Intestinal biodegradable stents

Initial experience in the Czech Republic

Stanislav Rejchrt[1], Marcela Kopáčová[1], Jolana Bártová[1], Zdeněk Vacek[2], Jan Bureš[1]

[1]2nd Department of Internal Medicine, Charles University in Praha, Faculty of Medicine at Hradec Králové, University Teaching Hospital, Hradec Králové, Czech Republic
[2]Department of Radiology, Charles University in Praha, Faculty of Medicine at Hradec Králové, University Teaching Hospital, Hradec Králové, Czech Republic

Summary

Objective: *Bio-degradable (BD) stents can be considered as a new therapeutical option for treatment of tight benign stenoses of the gastrointestinal tract. These stents can be made of different synthetic polymers (like polylactide, polyglycolide) or their co-polymers (polydioxanone). This paper is a feasibility study of implantation of BD stents into benign small and large intestinal stenoses.*

Methods: *Three patients with stenosing Crohn's disease (30, 33 and 54-year-old) entered the study, with stenotic ileocolonic anastomosis (11 and 23 years after previous surgery) or with a primary tight stenosis of the transverse colon (without previous surgery). BD stents made of polydioxanone were used in all patients. Stents were introduced by means of double balloon enteroscopy, using anal approach. Intestinal stenoses were dilated first by through-the-scope balloon dilation, distal margins of stenoses were marked with metallic clips and/or lipiodol injection. BD stents were implanted over a stiff guide wire by means of special introducer, inserted into the overtube after endoscope removal. Stent placement was accomplished under fluoroscopy control.*

Results: *Insertion of BD stents was successful at the first attempt in all cases. The mean time until stent degradation was four months. We did not observe any stent migration and/or any major complications like mucosal in-growth, perforation, bleeding or luminal obstruction with stent fragments. Kinking of the balloon overtube mainly at the splenic flexure during the introducer insertion was the only technical problem.*

Conclusions: *Endoscopic introduction of BD stents into small and large intestinal stenoses is feasible. Initial experience is promising. Proof of the long-term efficacy and safety requires further study.*

Key words: *biodegradable stents, Crohn's disease, double balloon endoscopy, polydioxanone, small and large intestinal stenoses*

Souhrn

Intestinální biodegradabilní stenty

Východiska: *Biodegradabilní (BD) stenty představují novou terapeutickou možnost v léčbě těsných benigních stenóz gastrointestinálního traktu. Tyto stenty mohou být vyrobeny z různých syntetických polymerů (polylaktid, polyglykolid) nebo jejich kopolymerů (polydioxanon). Cílem této práce bylo ověřit technickou proveditelnost zavedení BD stentů do stenóz tenkého a tlustého střeva.*

Metodika: *Do studie byli zařazeni tři pacienti s Crohnovou chorobou (ve věku 30, 33 a 54 let), s těsnou stenózou ileokolické anastomózy (11 a 23 let po operaci) a s primární stenózou transverza (bez předcházející operace). U všech nemocných byly použity BD stenty z polydioxanonu. Byly zavedeny pomocí dvojbalonové enteroskopie análním přístupem. Stenózy byly nejprve rozdilatovány, distální okraje byly označeny metalickými klipy a lipiodolem. BD stenty byly zavedeny po tuhém vodiči pomocí speciálního zavaděče. Přesná poloha stentu byla kontrolována skiaskopicky.*

Výsledky: *Zavedení BD stentů bylo na první pokus úspěšné u všech nemocných. Průměrná doba k degradaci BD stentů byla čtyři měsíce. Nepozorovali jsme migraci stentu ani žádnou jinou závažnou komplikaci (slizniční přerůstání, perforaci, krvácení nebo obstrukci lumina fragmenty stentu). Jediným technickým problémem byla tendence k zalomení převlečné trubice během zavádění zaváděcího systému (zejména v lienálním ohbí).*

Závěry: *Endoskopické zavedení BD stentu do tenkého a/nebo tlustého střeva je technicky proveditelné. Iniciální výsledky jsou povzbudivé. Nicméně průkaz dlouhodobé účinnosti a bezpečnosti budou vyžadovat další studie.*

Klíčová slova: *biodegradabilní stenty, Crohnova choroba, dvojbalonová enteroskopie, polydioxanon, stenózy tenkého a tlustého střeva*

