Effectiveness of Oral Route Isosorbide 5-Mononitrate on Peritoneal Solute and Fluid Transports in CAPD Patients

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Background: *Addition of sodium nitroprusside (NaNTP), a nitric oxide (NO) donor, to peritoneal solution could enlarge the effective peritoneal surface area and the peritoneal pore size. This would be leading to increased clearance of all solutes. Generalized clinical usage of NaNTP in CAPD patients however is not practical because it has a very short half-life and needs a specific route of administration. Organic nitrate, another NO donor, has a longer half-life and could be more easily absorbed via many routes.*

Objective: *The present study was conducted to determine the effect and mechanism of oral active nitrate (isosorbide 5-mononitrate: ISMN) on solute and fluid transports in stable CAPD patients.*

Material and Method: *A prospective randomized placebo control with a crossover study was performed in nine stable CAPD patients. In group 1 (n = 4), the treatment included 1) oral ISMN at the dose of 20 mg bid for 5 days 2) wash out period for 7 days, and 3) placebo for 5 days. In group 2 (n = 5), the treatment regimens were placebo, wash out, and ISMN periods.*

Results: *The MTACs of low molecular weight (LMW) solutes in the ISMN period were greater than the placebo period: median urea, 16.7 vs 13.8 ml/min; creatinine (Cr), 7.9 vs 6.9 ml/min; and urate, 6.1 vs 5.5 ml/min ($p < 0.05$ for all except MTAC of urea). Administration of ISMN could also enhance the clearances of high molecular weight (HMW) solute with a magnitude of increase as follows: 10% for β_2-microglobulin, 50% for albumin, and 15% for immunoglobulin G ($p < 0.05$ for all). However, the values of restrictive coefficient of LMW as well as HMW solutes of both groups were not different, indicating that the increased solute transports are not due to alteration in the peritoneal membrane permeability. Despite the increased peritoneal solute clearance, net ultra filtration (UF) was unchanged after drug administration, 110 (ISMN group) vs 120 ml (placebo group), (NS).*

Conclusion: *ISMN has a similar effect as NaNTP in enhancing peritoneal clearances of both LMW and HMW solutes. The effect of ISMN, however, is mediated only via expansion of peritoneal surface area without significant change in pore size. As such, administration of oral ISMN to stable CAPD patients would be practically beneficial in enhancing the achievement of target solute clearances suggested by NKF- DOQI Guidelines.*

Keywords: *Isosorbide 5-mononitrate, MTAC, Peritoneal solute transport, Fluid transport, CAPD*

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The results from the CANUSA study[1], one of the most prestigious prospective multicenter cohort studies, have demonstrated the correlation between small solute clearances and the mortality rate of CAPD patients. Thus, every 0.1 decrement in total weekly Kt/V urea and 10 L decrement in total weekly normalized creatinine clearance (nCrc) are associated with 5% and 7%, respectively, decreases in patient survival. These data have supported the view that the more dialysis doses, the better outcome. Based on this evidence-based clinical outcome, NKF-DOQI[2] has recently

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recommended that the minimum delivered dose target of Kt/V urea should be 2.0 per week while the minimum weekly total Crc should be 60 L/1.73 m^2. It seems, however, hard to achieve these targets in CAPD patients who have a trivial amount or no residual renal function and currently receive standard treatment doses, four 2-litres exchanges.

Theoretically, the amount of a solute that could traverse the peritoneal membrane during peritoneal dialysis would depend on the effective vascular surface area as well as the intrinsic permeability of the peritoneal membrane to that solute[4]. Vasoactive substances could influence both membrane parameters[5-10]. Intraperitoneal administration of sodium nitroprusside (NaNTP)[11-19], a direct nitric oxide (NO) donor, has been shown to markedly increase peritoneal clearances of both low and high molecular weight (LMW and HMW, respectively) solutes, in animals as well as in intermittent peritoneal dialysis and CAPD patients.

