Lingual Mucosal Graft as a Long Segment Ureteric Replacement: An Experimental Study in Dogs

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Abstract: Objective: The present study was conducted to evaluate the exact healing and tissue integration process of lingual mucosal graft (LMG) when used to reconstruct the long segment ureteric defects in dogs. **Materials & Methods:** Nine cross-breed clinically healthy adult dogs (5 males and 4 females) were used. The required grafts were harvested and over a double J ureteral stent, the free LMG replaced a 10 cm. in length of the right ureteral defect as onlay graft. Intravenous pyelography (IVP) was performed at the 4th, 8th and 12th weeks. At the 12th week, all dogs were euthanized to evaluate potency of the right ureter and the kidney as well as to get specimens for histopathological analysis. **Results:** There were no evidence of postoperative complications. IVP showed good drainage of the kidney with intact right ureter**.** Necropsy findings revealed maintenance of a wide right ureteral calliber without any sings of stricture or extravasation. The typical sequamous epithelium of lingual mucosa and patent junction of the LMG with the reconstructed ureter were identified histopathologically. **Conclusions:** Lingual mucosal free onlay graft is a safe and effective reconstructive procedure in dogs with long segment ureteral defects.
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Key words: Lingual mucosal graft- Ureter- Dogs.

1. Introduction

Common indications for the long segment ureteric replacement are ureteral srictures disease secondary to retroperitoneal fibrosis, surgical trauma, ureteral obstruction due to ureteritis, iatrogenically induced ureteral injury, recurrent ureteropelvic junction obstruction and ureteral carcinoma **(Wen et al., 1999; Brandes 2004; Low et al., 2010 and Berent, 2011).** Removal of solid tumours of the pelvis or abdominal cavity may require resection of an involved ureteral segment **(Steffey et al., 2004)**. The veterinary literature is scarce on the use of interventional endourological techniques for the treatment of long segment ureteral defects **(Berent, 2011).** Options for ureteral replacement traditionally include psoas hitch, boari flap, the Monti tube, use of the appendix, reconfigured colon or ileal segment **(Pope & Koch, 1996; Mathews & Marshal, 1997; Jeffrey et al., 2000; Ali-El-Dein & Ghoneim, 2003 and Armatys et al., 2009).** Management of complicated ureteral strictures defects, especially the upper third of the ureter may create a great dilemma for urologists since treatment by bowel interposition or auto-transplantation is required. Both procedures are of considerable surgical magnitude and entail long-term complications **(Evangelson et al., 2001; Brandes, 2004 and Chung et al., 2006).**

Naude (1999) and Hensle et al., (2002) treated patients with segment ureteral loss using bucal mucosal grafts (BMGs) applied as a patch wrapped with omentum. However, **Badawy et al., (2010) and Berent, (2011)** reported a series of patients who presented with extensive ureteral strictures who had BMGs laid and fixed to the ureteral adventitia and tubularized over a double J stent.

The mucosa covering the tongue has no particular functional features and like buccal mucosa. Lingual mucosa has constant availability, is easy to harvest and has favorable immunological properties (resistance to infection) and tissue characteristics (a thick epithelium, high content of elastic fibers, thin lamina propria and rich vascularization) **(Burkitt et al., 1993; Dyce et al., 2002; Rudney, 2005; Eurell and Frappier, 2006 and Michael et al., 2007).** As the lining of the oral cavity is limited, buccal mucosal graft might not be adequate for treating complicated lengthy urethral strictures that require a larger supply of graft tissue. An ideal donor site for substitution urethroplasty is LMG which has characteristics comparable to buccal mucosa, but be providing grafts of sufficient dimensions **(Lizuka et al., 1996; Simonato et al., 2006; Song et al., 2007; Barbgli et al., 2008; Kumar et al., 2008 and Simonato et al., 2008).**

The main objective of this study was to investigate the reproducibility, tolerability, safety, and efficacy of LMGs as a long segment ureteric replacement in dogs.