Use of stents for treatment of benign stenoses of the gastrointestinal tract is associated with several problems and drawbacks. Uncovered metallic stents induce early mucosal hyperplastic reaction (with over- and/or ingrowth); covered metallic and plastic stents are associated with a higher risk of migration and lower flexibility and shorter/lower radial force. Reports on their use provide controversial results [2,7,13,15,17]. Stents made of biodegradable materials could theoretically overcome the above-mentioned shortcomings [1]. Fry et al [5] were the first who introduced a biodegradable stent made of poly-L-lactide for a refractory benign oesophageal stricture. The stent disintegrated six weeks later and obstructed the oesophageal lumen [5]. Lauk-

karinen et al [10,11] tried a biodegradable polylactide stent in the biliary and pancreatic ducts in animal models. To the best of our knowledge there are no data on the use of biodegradable stents in the small and/or large bowel. This paper reports on a feasibility study of implantation of biodegradable stents into benign tight small and large intestinal stenoses.

MATERIAL AND METHODS

Biodegradable stents

Biodegradable stents made of polydioxanone (SX-ELLA BD biodegradable stent, ELLA-CS, Hradec Králové, Czech Republic) were used in all patients (Fig. 1). These stents provide an extended period of dilation compared to conventional methods. Stent integrity and radial force were maintained for 6–8 weeks after implantation. Stent degradation and fragmentation occurs 11–12 weeks after its insertion, the speed of degradation is pH-dependent (faster in lower pH). The dual flared-end stent design reduces the risk of migration [3].

We used different sizes of stents for each patient according to the size of the stenosis and introducer system with outer diameter 18–25 mm (flare ends 23–27 mm) and length from 40 to 80 mm. Stents are fitted with radio-opaque markers at each end and the mid-point to enable precise stent positioning under fluoroscopy control. The standard delivery system for oesophageal implantation, which may be used in case of distal (rectal) stenoses, consists of a shaft (outer diameter 28 French, length 75 mm) with a detachable olive. For proximal stenoses, a special introduction system for stent insertion through the balloon overtube was developed. The stent must be loaded just before implantation.

Patients

Three patients with stenosing Crohn's disease entered the study: a 54-year-old man with a stenotic ileo-ascendento-anastomosis (23 and 11 years after previous surgery), a 33-year-old woman with a stenotic ileo-rectal anastomosis (10 years after surgery) and a 30-year-old woman with a primary tight stenosis of the transverse colon (without previous surgery).

Endoscopy

A double balloon enteroscopy system (Fujinon, Saitama, Japan) was used in all cases. All procedures were accomplished under conscious sedation (i.v. midazolam and pentazocine) by means of anal approach. A therapeutic enteroscope EN 450T5 (working channel 2.8 mm, outer diameter 9.4 mm, working length 200 cm) was inserted through an overtube (TS-13140, outer diameter 13.2 mm, length 145 cm). Intestinal stenoses were dilated first by through-the-scope balloon dilation (Rigiflex, Boston Scientific, Natick, USA), distal margins of stenoses were marked with metallic clips and/or lipiodol injection. The inflated balloon on the tip of the overtube secured the correct stable position during the procedure. Biodegradable stents were implanted over a stiff guide wire by means of special introducer, inserted into the overtube after endoscope removal. Stent placement was accomplished under fluoroscopy control. Kinking of the balloon overtube mainly at the splenic flexure during the introducer insertion was the only technical problem. The enteroscope, which was used without a distal balloon to allow its smooth pull-out through an overtube, was immediately reinserted via this overtube to check correct stent position (see Fig. 2–7 for details).

Ethics

The study was approved by the Joint Ethical Committee of the Faculty of Medicine, Charles University and University Teaching Hospital, Hradec Králové.

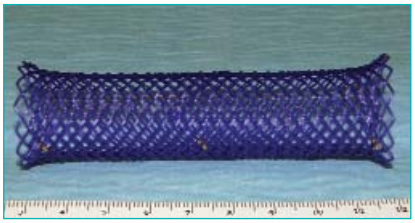

Fig. 1./Obr. 1.
A biodegradable stent made of polydioxanone with three radio-opaque markers.
Bio-degradabilní stent z polydioxanonu se třemi rentgen-kontrastními značkami.