Despite such salutary effects of NaNTP[19], there are several limitations for clinical use in general practice. First, the only administration route of the drug is intraperitoneally. Second, the drug has a very short half-life (2-3 seconds). Lastly, the drug could cause serious side effects including cyanide and thiocyanate intoxications and severe systemic hypotension, particularly in anuric patients. In contra-distinction, organic nitrate, another NO donor[19-21], could be easily absorbed via many routes, has a longer half-life, and has fewer systemic side effects than NaNTP. Thus, oral organic nitrates might be used as a clinically beneficial enhancer of solute transports in CAPD patients.

The present study was performed to investigate a possible role of oral IsoSorbide 5-MonoNitrates (ISMN) in the regulation of the peritoneal solute and fluid transports in stable CAPD patients.

Material and Method

Patients

The effects of oral route ISMN on peritoneal solutes and fluid transports were conducted in 9 stable CAPD patients (female = 4 and male = 5), who were treated at King Chulalongkorn Memorial Hospital, Bangkok Thailand between January 1st, 2000 and December 31st, 2000. The present study was approved by the Ethical Committee, Faculty of Medicine, Chulalongkorn University, Bangkok Thailand. Informed consent was obtained from all patients. The studied patients had a median age of 58 years (ranged 24-75 years) and were treated with CAPD for a duration ranging from 3 to 56 months (median 11 months). The underlying diseases of end stage renal disease included diabetic nephropathy[4], hypertensive nephrosclerosis[1], and unknown[4]. The characteristics of the transporter in each patient were assessed by a standard peritoneal equilibrium test[22] prior to the present study: low average = 5, high average = 3, and high = 1. All patients were free of peritonitis at the time of the present study as well as in the four preceding weeks. The exclusion criteria were active systemic inflammatory diseases, unstable vital signs, contrain-dications of nitrates therapy[19,21] (hypertrophic cardiomyopathy, diastolic heart failure, constrictive pericarditis and restrictive cardiomyopathy), allergy to nitrates, and ongoing nitrates.

Method

To circumvent interpatient variation, the study protocol included two-drug administration, placebo and ISMN, in a crossover fashion on separate periods (Fig. 1). Thus, the patients were randomized into 2 groups. Transports of LMW as well as HMW solutes were determined by peritoneal function test, performed as previously described by Krediet RT, et al[23]. In brief, the peritoneal cavity was rinsed with two liters of 1.5 % dialysis solution before installation of the test solution into the abdomen. This rinsed solution was completely drained over 20 min. in the sitting position, inverting the bag three times for mixing the drainage dialysate, and, then, dialysate sample was collected. A blood sample was obtained at the end of drainage. Two liters of 1.5% dialysis solution was infused in portions of 400 mL per 2 min over a total of 10 min. The patient was in the supine position during infusion and rolled from side to side after infusing each 400 mL for better mixing of the residual peritoneal volume and the new infused solution. At the completion of infusion (0-dwell time), exactly 10 min after the start of infusion, 200 mL of solution was drained into the bag, mixed by inverting the bag three times, 10 mL sample of dialysate was taken and the remaining 190 mL was reinfused. The patient was ambulatory during the dwell period. After a 4-hour dwell time, the dialysis was drained over 20 min while the patient was in the sitting position, the total volume was measured and a sample was taken. The total time of the exchange was 270 min. A blood sample was obtained at the end of drainage. A sample of dialysis was taken from the post test rinsed bag to be infused, and two liters of fresh solution were infused over 10 min with the same technique as for the test solution exchange; immediately drained over 20 min in

