nitate, also decreased for 2 h after a dose. Concentrations of physiological ketone bodies in the cerebrospinal fluid were 23% of those in plasma (patient 1).

These three patients had a severe infantile form of riboflavin-unresponsive MADD. Four siblings of patients 2 and 3 had died in infancy and all our patients had received intensive conventional treatment, despite which all were very sick when sodium-D,L-3-hydroxybutyrate was started.

We gave the racemic mixture of D-3-hydroxybutyrate and L-3-hydroxybutyrate. Although fatty acids do not cross the blood brain barrier, ketone bodies do enter the brain, and this process is even better in childhood. They are used by heart, kidney, and fat tissue, and, to a lesser extent, by muscle. All brain cells use ketone bodies for energy. Rat brain also uses both D-3-hydroxybutyrate and L-3-hydroxybutyrate for synthesis of lipids; the increase of this in infancy is even more pronounced for L-3-hydroxybutyrate than for D-3-hydroxybutyrate, making it particularly suited for restoration of myelination.1

Use of fatty acids is reduced in the myocardium of patients with defects in oxidation of fatty acids, and cardiomyopathy is a frequent cause of death in MADD2 warranting experimental treatment. D,L-3-hydroxybutyrate treatment resulted in substantial and persisting improvement of cardiomyopathy in these infants who were critically ill. D,L-3-hydroxybutyrate also improved hypotonia and feeding tolerance in a patient with MADD.2 Administration of ketone bodies to human volunteers decreases lipolysis with decreased free fatty acids in plasma. End product administration not only restores a deficit, but also through feedback inhibition reduces formation of toxic precursors as indicated by decreased decanoylcarnitine.

Our observations and results of other studies suggest that treatment with D,L-3-hydroxybutyrate is safe and effective. It was not associated with adverse side-effects. D,L-3-hydroxybutyrate is an additional therapeutic option for cardiomyopathy and cerebral dysfunction in severe fatty-acid oxidation defects.

Contributors

J L K Van Hove and J V Leonard designed and implemented the study and wrote the report. J Jaeken and S Grünewald assisted in the clinical study and writing of the report. J E Deanfeld did the echocardiograms and managed the cardiomyopathy, P Demaerel did the brain MRI studies. P E Declercq, P Bourdoux, and K Niezen-Koning did the laboratory studies and the drug and metabolite measurements.

Conflict of interest statement

None declared.

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Control of encrustation and blockage of Foley catheters

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Urinary catheters often become encrusted and blocked by crystalline Proteus mirabilis biofilms. Results of experiments in a laboratory model of a Foley catheterised bladder infected with P mirabilis showed that when retention balloons were inflated with a solution of triclosan (10 g/L), the catheters drained freely for at least 7 days. Triclosan became impregnated throughout the silicone catheter material and completely inhibited the formation of crystalline biofilm, whereas catheters inflated with water became blocked in 24 h. Our observations suggest a way to control a common complication in patients with long-term indwelling bladder catheters.

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Many patients undergoing long-term bladder catheterisation experience encrustation of their catheters. The problem stems from infection by Proteus mirabilis or other urease-producing bacteria such as Providencia spp and Morganella spp. These organisms colonise catheter surfaces, forming biofilm communities embedded in a polysaccharide matrix. Urease generates ammonia and raises the pH of urine and biofilm. Under these conditions, crystals of magnesium and calcium phosphates form and become trapped in the organic matrix and can eventually block the catheter. This complication can seriously compromise patients’ health and welfare.1 There are no effective procedures for controlling this problem, to which all types of Foley catheter are vulnerable.2

Bibby and colleagues3 suggested that to control catheter encrustation, the retention balloon should be inflated with an antimicrobial solution rather than with water. Thus, delivery of the agent to the urine might be achieved by diffusion through the balloon. In an in-vitro model, low concentrations of mandelic acid were shown to diffuse through the balloon. In an in-vitro model, low concentrations of mandelic acid were shown to diffuse through the balloon.
through the balloon. Mandelic acid has been used as an antibacterial bladder irrigant but has little activity against *P mirabilis* (minimum inhibitory concentration [MIC] of 5 g/L). It is bacteriostatic provided that pH is maintained below 5·5.