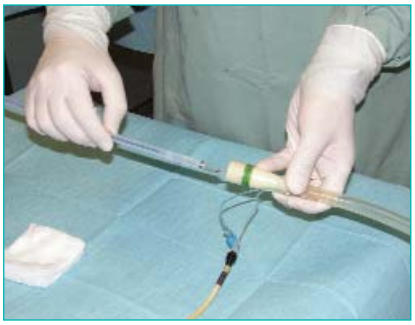

Fig. 2./Obr. 2.
Introducer system with an inflated balloon at its end before insertion into the endoscopic overtube.
Zaváděcí systém zakončený balonkem před zasunutím do endoskopické převlečné trubice.

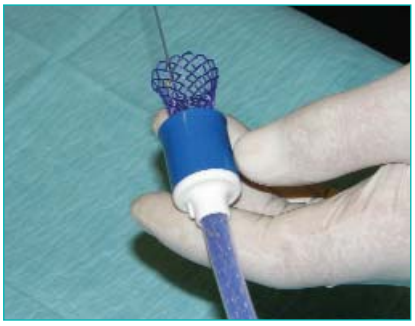

Fig. 3./Obr. 3.
Loading of the biodegradable stent into the introducer.
Zasouvání biodegradabilního stentu do zavaděče.

RESULTS

Insertion of biodegradable stents was successful at the first attempt in all cases. We have not registered any immediate complication of the procedure. Early short-term mild dull abdominal pain did not require pain killers. Biodegradable stent insertion provided rapid clinical improvement and symptom relief in all patients. The mean time until stent degradation was four months. In one case (a 33-year-old woman with ileo-sigmoideal stenosis), two months after

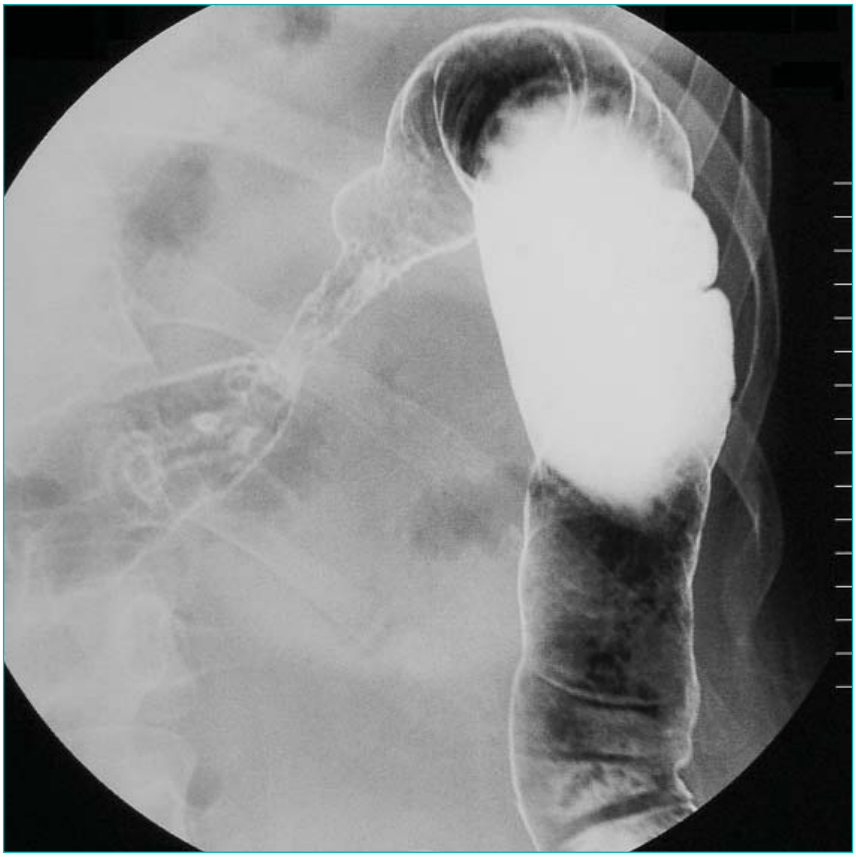

Fig. 4./Obr. 4.
A tight stenosis of the transverse colon close to the splenic flexure.
Stenóza na příčném tračníku před lienálním ohbím.