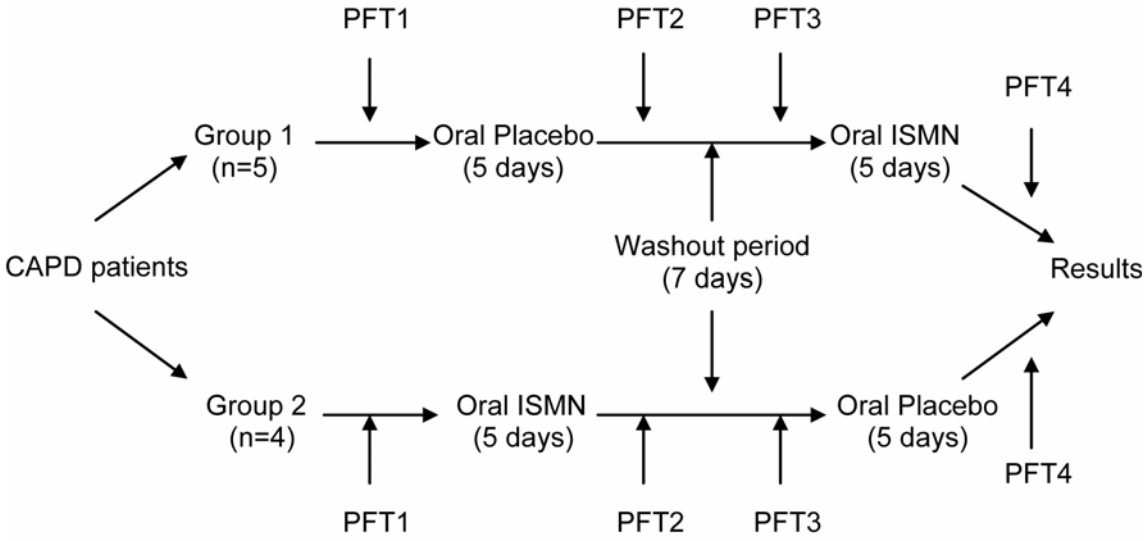

Fig. 1 Summary of protocol study

the sitting position. Pulse rate, body weight, and blood pressure while sitting and lying were measured before inflow of the first rinsed bag and during outflow of the last rinsed bag.

UF was assessed by direct measurement of the difference between the drained and infused dialysate volume.

Measurements

Theoretically, the main solute transport mechanism across peritoneal membrane depends on diffusion, which occurs bi-directionally via both small and large pores[5,24,25]. The products of the Mass Transfer Area Coefficient (MTAC) and the concentration gradient determine the rate of diffusion. In a situation where equilibrium is not present between plasma and dialysate concentration as occur in a case of HMW solutes transport, the authors can approximate MTAC by using clearance. In general, the MTACs as well as clearance of solutes depend on both effective peritoneal vascular surface area and intrinsic permeability of the peritoneum. The latter is inversely proportionate with Restriction Coefficient (RC).

The LMW solutes examined in the present study included urea, Cr, and urate while the large solutes comprised β_2-microglobulin, albumin, and immunoglobulin G (IgG). The MTAC of urea, Cr, and urate were calculated according to the model of Garred et al[4,26]. Peritoneal clearances of β_2-microglobulin, albumin, and IgG were determined using the equation.

$$\text{Clearance (mL/min)} = \frac{(C_{Dt} - C_{Do}) \times V_d/t}{C_B}$$

C_{Dt} = the dialysate concentration at t hour dwelled, C_{Do} = the dialysate concentration at complete infused of test solution, C_B = the plasma concentration, V_d = the dialysate volume, and t = the dwell time.

To calculate the RC of the LMW solutes, the MTACs of urea, Cr, urate, and β_2-microglobulin were used. The clearances of β_2-microglobulin, albumin, and IgG were used to calculate the RC of peritoneal membrane to these macromolecules. RC is calculated by the slope of power relationship of peritoneal MTACs (LMW solutes) or clearances (HMW solutes), and their free Diffusion coefficient in water ($D_{20,W}$) when plotted on double logarithmic scale, according to the equation: MTAC or Clearance = constant x $D_{20,W}^{rc}$.

Net UF was calculated by subtracting drained volume with infused volume. Urea, Cr, and glucose in both plasma and dialysate were immediately measured with enzymatic method, while urate was measured by alkaline phosphotungstate reaction, and albumin by Bromcresol green dry binding method. Serum and dialysate samples of β_2-microglobulin and IgG were frozen at -70°C until assays were examined, usually within one month. When the samples were ready to test, the samples were thawed at 20-25°C by Waltex machine for 30 min. and mixed vigorously before the assays were performed. β_2-microglobulin was determined on COBAS COREII system using a Microparticle

Enzymatic Immunoassay. IgG was measured with Behring Nephrelometer-100 Analyzer.