Triclosan (2,4,4'-trichloro-2'-hydroxydiphenylether, C₁₂H₇Cl₃O₂) is used at 0·3–2·0% weight/volume in soaps, surgical scrubs, deodorants, toothpaste, and mouthwashes. It is sparingly soluble in silicone and organic solvents such as polyethylene glycol. Triclosan’s safety has been established through extensive acute and long-term toxicity, carcinogenicity, reproduction, and teratology studies and the USA Food and Drug Administration has approved its use in oral care products.4 Isolates of *P mirabilis* from encrusted catheters are extremely sensitive to triclosan (MIC 0·5 mg/L).5 Therefore, we decided to examine the ability of triclosan to prevent catheter encrustation by *P mirabilis*.

We used a laboratory model of a catheterised bladder6 to test the ability of triclosan to diffuse through the balloon into urine. The model consists of a glass bladder chamber maintained at 37°C by a water jacket. Urine is pumped in and then drains through a catheter inserted into the base of the chamber. Test catheters (size 14 all-silicone catheters, Bard; Crawley, UK) were inflated with 10 mL of triclosan solution (10 g/L in 5% weight/volume polyethylene glycol). Control catheters were inflated with water. We supplied models with artificial urine at 0·5 mL/min and infected them with 10 mL of a 4-h urine culture of *P mirabilis* B2 (an isolate from an encrusted catheter). We did four replica experiments with a test and control catheter to calculate the time taken for catheters to become blocked. We used scanning electronmicroscopy (SEM) on catheter sections to visualise biofilm colonisation or encrustation.

In a second set of experiments (three replicates), catheters were inflated with triclosan solution, inserted into sterile models, and supplied with sterile urine for 24 h. Catheters were then deflated and the balloon washed thoroughly with water and reinfated with water. We infected these models and models fitted with control catheters with 10 mL of a 4-h urine culture of *P mirabilis* B2 and supplied them with urine at 0·5 mL/min. Catheters were removed from the test models and cut into 1 cm sections, which were placed on tryptone soya agar plates that had been inoculated with lawns of *P mirabilis* B2 and incubated overnight at 37°C.

On incubation, urinary pH in the control catheters rose from 6·1 to 8·6 and the catheters became blocked with crystalline biofilm in a mean of 24 h 15 min (SD 1 h 40 min). When catheters were inflated with triclosan solution, urine remained acid (pH 6·7) for 7 days and the catheters were draining freely at the end of the experiment. SEM on catheter sections revealed little evidence of biofilm colonisation or encrustation.

In the second set of experiments, control models became blocked at 29 h (10 h 18 min) and the pH rose to 8·4. Catheters that had been inflated for 24 h with triclosan drained freely for 7 days and the pH remained at 6·2. Low vacuum SEM on cross-sections of triclosan-treated catheters revealed little sign of encrustation compared with controls (figure 1). Large zones of bacterial inhibition were produced around test catheter sections from the length of the catheter (figure 2). Sections from control catheters produced no such zones.

These results show that antibacterial concentrations of triclosan can diffuse through the catheter inflation line and balloon into urine. Triclosan can control the urinary pH preventing the alkaline conditions that precipitate encrustation. Additionally, triclosan becomes impregnated throughout the length of the catheter and crystalline biofilm formation is completely inhibited. Triclosan is retained in the catheter material for at least 7 days in situ in the model. The model simulated a heavy infection (10⁸ colony forming units/mL urine) with a pure culture of *P mirabilis*. In urine at pH 8·4 to 8·6, encrustation is rapid and catheters block more rapidly than they do normally. Under these conditions, triclosan-treated catheters drained freely for at least 7 days, and showed no sign of encrustation at the end of the experiment.