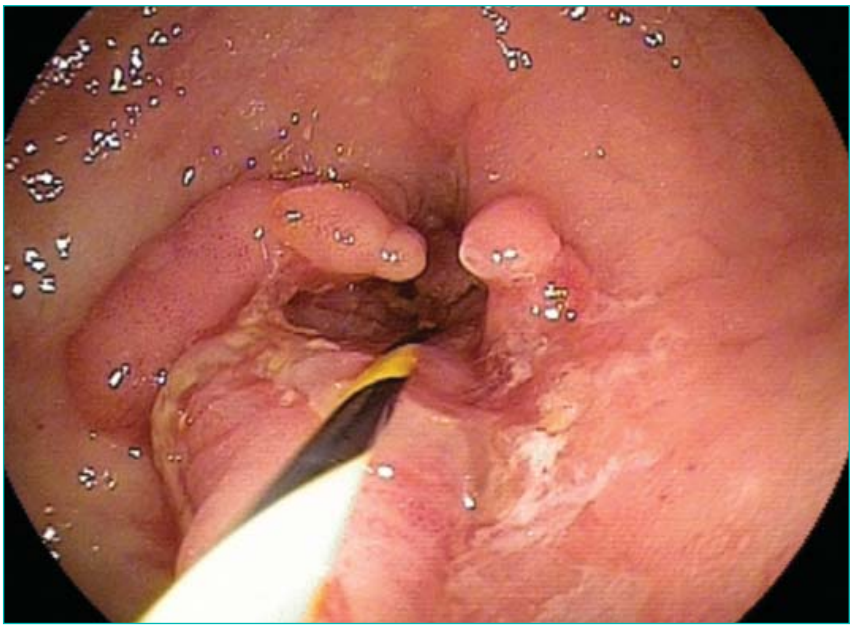

Fig. 5./Obr. 5.
Inflammatory polyps in front of the stenosis. A guidewire is introduced into the stenosis.
Zánětlivé polypy před stenózou příčného tračníku. Ve stenóze je zaveden vodič.

implantation, the proximal flared end of the stent came into contact with the intestinal wall (without stent migration) and caused intermittent transit obstruction. The proximal end of the stent was cut off endoscopically by means of hot biopsy forceps and the stent discharged spontaneously five days later. The favourable effect of previous dilation has been persisting after stent expulsion even in this case. We have not recorded any stent migration in any of the patients. Long-term efficacy and safety results are not available yet.

DISCUSSION

We report our initial experience with intestinal implantation of biodegradable stents in this study. We chose patients with tight benign intestinal stenoses as a complication of Crohn's disease. Insertion of biodegradable stents was successful in all cases and was not associated with any major complication.

Tight intestinal Crohn stenoses and strictures complicating other diseases might cause significant problems. Previously, they were solved by surgical resections (often extensive) or stricturoplasty, nowadays they can be dilated endoscopically [8,9,12]. However, the long-lasting effect of this treatment may be limited and repeated dilations with perforation risk are necessary. Biodegradable stents can be considered as a new therapeutical option. These stents can be made of different synthetic polymers (like polylactide, polyglycolide) or their co-polymers (polydioxanone). Their degradation is a hydrolytic one, first the amorphous and then the crystalline structure is broken down. The speed of biodegradation is dependent not only on the size and structure (crystallinity, porosity, hydrophilic backbone etc.) but also influenced by temperature, pH and type of body tissue/fluid [4,6]. To date, biodegradable stents are mostly tried for benign refractory oesophageal strictures [1,5,14,16].

We are fully aware of the possible limitations of this very initial study. Only a limited number of patients were included and long-term efficacy and safety results cannot be evaluated yet. Nevertheless, this was a feasibility study and thus it fulfilled its objective. Intestinal implantation of a biodegra-