Statistical analysis

One-sample Kolmogorov-Smirnov test was used to test data distribution. Gausian distribution results were reported as mean and standard deviation, while non-Gausian distribution results were expressed as median and range. Crossover analysis of variances was employed for testing hypothesis. Either pair T-test or Wilcoxon matched pairs rank sum test was used to compare the difference in side effects of ISMN and placebo depending on data distribution, with $p < 0.05$ as the significant level.

Results

Transports of LMW solutes

Following 5 days of treatment with oral ISMN, the MTACs of Cr and urate were significantly increased ($p < 0.05$) (Table1). There was a trend for the MTAC of urea to increase although the statistical significance was not attained. Of interest, the median MTAC increases of Cr was 14%, of urate was 11%, and of urea was 21%. The increase in Urea was much higher than the former two. The glucose absorption during oral ISMN period was not significantly increased (Table 1).

Transport of HMW solutes

After ISMN therapy, there were also significant increases in the clearances of the HMW solutes. The β_2-microglobulin increased by 10%, albumin by 49% and IgG by 15% (Table 2). The 4-hour albumin loss was 1.1 gram during the ISMN period compared with 0.8 gram in the placebo period.

The values of RC of LMW as well a.0s HMW solutes were not significantly changed after treating with ISMN (Table 3).

Fluid transport

As shown in Table 4, there were no significant differences of median and range values of net UF between the two periods.

Side effects

Following ISMN treatment, two of nine patients developed minor side effects consisting of mild degree

Table 1. Mass transfer area coefficient (MTAC) of the low molecular weight solutes and the percentage of glucose absorption in the oral ISMN and placebo groups

	ISMN (N = 9)	Placebo (N = 9)	Percent change of transport rate	p-value
MTAC (ml/min)				
Urea	16.7 (12.3-29.3)	13.8 (11.2-20.7)	+21	NS
Creatinine	7.9 (5.6-15.1)	6.9 (5.7-12.5)	+14	<0.05
Urate	6.1 (4.5-11.1)	5.5 (3.8-8.6)	+11	<0.05
Glucose absorption (%)	52 (43-61)	49 (42-61)	+6	NS

The data were expressed as median (range)
Abbreviation: NS = Non significant ($p > 0.05$)

Table 2. Clearance of high molecular weight solutes and 4-hour albumin loss in the oral ISMN and placebo groups

	ISMN (N = 9)	Placebo (N = 9)	Percent change of clearance	p-value
Clearance (μl/min)				
β_2 microglobulin	790 (676-1327)	721 (437-1116)	10	<0.01
Albumin	125.7 (66.2-352.9)	84.3 (31.2-312.5)	49	<0.05
IgG	36.0 (23.8-96.7)	31.2 (15.9-69.9)	15	<0.01
Albumin loss (gm/4 hr)	1.1 (0.5-2.5)	0.8 (0.2-2.0)	38	<0.05

The data were expressed as median (range)

Table 3. Low and high molecular weight (LMW and HMW, respectively) solute's restrictive coefficient in the oral ISMN and placebo groups

	ISMN (N = 9)	Placebo (N = 9)	p-value
Restrictive coefficient			
LMW solutes	1.3 (1.2-1.4)	1.3 (1.1-1.4)	NS
HMW solutes	2.5 (2.3-2.9)	2.6 (2.2-3.1)	NS

The data were expressed as median (range)
Abbreviation: NS = Non significant ($p > 0.05$)

Table 4. Net ultrafiltration during 4-hour dwelling in the oral ISMN and placebo groups

	ISMN (N = 9)	Placebo (N = 9)	p-value
Net ultrafiltration (mL)	120 (100-240)	110 (80-200)	NS

The data were expressed as median (range)
Abbreviation: NS = Non significant ($p > 0.05$)

Table 5. Mean arterial blood pressure (mABP) and pulse rate in the oral ISMN and placebo groups

	ISMN (N = 9)	Placebo (N = 9)	p-value
mABP * (mmHg)	101 $\pm$ 18.2	106 $\pm$ 21	NS
Pulse rate ** (BPM)	74 (56-100)	76 (70-96)	NS

* Mean $\pm$ (standard deviation)
** Median (range)
Abbreviations: NS = Non significant ($p > 0.05$), BPM = Beat per minute

of nausea, vomiting and sweating. Both patients, however, could continue the drug without additive symptoms until the present study was finished. Neither pulse rate nor blood pressure while sitting and lying were altered after the patients completely received ISMN (Table5).