2. Materials and Methods

This study was performed on 9 cross-breed clinically healthy dogs (5 males and 4 females) of varying body weight from 14 to 19 Kg. and age ranged from 2-2.5 years. All dogs were fasted overnight before operations. Venous catheters were placed before the operated dogs pre-medicated with IV injection of a 0.5

mg/Kg. b.wt. Diazepam, 0.1 mL/Kg. b.wt. Polamivet and 0.05 mg/Kg. b.wt. of atropine sulphate. General anesthesia was induced by IV injection of Ketamie in a dose of 10mg/Kg. b.wt. until the main reflexes were subsided. For LMG harvesting, the apex of the tongue was passed through direct traction with a Babcock clamp to expose the ventro-lateral mucosal surface of the tongue. The required graft was measured and marked with a surgical pen (10 cm. in length and 1-1.5 cm. in width) **(Fig. 1A).** The graft edges were incised with a scalpel (dissection was facilitated by prior submucosal injection of saline solution) **(Fig. 1B).** Full-thickness mucosal grafts were harvested using sharp instruments **(Fig. 1C).** The donor sites were carefully examined for bleeding and easily closed with interrupted polyglactin 3-0 sutures. The graft was then defatted on the finger using tenotomy scissors to remove remnants of fatty tissue and strands of muscle**.** The harvested grafts were placed in isotonic saline and kept wet, thus preventing desiccation. Ventral midline laparotomy to expose the right ureter was done. Excision a 10 cm. length from the exposed uterter then over a double J ureteral stent, the free LMG replaced the ureteral defect as onlay graft (the mucosal surface of the graft was always placed as the lumen of the reconstructed ureter) and the anastomosis was done with 6/0 polyglycolic acid suture **(Fig. 2A&B)**. Once the anastomosis was completed the graft was covered with omentum. Closure of the abdomen was made with bubal drain 18 french. IV fluids for the first 24 hours as well as tramadol hydrochloride (Tramal) 100 mg. and Cefotaxime (Cefotax) 1gm/12 hrs were given IM for 3&5 successive days post-operative respectively. The double J stent removed after 4 weeks. IVP (using Urografine 76% in a dose of 825 mg/Kg. b.wt.) was performed after 4, 8 and 12 weeks from the operation time. At the 12th weeks, all dogs were euthanized, with over doses of thiopental sodium 5%, to evaluate potency of the right ureter and the kidney macroscopically as well as to get specimens for histopathological analysis. Histopathological examination of the specimens was carried out to evaluate the viability of the grafts and changes that may occur in the surface epithelium, the submucosa and the fibrous tissue deposition during healing process. The specimens were stained using Hematoxylen & Eosin (H&E) and Sirus Red stains.

3. Results

There were no difficulties associated with LMG harvesting. All dogs of this study had a successful outcome of the procedure and survived their intended survival period (12 weeks) without evidence of early or late postoperative complications, such infection or wound healing abnormalities on the harvest site related to the tongue surgery or on the perineum. The animals started oral feeding one day post-operatively. IVP showed a good drainage of the kidney without dilatation of the renal pelvis with intact right ureter **(Fig. 3A&B).** Necropsic findings revealed maintenance of a wide right ureteral calliber without any sings of stricture or extravasation **(Fig. 4A&B)**. Histopathological examination revealed disappearance of covering keratin layer of the lingual mucosal grafts and the transitional metaplasia of the squamous epithelium was observed. Few muscle fibers start to invade the graft from the native ureteral edge. Few vascular capillaries were observed in the submucosa of the graft. The collagen fiber deposited in and around the graft during healing is similar to that present in the wall of the native ureter **(Fig. 5A&B)**.

