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Review

Long-term complications arising from bowel interposition in the urinary tract

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HIGHLIGHTS

- The use of bowel in urologic reconstructive surgery is not devoid of complications.
- Their pathophysiology is related to bowel's mucosa and length of the segment used.
- Acid-base imbalance, B12 malabsorption, nephrolithiasis, are commoner with ileum use.
- Hypokalemia and neobladder stones are commoner with colon.
- Surgeons should consider those complications to tailor the best surgery to each patient.

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ABSTRACT

After radical cystectomy or pathologies affecting the ureter(s), bowel segments can be employed to restore the natural urine flow or to create an external urinary diversion.

Nevertheless, the interposition of bowel segments in the urinary tract is not devoid of complications.

In fact, bowel's microstructure differs from the urothelium; specifically its mucosa is aimed at reabsorption, rather than storage.

The aim of this paper is to revise the pathophysiology of complications related to bowel's mucosal properties. Those are: metabolic imbalance, malabsorption of vitamins, cholelitiasis, nephrolitiasis and infections. Their entity varies according to the segment used and to its length, which reflects the surface in contact with urine. Mostly, they occur on the long-term, but metabolic imbalances might occur soon after surgery as well.

1. Introduction

The interposition of bowel segments in the urinary tract, and, especially, neobladder reconstruction, exposes to long-term complications such as metabolic imbalance, malabsorption of vitamins, cholelitiasis, nephrolitiasis and infections [1,2].

The spectrum of those complications depends on the segment used and on its length. Thus they are more pronounced when an orthotopic neobladder or a heterotopic neobladder (pouch), for urinary diversion, are reconstructed.

Herein we are going to focus on the mechanisms underlying complications that arise in patients with a bowel segment interposed within the urinary tract. Most studies have been conducted on patients with a neobladder [1,3], but the same considerations that apply for neobladders are valid also for pouches, uretero-ileal substitution and conduits. In the latter circumstances, mostly a modest and generally insignificant metabolic imbalance may occur.

While one can modify the segment by detubularization thus avoiding issues peristalsis and high-pressure related, none can modify in any way the mucosal properties of the bowel. Although with time mucosal changes have been described [4], the intrinsic intestinal mucosal properties are the very responsible for the main complications [1,3].

2. Discussion

2.1. Acid base imbalance

Hyperchloremic metabolic acidosis is a well known bowel interposition-related complication [1,3]. This occurs if ileum or

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colon, as either proximal or sigmoid, are used and nowadays these are the two most utilized segments. The probability of developing acid-base imbalance is low if kidney and hepatic function are not impaired [3].

In 1931 Julian Boyd reported a case of rickets, secondary to chronic acidosis, in a young patient who had underwent ureterosigmoidostomy; he appropriately pointed out that there were no evidence that renal impairment was the cause of such metabolic imbalance [5]. Thus he anticipated the concept of acid-base imbalance secondary to urinary diversion.

Urine contact with bowel mucosa results in the absorption of its components; its entity depends on surface extension, mucosal characteristics, time of contact and initial urine composition [6].

Ammonium transport is the main culprit of the genesis of acidosis in ileal and colonic neobladders [1,3]. Luminal epithelial cells express, among other proteins, a sodium/hydrogen antiport and a chloride/bicarbonate one. Urinary ammonium competes with sodium for the sodium/hydrogen antiport, determining ammonium absorption and hydrogen luminal excretion. In order to keep electroneutrality, a molecule of bicarbonate is expelled and a molecule of chloride reabsorbed [7,8]. The net gain of ammonium chloride and net loss of sodium bicarbonate are the main responsible for acid-base alteration [9,10]. Moreover, ammonia can freely diffuse through luminal cells and ammonium can also compete with potassium for potassium channels [3,7].

Absorbed ammonium reaches the liver through the portal system, here it enters the urea cycle and a proton is generated for each catabolized ammonium molecule.

Normally 2NADH and $2H^+$ are produced during the urea cycle, the first NADH molecule is produced by glutamate dehydrogenase, the second is produced by malate dehydrogenase: when fumarate is released into the cytosol, it is converted by cytosolic fumarase to malate, its reduction to oxaloacetate reduces a NAD^+ molecule to $NADH + H^+$ [11].

When a free ammonium molecule enters the urea cycle, originating from ammonium reabsorption, the first NADH production through glutamate dehydrogenase is missing, so one proton is generated for every reabsorbed ammonium metabolized. This acid load is titrated by serum bicarbonate, the so produced carbon dioxide is expelled by lungs. Untreated metabolic acidosis is compensated by lungs resulting in a chronic respiratory alkalosis.