Discussion

The results in the present study, performed in stable CAPD patients, have shown that following treatment with oral ISMN for 5 days: 1) the MTAC's of LMW solute including Cr and urate are increased and there is a trend of increased urea MTAC, 2) the clearances of the HMW solute comprising β_2-microglobulin, albumin, and IgG are enhanced, 3) the RC values of LMW and HMW solutes remained unchanged, 4) glucose absorption and net UF are unaltered, 5) there are acceptable minor side effects after drug treatment.

The increases in both LMW and HMW solutes transports observed in the present work would be of significance in clinical practice. Regarding to LMW solutes, for example, there was a 14 percent or approximately 1 ml/min increase in peritoneal Crc (Table1). One could extrapolate that the continuous use oral ISMN for one week would add 10 liters per week (1 x 60 x 24 x 7) to the baseline peritoneum Crc. This might convert the patient from being in the range of inadequate dialysis to the state of having adequate dialysis dose.

Regarding HMW solutes, prolonged exposure of high plasma level of β_2-microglobulin is related to a well-recognized complication of long-term dialysis, particularly dialysis-related amyloidosis. In several studies[28-32], it was found that increasing β_2-microglobulin removals via many modalities of hemodialysis is able to prevent or delay onset of dialysis-related amyloidosis. However, the correlation between amount of amyloid deposition and plasma β_2-microglobulin concentration are not strong[33]. Moreover, recent immunohistochemical and chemical analyses have indicated that β_2-microglobulin amyloid deposits are modified by advanced glycation end products, implying that the modified β_2-microglobulin might have an active

pathogenic role in dialysis related-amyloidosis[34-38]. It can be expected that the usage of oral ISMN, which enhances 10% increment of peritoneal clearance of β_2-microglobulin, might have a beneficial effect in dialysis-related amyloidosis at least in aspect of reduction of precursor of modified β_2-microglobulin.

One might concern the clinical impact of the 49 percent increase in peritoneal albumin clearance following ISMN therapy. In this regard, the median value of the actually increased amount of the peritoneal albumin loss was 0.3 gram, 1.1-0.8 = 0.3, per four hours exchange (Table 2). This would cause increased peritoneal albumin loss from 4.8-6.6 grams per 24 hours. Such values, however, are less likely to affect the serum albumin levels. Indeed, a recent work has demonstrated that albumin synthesis in CAPD patients is enhanced despite increased albumin loss[39]. Moreover, several studies have shown that the main determinants of serum albumin concentration in CAPD patients are age and the presence of systemic disease including diabetes mellitus. Peritoneal albumin loss is a minor contributing factor[40,41].

Another concern with the increase peritoneal LMW solute transport following oral ISMN is the possibility of the worsening in net UF. Of interest, there is no significant change in the net UF. Such effect of ISMN is similar to that of low dose sodium nitroprusside (NaNTP) administered intraperitoneally in an animal study described by Wang T[13]. Indeed, the net UF is mainly dependent on net glucose absorption from peritoneal cavity to blood circulation, which is unaltered after 4-hour dwelling (Table 1). Indeed, the net glucose absorption is not as simple and/or passive as peritoneal urea, urate, and Cr transports, but is affected mainly by insulin and glucose concentration[42]. Glucose is taken up by cells and used as an energy source. Glucose transporters, which facilitate glucose transport into the cells, mediate intracellular glucose uptake[43]. The peritoneal permeability to glucose is decreased with the inhibition of glucose transporters[44,45]. Of interest, using a glucose transporter inhibitor could reverse the increased peritoneal glucose absorption observed after long-term use of glucose-containing dialysis solutions[45]. This observation does not occur in other LMW solutes transport.