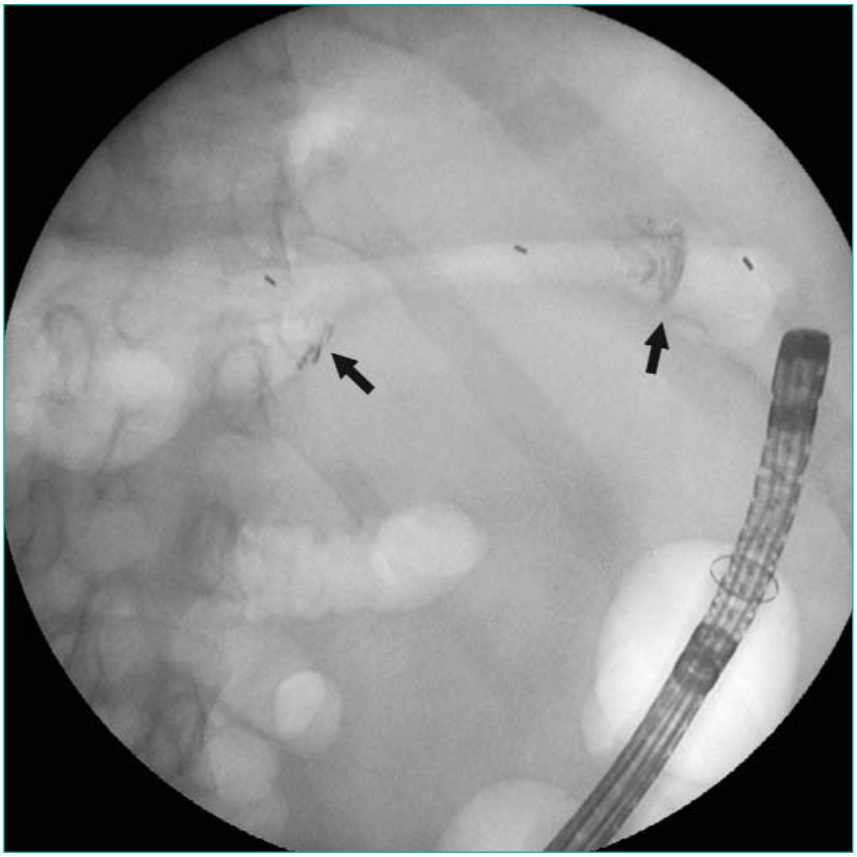

Fig. 6./Obr. 6.
Biodegradable stent with three radio-opaque markers in the stenosis marked with lipiodol at both ends (arrows).
Bio-degradabilní stent se třemi rentgen-kontrastními značkami uvolněný ve stenóze označené injekcí lipiodolu na obou koncích (šipky).

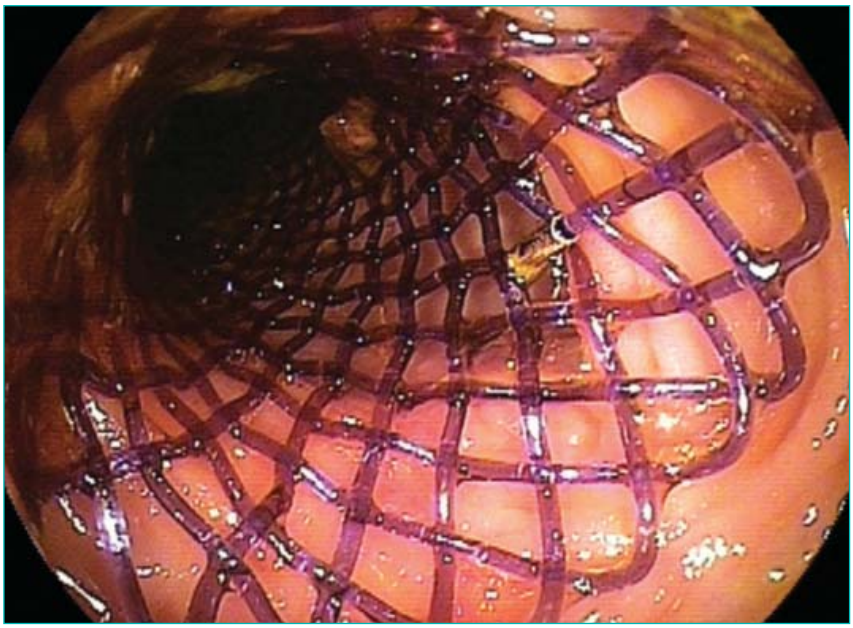

Fig. 7./Obr. 7.
Endoscopic view of biodegradable stent inserted into the tight stenosis of the transverse colon (same patient as seen on Fig. 4–6).
Endoskopický pohled na bio-degradabilní stent zavedený do těsné stenózy transverza (stejný pacient jako na obr. 4–6).

dable stent is technically possible and relatively simple. We did not observe any stent migration and/or any major complications like mucosal in-growth, perforation, bleeding or luminal obstruction with stent fragments.