Concerning neobladders, the highest risk of metabolic acidosis is encountered when Hautmann technique is adopted, because it requires an ileal segment up to 60 cm long [12].

Reabsorbed ammonium load seems to be higher if urea-splitting organisms are present inside neobladder [13].

When colon is adopted, the rate of metabolic imbalance is lower and chronic oral therapy with bicarbonate is generally not required [14]. In order to treat metabolic acidosis, one can administer oral sodium bicarbonate or sodium citrate plus citric acid known as Shole's solution. Patients under sodium restriction diet can undertake a combination of sodium citrate and potassium.

Patients under sodium and potassium restriction diet can undertake Chlorpromazine [15] or Nicotinic Acid [16]. Rationale for that relies on the reduced synthesis of cAMP in intestinal epithelial cells, resulting in chloride/bicarbonate reduced activity.

2.2. Electrolyte imbalance

The net movement of electrolytes is aimed at reaching electoneutrality. Water tends to move accordingly to concentration gradient. Urine is generally hypertonic, thus there is a potential risk concerning loss of water. When colon is used, the probability of water loss is low because of the epithelial cell tight-junctions that virtually prevent water luminal diffusion. Advising patients to drink an adequate amount of water can prevent problems related to water loss.

Regarding electrolyte imbalance, hypokalemia can occur, its probability is higher when colon is used [1,3]. The mechanism has not been fully elucidated, it seems that when high potassium solution is in contact with bowel mucosa, ileum can reabsorb this ion better than colon does, thus, in case of potassium waste, colonic neobladder predisposes to hypokalemia [17].

2.3. B12 malabsorption

When colon is used, for anatomical and physiological reasons, B12 absorption is intact. When ileum represents the segment of choice, B12 malabsorption may occur, its entity is higher if a 60 cm or longer segment is employed [18,19]. It has been noted that the sparing of the terminal 15 cm ileum is not enough to avoiding such complication, even if its entity is lower [20].

2.4. Cholelithiasis, nephrolithiasis and neobladder calculi

Up to 95% of bile acids are reabsorbed in the ileum, the absorption process is higher in its distal part [3]. Alterations in the entero-hepatic bile acids cycle predisposes to cholelithiasis [21,22], the entity of which is difficult to evaluate since most of the times gallbladder stones do not cause symptoms.

Theoretically alterations in the bile acids reabsorption process should predispose to fat soluble vitamins malabsorption as well, but no studies have evaluated this complication.

The same mechanism is implicated in the pathogenesis of nephrolithiasis: not reabsorbed bile acids and not reabsorbed fatty acids compete with oxalate for binding to intraluminal calcium and so are excreted; an increased amount of free oxalate is thus ready to be reabsorbed, this process is enhanced by the contact between bile acids and colonic mucosa that increase permeability to oxalate [23,24]. Oxalate excess is expelled by kidneys thus predisposing to oxalate calculi formation.

Neobladder or pouches stones formation is due to the presence of wires and stapler clips and to mucus alteration, especially secondary to obstruction or infections [25], they are more likely to develop in patiens with colonic neobladder which is more prone to produce great amount of mucus.

2.5. Infections

For what concerns infections, the incidence in neobladder patients is increased. Nakano et al. found an increased urinary level of IL-1β IL-6 and IL-8 in patients with ileal neobladders compared to patients with sigmoid one, consistent with chronic inflammation. The enhanced production of IL-6 and IL-8 are associated with chronic bacteriuria, thus the sigmoid neobladder exposes to a lower risk of chronic bacteriuria when compared to ileum [26].

2.6. Drugs reabsorption

Excreted unchanged drugs can be reabsorbed from inside the neobladder, this is valid if an ileal neobladder is reconstructed, because the absorption of drugs at colonic level is negligible. Enhanced methotrexate toxicity has been described in patients with Bricker conduit [27,28]. It is common knowledge inserting a urinary catheter if a patient after neobladder reconstruction must undergo chemotherapy.

3. Conclusion

The pathophysiology of complications related to the

interposition of bowel segments within the urinary tract helps surgeons to remind them.

Theoretically, the use of the ileum, for its anatomical and physiological properties tends to expose to a greater likelihood of long-term complications if compared to the colon. The rate of these complications can be reduced with an appropriate medical therapy and patients' education.

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Alberto Martini: Manuscript writing/editing.
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Conflicts of interest

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