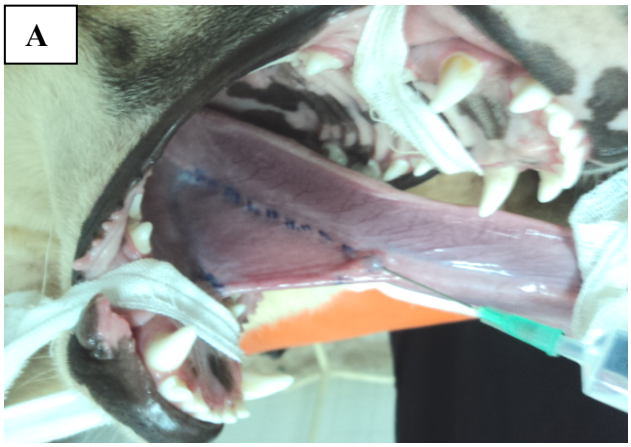

Fig. (1A). Lingual mucosa donor site exposure.

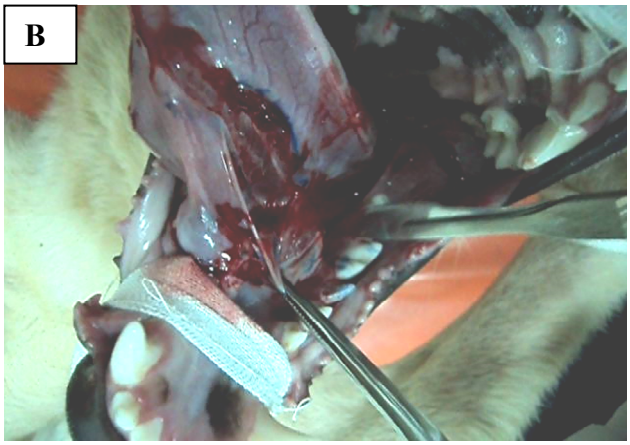

Fig (1B): Showing incision of the marked LMG.

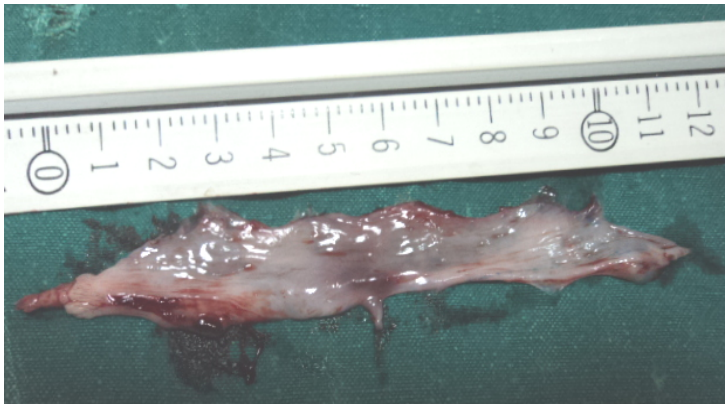

Fig. (1C). LMG being harvested.

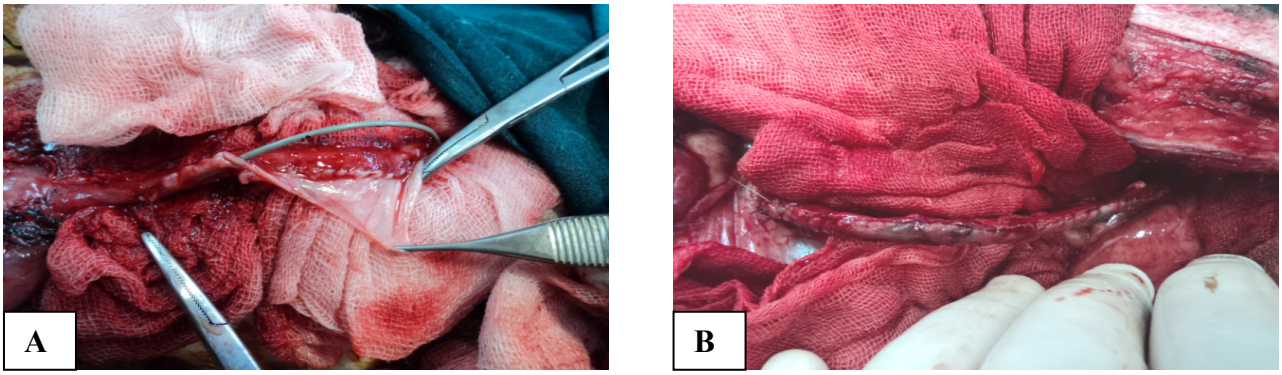

Fig. (2A&B): Showing the replacement of the ureteral defect using a free LMG over a double J ureteral stent.