CONCLUSIONS

Endoscopic introduction of biodegradable stents into small and large intestinal stenoses is feasible. Initial experience is promising. Proof of the long-term efficacy and safety requires further study.

Acknowledgement

The study was supported by research project MZO 00179906 from the Ministry of Health, Czech Republic.

References/Literatura

1. Bhasin DK, Rana SS. Biodegradable pancreatic stents: are they a disappearing wonder? Gastrointest Endosc 2008; 67(7): 1113–1116.
2. Dua KS, Vleggaar FP, Santharam R, Siersema PD. Removable self-expanding plastic esophageal stent as a continuous, non-permanent dilator in treating refractory benign esophageal strictures: a prospective two-center study. Am J Gastroenterol 2008; 103: 2988–2994.
3. England R. Implant of SX-ELLA BD biodegradable stent in patient with post radiotherapy benign oesophageal stricture. BD Clinical Bulletin A44pp. UK Medical Limited: Sheffield 2008.
4. Freudenberg S, Rewerk S, Kaess M et al. Biodegradation of absorbable sutures in body fluids and pH buffers. Eur Surg Res 2004; 36(6): 376–385.
5. Fry SW, Fleischer DE. Management of a refractory benign esophageal stricture with a new biodegradable stent. Gastrointest Endosc 1997; 45(2): 179–182.
6. Gunatillake P, Mayadunne R, Adhikari R. Recent developments in biodegradable synthetic polymers. Biotechnol Annu Rev 2006; 12: 301–347.
7. Holm AN, de la Mora Levy JG, Gostout CJ et al. Self-expanding plastic stents in treatment of benign esophageal conditions. Gastrointest Endosc 2008; 67(1): 20–25.

8. Kopacova M, Bures J, Vykouril L et al. Intraoperative enteroscopy. Ten years' experience at a single tertiary center. Surg Endosc 2007; 21(7): 1111–1116.
9. Kopacova M, Rejchrt S, Tacheci I, Bures J. Hyperamylasemia of uncertain significance associated with oral double-balloon enteroscopy. Gastrointest Endoscopy 2007; 66(6): 1133–1138.
10. Laukkarinen J, Lämsä T, Nordback I et al. A novel biodegradable pancreatic stent for human pancreatic applications: a preclinical safety study in a large animal model. Gastrointest Endosc 2008; 67(7): 1106–1112.
11. Laukkarinen J, Nordback I, Mikkonen J et al. A novel biodegradable biliary stent in the endoscopic treatment of cystic-duct leakage after cholecystectomy. Gastrointest Endosc 2007; 65(7): 1063–1068.
12. Rejchrt S, Kopacova M, Tacheci I, Bures J. Interventional double balloon endoscopy for Crohn's, gastrointestinal bleeding, and foreign body extraction. Tech Gastrointest Endoscopy 2008; 10(3): 101–106.
13. Repici A, Conio M, De Angelis C et al. Temporary placement of an expandable polyester silicone-covered stent for treatment of refractory benign esophageal strictures. Gastrointest Endosc 2004; 60(4): 513–519.
14. Saito Y, Tanaka T, Andoh A et al. Novel biodegradable stents for benign esophageal strictures following endoscopic submucosal dissection. Dig Dis Sci 2008; 53(2): 330–333.
15. Siersema PD. Stenting for benign esophageal strictures. Endoscopy 2009; 41(4): 363–373.
16. Tanaka T, Takahashi M, Nitta N et al. Newly developed biodegradable stents for benign gastrointestinal tract stenoses: a preliminary clinical trial. Digestion 2006; 74(3–4): 199–205.
17. Tierney W, Chuttani R, Croffie J et al. Enteral stents. Gastrointest Endosc 2006; 63(7): 920–926.

Correspondence to/
Adresa pro korespondenci:
Assoc. Professor Stanislav Rejchrt, MD, PhD
2nd Department of Internal Medicine
Charles University Teaching Hospital
Sokolská 581
500 05 Hradec Králové
Czech Republic
e-mail: rejchrt@lfhk.cuni.cz