Renal Function After Dopamine and Fluid Administration in Patients with Malignant Obstructive Jaundice. A Prospective Randomized Study

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Abstract

Background and Aims: Acute renal failure is a relevant complication in obstructive jaundice (OJ). The extracellular water volume (ECW) depletion and myocardial dysfunction affects haemodynamic and renal disturbance in patients with OJ. **Methods**: A prospective open randomised study was conducted to evaluate the effect of peridrainage saline infusion associated with dopamine administration on hormonal and renal function derangements in 102 patients with malignant OJ. Patients were randomly distributed according to whether (n=64) or not (n=38) received dopamine with saline solution before endoscopic biliary drainage. Furthermore, patients receiving dopamine were randomly distributed whether (n=31) or not (n=33) received additional dopamine administration during the postdrainage phase. Different parameters such as ECW, serum levels of aldosterone, renin, atrial natriuretic peptide (ANP), antidiuretic hormone (ADH), endothelin-1 (ET-1), urine PGE2 and creatinine clearance (CrCl) were analyzed. **Results**: Fluid administration was accompanied by an increase in the ECW (p=0.01) and an improvement in the CrCl (p=0.01). Dopamine increased CrCl by 11% (p=0.04) and reduced urinary PGE2 concentration (p=0.02). After drainage, a transient worsening of CrCl was seen in patients on i.v. fluid infusion alone but not in dopamine groups (p=0.001). Improvement of CrCl after dopamine administration was found in patients with serum bilirubin > 16 mg/dl and sodium urine excretion <145 mEq/l. **Conclusions**: The administration of dopamine associated with appropriate i.v. fluid infusion in the peridrainage period has an impact on renal function only in selected patients with malignant biliary obstruction. This effect is more relevant in patients with higher marked cholestasis.

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Key words

Cholestasis – renal dysfunction – dopamine – volume depletion.

Introduction

The association between obstructive jaundice (OJ) and renal failure has been recognized since 1910 when Clairmont [1] reported the development of acute renal failure, with subsequent death, in five patients following surgery for OJ. Although the aetiology of renal dysfunction is multifactorial [2], it is strongly associated with haemodynamic and body fluid disturbances [2-5]. The presence of extracellular fluid (ECW) depletion [6-8] and myocardial dysfunction [9, 10] has been recently pointed out to be relevant for haemodynamic and renal disturbances in patients with OJ. Moderate volume depletion has been observed in these patients measured by tracer dilution techniques [6] and endocrine markers such as renin plasma levels [11-15]. The administration of intravenous (i.v.) fluids expands the ECW in the perioperative period. However, this strategy has been shown to fail in improving renal function in 30% of patients [16]. This suggests that other active sodium and water balance regulatory hormones, such as endothelin-1 (ET-1) may also play a role during perioperative renal failure [17, 18]. Volume depletion is related to a rise in ET-1 blood concentration which causes renal vasoconstriction and a reduction of the glomerular filtration rate. This might explain the compensatory elevation of urinary PGE2 observed in these patients [19].

The addition of a renal vasodilator agent such as dopamine could counteract the renal vasoconstriction associated with ET-1 activity. This effect of dopamine has been observed in experimental studies of chronic OJ [20]. The administration of dopamine during postoperative period has not showed any significant improvement of renal function in patients with perioperative renal dysfunction [7, 21]. However, the effect of dopamine administered before biliary drainage or surgery in patients with OJ on the renal and endocrine derangements has not been assessed. The present study was therefore

designed to analyse the effect of dopamine associated with fluid administration on ECW, water and sodium regulating hormones and renal function alterations in patients with OJ undergoing endoscopic internal biliary drainage.

Methods

Design

The study was designed as a prospective, open, randomised trial including patients with malignant OJ, a bilirubin concentration higher than 6 mg/dl, ultrasound evidence of extrahepatic and intrahepatic bile duct dilation (more than 8 mm and 4 mm, respectively) and feasibility of internal endoscopic biliary drainage. The exclusion criteria were cholangitis, acute pancreatitis, heart disease, arterial hypertension, chronic lung disease, use of diuretics and chronic renal failure. The informed consent was obtained from all patients as well as permission to publish the results of the investigation. The study was approved by the Hospital Clinical Trials and Ethics Committee. The registration number of the clinical trial was ISRCTN14198655.