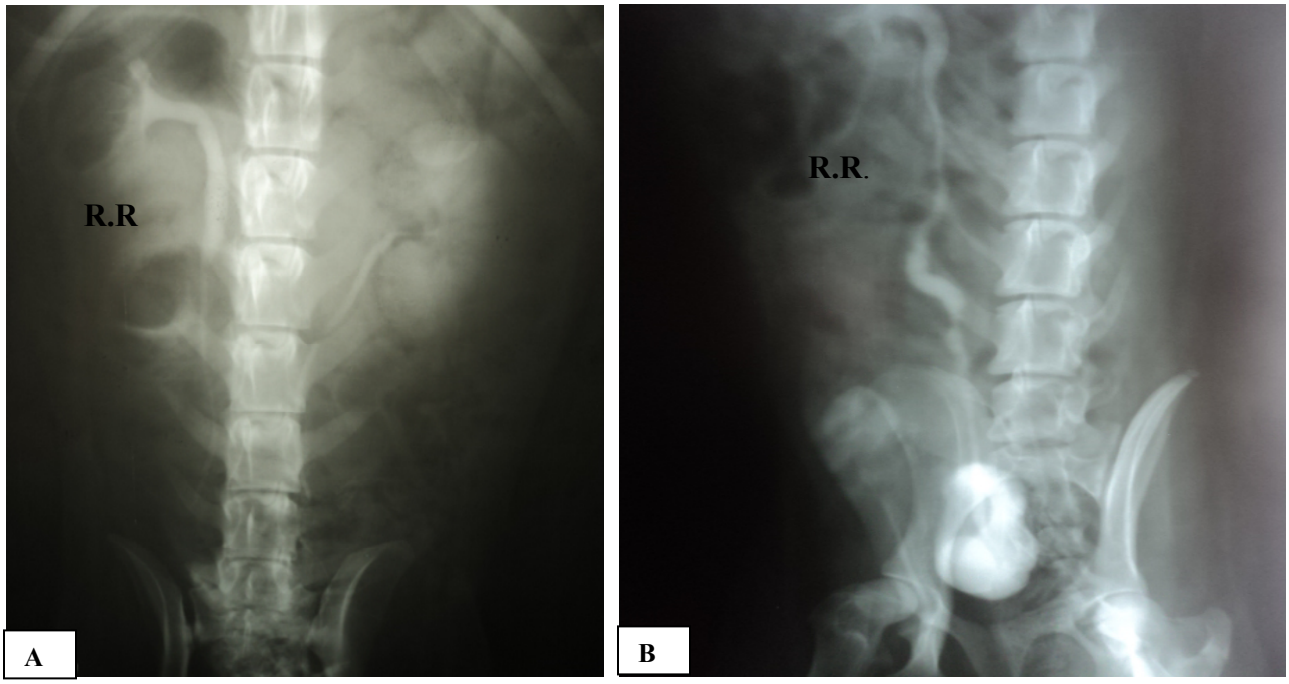

Fig. (3A&B): I.V pyelograms showing a good drainage of the kidney with intact right ureter (R.R) at 4 and 12 weeks post operative respectively.