As such, the beneficial effects of ISMN on clearances of both LMW solutes as well as β_2-microglobulin would outweigh the limited unfavorable results of ISMN on peritoneal albumin loss.

As stated earlier, solute transport across the peritoneal membrane depends on the effective vascular surface area and the intrinsic permeability of the peritoneum, which is governed by RC. The unchanged RC values of both solutes noted in the present study would indicate that oral ISMN enhances LMW as well as HMW solutes transports by increasing effective vascular surface area. Such findings are expected since the rate of transport of LMW solutes mainly depends on the effective vascular surface area, while the rate of transport of HMW solutes is determined on both peritoneal factors.

The RC represents the size selective permeability of the peritoneal membrane[4,26,27]: high values mean a low permeability. The RC value equal to 1.0 means a linear relationship between MTAC and free diffusion coefficient, and no hindrance by the size selective restriction barrier. This occurs in case of LMW solutes transport. On the contrary, HMW solutes have RC of much greater than 1, indicating the characteristic hindrance to diffusion process[4,26,27].

Regarding mechanism of action, ISMN and NaNTP have similar active NO. In animal models[46], the increased effective surface area following NaNTP treatment is likely caused by an increment in the number of newly opened capillaries. NaNTP donates NO, a free radical gas derived from a guanidine nitrogen of L-arginine by a five-electron oxidation reaction. NO could activate guanylate cyclase enzyme that, in turn causes an accumulation of intracellular cyclic guanosine 3', 5' Mono Phosphate (cGMP). Smooth muscle cell relaxation is induced by cGMP through fluxes in intracellular calcium, resulting in vasodilatation[19-21]. Opening the previously not perfused capillaries would increase the total number of pores without significant changes in the pore property. As obviously demonstrated in the present study, the enhancing effect of ISMN on both LMW and HMW solute transports without altered RC would be mediated via such mechanism. Several studies, however, have further shown that NaNTP, in addition to increase effective peritoneal vascular surface area, could also simultaneously reduce the RC of both solutes.

There are certain different effects on solute transports between ISMN and NaNTP[11,12,15]. 1) NaNTP causes greater increases in MTACs of LMW solute: 43% for Cr and 22% for urate and also significant increase in MTAC of urea. 2) NaNTP has much greater increases in clearance of HMW solute: 34% for β_2-microglobulin, 70% for albumin and 77% for IgG. 3) NaNTP enhances solute transports with a trend to be proportionately greater with increasing solute molecular weight.

These discrepancies might be caused by the disparity in the aforementioned mechanism of action between the two drugs or by difference in the route of administration. According to the latter factor, most NaNTP data[11-18] have demonstrated the beneficial effects of intraperitoneal route, while ISMN is administered via the oral route. Intraperitoneal route may have greater benefits than oral route by many reasons including higher dose, accurately intraperitoneal drug levels, and more direct contact with peritoneal membrane.

In conclusion, the addition of oral route, ISMN could enhance both LMW and HMW solute transports, the mechanism mediated via increased effective peritoneal vascular surface area without significant change in peritoneal pore size. ISMN treatment has no effects on UF rate and net glucose absorption. Furthermore, no significant side effect was found.

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การบริหารยาไอโซซอรไบด์โมโนไนเตรดทางปาก กับความสามารถของเยื่อบุผนังช่องท้องในการแลกเปลี่ยนของเสียและน้ำในผู้ป่วยไตวายเรื้อรังระยะสุดท้ายที่ได้รับการรักษาทดแทนด้วยการฟอกช่องท้องแบบถาวร