Patients

One hundred and two patients with malignant OJ were randomly distributed in two treatment groups according to whether they had (n=64) or not (n=38) received dopamine (3 µg/Kg/min) associated with saline solution infusion (45 ml/kg) for 48 hours before biliary drainage (Fig. 1). The patients receiving dopamine before biliary drainage were additionally randomly distributed according to whether they had (n=31) or not (n=33) received dopamine 72 h after postdrainage intervention. The patients without dopamine administration (n=38) did not receive dopamine administration after postdrainage intervention. The endoscopic biliary drainage was unsuccessful in 8 patients. Therefore, the postdrainage study groups (total n= 94) included patients with fluid infusion (n=35), fluid and dopamine predrainage administration (n=31) and fluid and dopamine (pre and postdrainage) administration (n=28) (Fig. 1). All patients were maintained under the same conditions. The patients were fasted for the first 12 h after endoscopic internal drainage, and then administrated with 2.5 l of glucosaline solution containing 150 mEq of NaCl until the following morning. On the second day, the i.v.

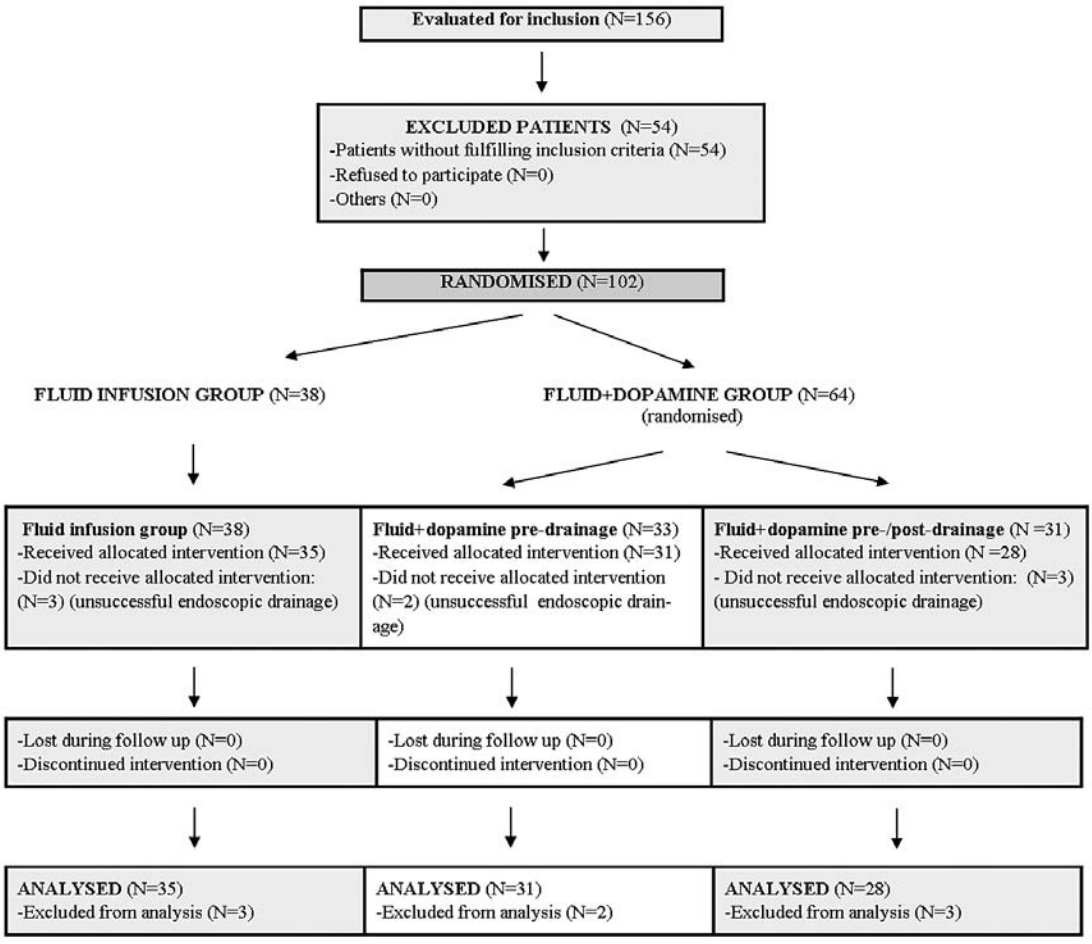

Fig 1. CONSORT flow diagram

infusion was stopped and patients received a 2000 kcal/day diet up to the 72 h when the study protocol was terminated. The sodium content of the diet was 80 mEq/day and a free fluid intake was allowed.

