be followed, and not alternative guidance that recommends its use in mild renal impairment. This should be taken forward to a full study

Introduction

Nitrofurantoin is an oral antibiotic that is only active in urine. Unlike other antibiotics for urinary tract infections (UTI), acquired resistance is limited.

It would be the agent of choice in our aging population, but its use is limited by the British National Formulary (BNF) saying to avoid in patient with mild renal impairment (e GFR <60ml/min). The Renal Drug Handbook recommends use if >20ml/min, but does not specifically reference the evidence base.

A Canadian study(Ajay Bains, 2009) retrospectively reviewed 356 patients and showed similar outcomes for those with eGFR above or below 50ml/min.

This pilot study was to look at the feasibility of repeating this on a larger scale with England to increase the evidence base to influence the BNF entry.

Methods

A single city centre general practice with 12,118 registered patients was used for the pilot study. All patients over 18 years of age who had received one of more nitrofurantoin prescriptions in the last year aged were reviewed.

Each patient had there eGFR reviewed. Where there was a low eGFR, a Cockcroft & Gault Creatine Clearance (C&G-IBW-ClCr) based on the ideal body weight (IBW) was performed. Success was assumed if there were no further antibiotics, no admission to hospital for related episode or recorded as still symptomatic on their medical records. No ethics committee approval was needed as this was an audit of current practice.

Results

164 adults received prescriptions for one or more scripts for nitrofurantoin in the last year. 37 patient records in 2hrs 4 mins. The average age was 72 years (range 21-100), and the median 80 years. The average eGFR/1.73 m^2 was 73.8ml/min (range 33-130) and the C&G-IBW-ClCr was 55ml/min (range 24-127).

There were 15 patients with C&G-IBW-ClCr >60ml/min. None needed further antibiotics or were recorded as still symptomatic.

In the 22 patients with a C&G-IBW-ClCr <60ml/min (average eGFR 61.7ml/min vs CrCl 38.7ml/min), eighteen (81.8%) had further antibiotics or recorded as still symptomatic.

12 patients received either 50mg qds or 100mg m/r bd, 2 on 100mg qds and 8 with no doses recorded. One had an admission into hospital but after a fall, so probably unrelated. However, only seven patients (31.8%) had an eGFR/1.73 m^2 <60ml/min.

Twelve patients had further courses of antibiotics (5 cefalexin or cefradine, 4 trimethoprim, 1 norfloxacin, 1 pivmecillinam, 1 amoxicillin). 3 patients were recorded as still symptomatic. 1 went into hospital.

1 patient went back onto prophylactic antibiotics. No samples stated nitrofurantoin resistance, but 6 samples specifically stated that nitrofurantoin was sensitive.

The patients that did not require additional antibiotics had an eGFR of 75, 57, 55, & 53ml/min//1.73 m^2 & a CrCl of 36, 39, 50 & 53ml/min.

Nitrofurantoin - at least 1 course in 2011 at one GP practice

CrCl C&G <60ml/min	CrCl C&G >60ml/min

Age	eGFR	C&G IBW	microbiology	Nitrofurantoin dose	no further treatment	needed further AB	comment
55	127	127	no growth		✓		
23	112	117	no growth		✓		
26			no		✓		
36	97	106	no growth		✓		
44	130	123	no growth		✓		
46	82	74	E coli sens N P res T C		✓		
58	75	68	coliform ++ sens N T		✓		
61	95	73	coliform sens T N P			7 days more nitr	
62	100	77	no		✓		post op urethral stent with infection
63	55	50	orgs ++ but no growth		✓		suspected uti
64	86	75	coliform ++ sens N res T		✓		
71	113	85	coliform sens T N		✓		
72	47	39	coliform Sens T, N, P			cefalexin	
77	53	41	mixed	100mgMR bd		trimethoprim	
79	73	53	mixed growth		✓		
79	57	39	coliform Sens N P C Res T	100mg MR bd	✓		prev trimethoprim
79	53	35	coliform Sens T, N, P	100mgMR bd, 50mg qds		still symptomatic	4 separate courses
80	39	31	mixed	100mg qds		amoxicillin	
80	66	48	no growth	50mg qds		still frequency and urge	
82	79	54		50mg qds			N not tolerated
82	76	52		100qds, 50qds, 50bd		still symptomatic	
83	57	40		50mg qds		2/7 cefalexin	
86	75	36	Coliform Sens NPC Res T	50mg qds	✓		
87	78	47	no	50mg qds		cephalexin	
87	75	42	no growth			cephradine	
87	73	41	coliform Sens T, N, P	50mg qds		cephalexin	
88	56	31	mixed growth sens T			trimethoprim	
88	66	35		50mg qds			referral to continence service
89	33	24	coliform Sens N, P, C Res T			trimethoprim	pt reported no improvement on nitro
92	63	29	hosp summary said positive				hosp adm with fall
93	68	33	coliform			trimethoprim	
93	64	31		50mg qds		pivmethicillin	
97	75	39				back to prophylactic	treat as uti'
100	39	20	12/11 Staph aureus	100mg bd		norfloxacin flucloxacillin	

Discussion & conclusion

Nitrofurantoin is not recommended in patients with impaired renal function because of the inability to get adequate levels in the urine.

This pilot study shows that eGFR is not a good indicator of renal function, and that CrCl should be used.

Over 80% with a CrCl<60ml/min needed further treatment. This will progress to a larger study.

References

Ajay Bains, D.B., Nathan A. Hoag, 2009. A retrospective review assessing the effi cacy and safety of nitrofurantoin in renal impairment. Can Pharm J, 142: 248-252.

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