Our observations suggest an approach that could have practical applications in controlling catheter encrustation. The method does not disturb the integrity of the closed drainage system and could be used to deliver other agents, including antibiotics, through retention balloons. Treatment of catheter-associated urinary tract infections by delivering antibacterials directly to the bladder could avoid the selection of antibiotic-resistant gut flora by oral administration of drugs.
Stapled versus excision haemorrhoidectomy: long-term follow up of a randomised controlled trial


Advantages of the stapling procedure for haemorrhoids include reduced postoperative pain and shortened convalescence; however, there are few data with respect to functional and symptomatic outcome. At a dedicated clinic, we reviewed patients between Dec, 2001, and March, 2002, who had taken part in a randomised controlled trial undertaken at the unit in 1999, which compared outcomes after open or stapled haemorrhoidectomy. We noted the presence or absence of haemorrhoidal specific symptoms, and assessed overall satisfaction, continence, and quality of life. Rigid sigmoidoscopy and an anorectal examination were also used to examine symptomatic recurrence and disease activity. At minimum follow-up of 33 months since surgery, both techniques seem to be equally effective.

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In 1988, the stapled haemorrhoidectomy procedure was introduced as a less painful option than the open Milligan-Morgan operation.1 The stapled technique offers an alternative approach to the management of large, prolapsing haemorrhoids. Pulling up the prolapsed haemorrhoidal tissue, removing redundant mucosa, and stapling off the end branches of the superior haemorrhoidal artery is thought to improve venous return and reduces vascular congestion. Results of randomised controlled trials have consistently shown a decrease in postoperative pain, procedure time, and an earlier return to normal activity with the stapled technique.2,3 However, long-term outcomes with respect to resolution of haemorrhoidal symptoms and potential complications, such as chronic pain, are unknown.4 Our aim was, therefore, to assess the long-term results of stapled haemorrhoidectomy in those patients who took part in a randomised controlled trial5 of this technique versus the open technique in 1999.

Between Dec 24, 2001, and March 22, 2002, we invited patients from both groups of the randomised controlled trial to attend an independent review clinic, led by a consultant surgeon (BJW) who was unaware of the original operative technique. The Cleveland Clinic faecal incontinence scores were recorded and each patient was asked to complete the previously validated short form 36 (SF-36v2) quality of life questionnaire and a linear analogue satisfaction score. We also recorded the presence or absence of haemorrhoidal specific symptoms, including pain, bleeding, prolapse, and pruritus. All clinic patients underwent rigid sigmoidoscopy and an anorectal examination. If for any reason a clinic review could not be arranged, we did a detailed telephone assessment. All patients provided written consent and the study was approved by the Hull and East Yorkshire NHS Ethics Committee.

We analysed data with SPSS (version 10), using the Mann-Whitney U test to compare faecal incontinence scores and quality life between the groups, and the χ² test for association. Fisher’s exact test was used for frequencies less than five. We judged a p value of 0·05 or less as significant.

We reviewed 36 of the 40 original trial patients (20 stapled and 16 open). The remaining four patients, all from the open procedure group, declined review. One of these patients is undergoing anorectal physiology to investigate sphincter disturbance, one reports persistent pain, and the remaining two declined for sociodemographic reasons. We followed up patients for a mean of 37 months (range 33–39, SD 1·6).

When comparing stapled versus excision haemorrhoidectomy, we aimed to assess the long-term outcomes with respect to resolution of haemorrhoidal symptoms and potential complications, such as chronic pain, and to determine the presence or absence of haemorrhoidal specific symptoms, including pain, bleeding, prolapse, and pruritus. All clinic patients underwent rigid sigmoidoscopy and an anorectal examination. If for any reason a clinic review could not be arranged, we did a detailed telephone assessment. All patients provided written consent and the study was approved by the Hull and East Yorkshire NHS Ethics Committee.