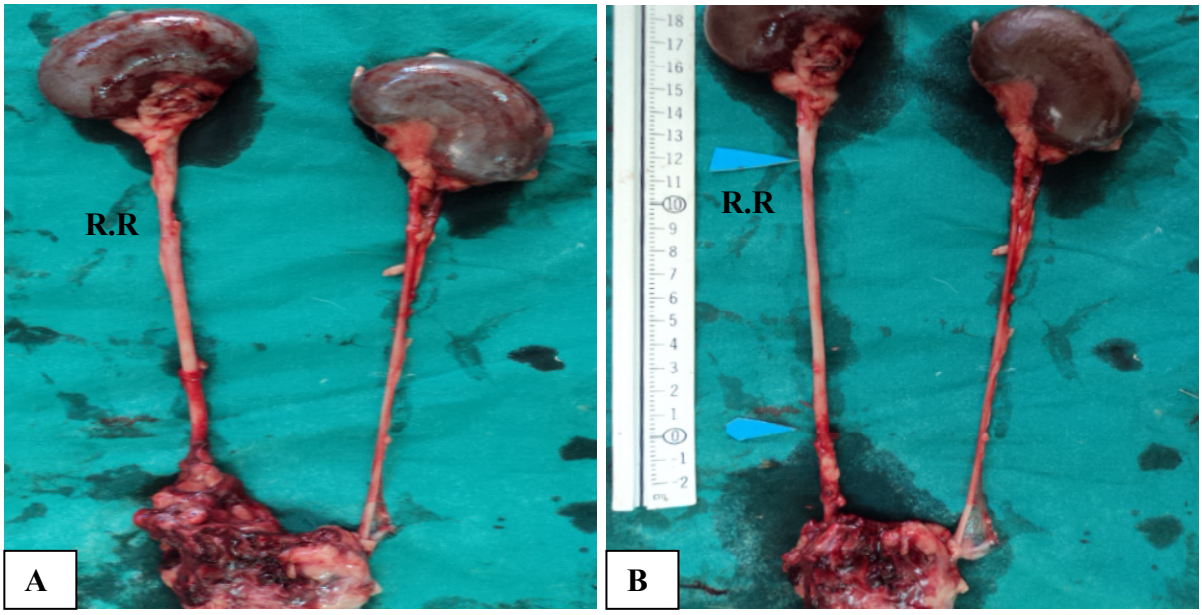

Fig. (4A&B): Necropsy findings at the 12th week revealed maintenance of a wide right ureteral calliber (R.R) without any sings of stricture.

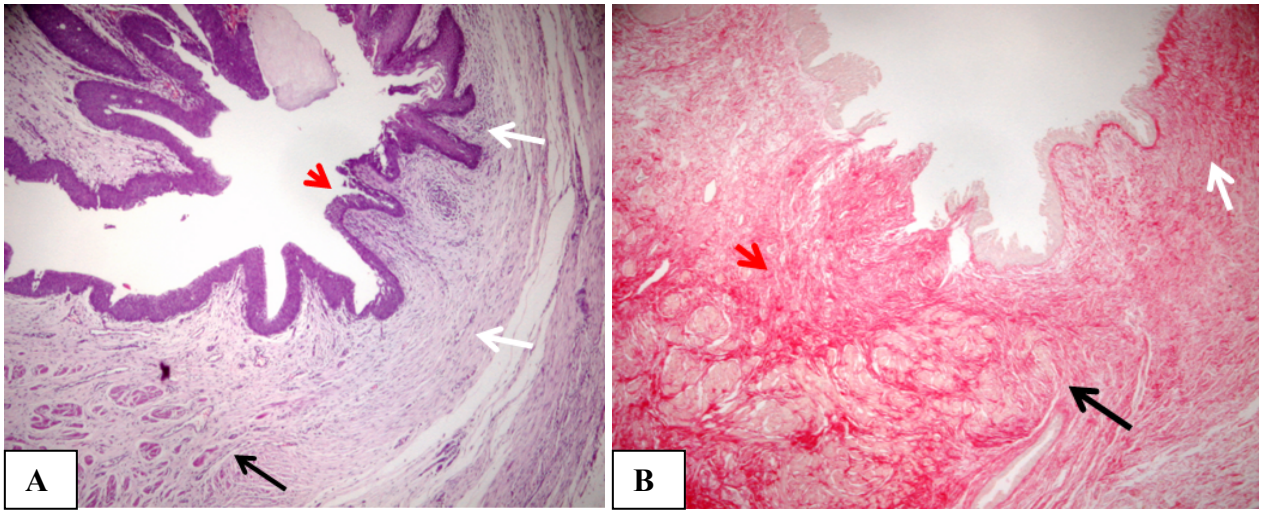

Fig. (5A&B): Lingual patch graft, early transitional metaplasia (short red arrow), the junction of the patch with the native ureter shows few muscle fibers migration towards the submucosa of the graft (long black arrow). White arrows denote capillaries in the submucosa of the graft (H&Ex40). Lingual patch graft shows deposition of mature collagen fibers in the submucosa of the graft and around it (white arrow) which is not denser than that of the native ureter (short red arrow); the black arrow denotes the junction between the graft and the native ureter (Sirus Redx40).