The endoscopic biliary drainage was considered successful if total bilirubin decreased around 30% and the size of the common bile duct diameter was significantly reduced by ultrasound 72 h after surgical intervention. The metallic self-expandable endoprosthesis (Wallstent®: 30 Fr) and plastic endoprosthesis (10 Fr) were implanted in 41 and 53 patients, respectively. Biochemical, hormonal and bioelectrical impedance analysis were performed at admission, before drainage, as well as 24 h and 72 h after biliary drainage.

Parameters analysed

Creatinine clearance (CrCl) was measured by the Modification of Diet in Renal Disease (MDRD) formula [22]. ECW was determined by bioelectrical impedance using a BIA-101S analyser (RJL System Inc MT Clemens MI USA) with the prediction equation of Lukaski and Bolonchuck [23]. All bioimpedance measurements were performed by the same experienced observer and ECW was reported as a percentage of body weight. The concentration of hormones was determined in the plasma. Blood was collected into chilled tubes containing EDTA (2 mg/ml) and aprotinin (Trasylol 400 KIU/ml, Sigma Chemical Co, St. Louis, MO, USA), and centrifuged at 3.000 rpm at 4°C for 10 min within 30 min of collection. The plasma was obtained and stored frozen at –70°C until measurements. The concentration of ANP (h-ANP, Cob. I-AR55 Co. Ltd., Tokio, Japan), endothelin-1 (RIA, Peninsula Laboratories Inc. RIK-6901 Human endothelin-1, California USA), renin (a-Renin IRMA 4K-REN-00, Future Diagnostics, Witjchen, The Netherlands), aldosterone (RIA DSL-8600 ACTIVETM Diagnostic Systems Laboratories, Inc. Webster, Texas; USA) and vasopressin (RIA , Península Laboratories Inc., cod. Rik-8 103 [Arg8]-Vasopressin, California,USA) was determined using commercial radioimmunoassay. The data was recorded by a γ-scintillator (Ultrogamma Counter-Ina, Crystal 2-5400 B-5412; Packard Instrument Company Inc., Canberra, Australia). The concentration of PGE2 in urine was measured by a commercial ELISA test (Rand D Systems Inc. Minneapolis, MN 55413, USA).

Statistical methods

The sample size was estimated on the assumption of 5% improvement on renal function after dopamine treatment [16]. Thus, a minimum of 21 patients was required in each group (bilateral contrast with α error <5% and power of 95%; n2/n1=1). Results are expressed as mean ± SD with 95% confidence intervals. The inter- and intra-group statistical analysis was carried out using the two-tailed Student's t test for unpaired and paired data. ANOVA for repeated measures and Newman-Keuls test were also used for post-drainage analysis. The statistical significance was set at $p<0.05$. The correlation of variables was assessed using Pearson's coefficient. The multivariate analysis was performed to determine factors that might predict an improvement in renal function after dopamine administration. CrCl was used as dependent variable. Variables for which $p > 0.1$ were excluded from the regression study using the stepwise method, and adjusted to the methodological selection procedure.

Results

Baseline data

The study group included 94 patients with malignant OJ with the presence of periampullary tumours (n=47), pancreatic cancer (n=35), ampuloma (n=12), cholangiocarcinomas (n=34) and gallbladder tumours (n=13). The study included men (n=33, 33%) and women (n=61, 67%) with a mean age of 71±8.8 years (range 35-76). The mean duration of jaundice was 14±8 days. The three groups were well matched for the most significant variables of the study (Table I).

Table I. Homogeneity of baseline parameters between the groups

	Fluid infusion (n=35)	Fluid+dopamine pre-drainage (n=31)	Fluids+ dopamine pre- +post-drainage (n=28)
Age (years)	68±5	73±9	74±9
Location of tumor (proximal/ distal)	13/22	15/16	15/13
Duration of jaundice (days)	12.5±9	16.5±7	15±8
Bilirubin (mg/dl)	14±6.5	18±5	15±4.5
ANP (ng/L)	139±24	136±31	140±36
Aldosterone (nmol/L)	2.3±0.5	1.9±0.8	2±0.5
Renin (µg/L)	0.042±0.01	0.045±0.02	0.046±0.03
ADH (ng/L)	16±4	15±5	16±6
ET-1 (pg/ml)	17.7 ±1.4	17.1±2	18±1.6
PGE2 (pg/L)	21113±735	20856±670	20930±710
CrCl (ml/min)	79±18	85±18	81±11
Urinary sodium (mEq/L)	153±42	167±47	160±44
Urine output (ml/24h)	1377±735	1415±859	1486±613
ECW (% body eight)	20.6±2	21.8±3	22±3