เถลิงศักดิ์ กาญจนบุษย์, สมชาย เอี่ยมอ่อง

พบว่าผู้ป่วยไตวายเรื้อรังระยะสุดท้าย ที่ได้รับการฟอกไตทดแทนด้วยการล้างช่องท้องถาวรอย่างไม่เพียงพอ มีอัตราการเจ็บป่วยและอัตราการตายสูง ดังนั้นจึงมีความพยายามที่จะเพิ่มความเพียงพอในการฟอกไตทางช่องท้อง โดยการบริหารยาเพื่อเพิ่มประสิทธิภาพในการแลกเปลี่ยนของเสียและน้ำของเยื่อบุผนังช่องท้อง นับแต่อดีตจนถึงปัจจุบันมีการทดลองใช้ยาจำนวนมากแต่มีเพียงยา nitroprusside เท่านั้นที่มีหลายการศึกษายืนยันถึงความสำเร็จ ยาดังกล่าวออกฤทธิ์ขยายหลอดเลือดผ่านการเพิ่มขึ้นของ nitric oxide เช่นเดียวกับยาในกลุ่ม nitrates จึงเป็นที่มาของการศึกษานี้ วัตถุประสงค์ของงานวิจัยนี้เพื่อศึกษาเปรียบเทียบความสามารถในการแลกเปลี่ยนสสารต่าง ๆ ของเยื่อบุผนังช่องท้องในผู้ป่วยไตวายเรื้อรังระยะสุดท้ายที่ได้รับการรักษาทดแทนด้วยการฟอกไตทางช่องท้องแบบถาวรของโรงพยาบาลจุฬาลงกรณ์ ก่อนและหลังการบริหารด้วยยา isosorbide 5-mononitrate (ISMN) ทางปาก การศึกษานี้เป็นการวิจัยแบบทดลองเพื่อเปรียบเทียบประสิทธิภาพของเยื่อบุผนังช่องท้องในการขจัดของเสีย และน้ำในผู้ป่วยไตวายเรื้อรัง ระยะสุดท้ายที่ได้รับการฟอกไตทดแทนทางช่องท้องถาวรในช่วงที่ได้รับยา ISMN และช่วงที่ได้รับยาหลอก จำนวนทั้งสิ้น 9 ราย ทุกรายจะได้รับทั้งยา ISMN ขนาด 20 มก. จำนวน 2 ครั้งต่อวันเป็นเวลา 5 วัน และ ยาหลอก 2 ครั้งต่อวัน เป็นเวลา 5 วัน แต่เป็นคนละช่วงเวลากัน (cross over design) ทำการหยุดยาเดิม 7 วันก่อนที่จะให้ยาใหม่เพื่อให้แน่ใจว่าไม่มีผลของยาเก่าเหลืออยู่ก่อนที่จะได้รับยาใหม่ ผลการศึกษา การบริหารยา ISMN ทางปากสามารถเพิ่ม 1) อัตราการขจัดของเสียที่มีโมเลกุลขนาดเล็กได้อย่างมีนัยสำคัญทางสถิติ ($p < 0.05$) วัดโดยมัธยฐานของ MTAC creatinine และ urate เพิ่มขึ้นร้อยละ 14 และ 11 ตามลำดับ 2) อัตราการขจัดของเสียที่มีโมเลกุลขนาดใหญ่ วัดโดยมัธยฐานของ clearance ของ β_2 microglobulin, albumin และ immunoglobulin G เพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติ ($p < 0.05$) เชื่อว่ากลไกการเพิ่มขึ้นของอัตราการขจัดของเสีย เกิดจากการเพิ่มพื้นที่ผิวของเยื่อบุผนังช่องท้องในการแลกเปลี่ยนของเสียและน้ำ เนื่องจากสัมประสิทธิ์ในการกั้นขวางคงที่ อย่างไรก็ดีการบริหารยา ISMN ทางปากไม่มีผลต่ออัตราการขจัดน้ำออกจากร่างกาย และไม่มีผลแทรกซ้อนที่รุนแรง โดยสรุปการบริหารยา ISMN ทางปากสามารถเพิ่มประสิทธิภาพของเยื่อบุผนังช่องท้องในการแลกเปลี่ยนของเสียทั้งโมเลกุลขนาดเล็กและโมเลกุลขนาดใหญ่จากการเพิ่มพื้นที่ผิวในการแลกเปลี่ยนสารและน้ำของเยื่อบุผนังช่องท้อง เชื่อว่าการบริหารยา ISMN ในระยะยาวจะสามารถเพิ่มความเพียงพอในการฟอกไตทางช่องท้องในผู้ป่วย ไตวายเรื้อรังระยะสุดท้ายได้