4. Discussion

Management of complicated ureteral strictures defects, especially the upper third of the ureter may create a great dilemma for urologists since treatment by bowel interposition or auto-transplantation is required due to their entail long-term complications (**Evangelson et al., 2001; Chung et al., 2006 and Armatys et al., 2009).** To overcome these adverse effects, previous researches have used BMGs, wheras **Naude (1999) and Hensle et al., (2002)** recorded that patients with segment ureteral loss were treated using BMGs applied as a patch wrapped with omentum. However, **Badawy et al. (2010) and Berent (2011)** reported a series of patients who presented with extensive ureteral strictures who had BMGs laid and fixed to the ureteral adventitia and tubularized over a double J stent.

Histopathologically, researchers recorded that the epithelium of the oral mucosa is stratified squamous and becomes keratinized in areas subject to considerable friction such as the palate. The oral epithelium is supported by a dense collagenous tissue **(Dyce et al., 2002 and Eurell and Frappier, 2006).** Oral epithelial cells are infused with polymicrobial intracellular and extracellular flora. Despite these harsh microbial exposures, inflammatory infiltrate is seldom witnessed under histological examination of oral mucosa in healthy individuals and the reasons for this are the suppressing activity mediated between polymicrobial flora, production of antimicrobial peptides by the epithelia **(Rudney, 2005 and Eurell and Frappier, 2006)**.

Michael et al. (2007) reported that, **t**he lamina propria of a welldefatted oral mucosa graft can be considered a secondary barrier preventing microorganisms from entering adjacent tissue layers and exhibits noteworthy antimicrobial properties including lymphocytes, immunoglobulin-synthesizing plasma cells, monocytes/macrophages, polymorphonuclear neutrophils, mast cells**.** Sebaceous glands are located in the lamina propria and it can be demonstrated through immunohistochemical staining that nerve fibers and blood vessels from the submucosa infiltrate into the lamina propria, therefore providing a mechanism for angiogenesis and revascularization of the tissue whilst grafting **(Burkitt et al., 1993 and Eurell and Frappier, 2006).** Oral mucosa is highly resilient and resistant to recurrent exposure to compression, stretching and shearing forces. This resilient and resistant can be partially credited to the lamina propria-oral epithelium interface, which consists of widespread projections of connective tissue into the epithelial layer, providing the oral mucosa's capacity to resist overlying forces **(Dyce et al., 2002; Eurell & Frappier, 2006 and Michael et al., 2007).** Though all these advantages, the lining of the oral cavity is limited and the BMG might not be adequate for treating complicated lengthy urethral defects that require a larger supply of graft tissue **(Lizuka et al., 1996; Song et al., 2007 and Simonato et al., 2008).**

Our findings agree with those reported by **Barbgli et al. (2008) and Kumar et al. (2008)** who found that **a**n ideal donor site for long segment uretral defects substitution is LMG which has characteristics comparable to buccal mucosa, but be providing grafts of sufficient dimensions. In the present study, all dogs had a successful outcome of the procedure without evidence of early or late postoperative complications.. Post-operative IVP revealed good execratory function of both kidneys and ureters. By gross examination of the upper urinary tracts after scarification of the animals showed no gross dilatation, stricture, shrinkage or extravasation. The typical sequamous epithelium of lingual mucosa and patent junction of the LMG with the reconstructed ureter were identified histopathologically.

In conclusion, it was found that surgical technique for harvesting a graft from the tongue is simple, safe and the replacement of long ureteral segment with lingual onlay mucosal graft is effective and provides good results.

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