*Unpaired Student's t test. Newman-Keuls; ANP: atrial natriuretic peptide; ADH: antidiuretic hormone; ET-1: endothelin-1; PGE2: prostaglandin E2; CrCL: creatinine clearance; ECW: extracellular

Pre-drainage study

The administration of fluid was accompanied by an increase in the ECW, diuresis, ANP levels and improvement of CrCl (Table II). The patients who received dopamine associated with fluid administration prior to drainage showed a significant improvement in CrCl accompanied by decrease in PGE2 concentration and an increase of urinary sodium

Table II. Effect of saline infusion and dopamine prior to internal biliary drainage

	Fluid infusion (n=35)	Fluid+dopamine pre-drainage (n=59)
Bilirubin (md/dl)		
baseline	14±6.5	17±5
pre-drainage	14±6	17±5
ANP (ng/L)		
baseline	139±24	138±31
pre-drainage	240±47[a]	140±38
Aldosterone (nmol/L)		
baseline	2.3±0.5	1.9±0.8
pre-drainage	2.4±0.6	2.2±0.8
Renin (µg/L)		
baseline	0.042±0.01	0.045±0.02
pre-drainage	0.022±0.01[b]	0.041±0.015
ADH (ng/L)		
baseline	16±4	15±5
pre-drainage	15±2	13±2
ET-1 (pg/ml)		
baseline	17.7±1.4	17.1±2
pre-drainage	15±1.3	13.1±1.7
PGE2 (pg/L)		
baseline	21113±735	20901±670
pre-drainage	19880±750	15870±520[a,d]
CrCl (ml/min)		
baseline	79±14	81±18
pre-drainage	97±31[b]	108±34[a,e]
Urinary sodium (mEq/L)		
baseline	153±42	157±47
pre-drainage	170±45	195±38[b,d]
Urine output (ml/24h)		
baseline	1377±735	1460±859
pre-drainage	1868±823[c]	2657±971[a,d]
ECW (% body weight)		
baseline	20.6±2.0	21.8±3.5
pre-drainage	24.7±2.8[b]	22±3.4[d]

*Paired Student's t test: (a): p=0.001 with baseline; (b): p=0.01 with baseline; (c): p=0.03 with baseline; (d): variation: p=0.02 with fluid infusion alone; (e) variation: p=0.04 with fluid infusion alone

excretion. Neither the ECW nor plasma renin showed significant changes (Table II).

Post-drainage study

The concentration of bilirubin, ANP, aldosterone and ET-1 in plasma levels, as well as PGE2 levels in urine showed a significant reduction after drainage (Table III). In patients treated only with saline administration, a transient impairment of CrCl was seen 24 h after drainage, but not in dopamine groups. There were no differences in CrCl between dopamine-treated groups. The proportion of CrCl determinations which showed a baseline 10% improvement was 69% in the group of fluid therapy alone versus 84% in the dopamine group pre-drainage (p=0.03) and 81% in patients with pre and post-drainage dopamine (p=0.03), respectively.

Multivariate analysis

Serum bilirubin (p=0.003) and urinary sodium excretion (p=0.01) proved to be reliable predictors of good response in renal function after treatment with dopamine in patients with OJ (Table IV). The logistic equation obtained for renal function was: CrCl increase (%): 0.31 + 0.90 (bilirubin) - 0.04 (urinary sodium excretion)

The sensitivity and specificity of the equation to detect renal dysfunction were 81% and 87%, respectively. Positive (bilirubin) and negative (urinary sodium excretion) predictive values of the equation were 87% (95% confidence interval = 74-96%) and 75% (95% confidence interval = 67-84%), respectively. The administration of dopamine increased greater than 10% CrCl in patients with baseline bilirubin >16 mg/dl and urinary sodium excretion <145 mEq/L.

Discussion

Patients with OJ frequently suffer haemodynamic and body fluid disturbances [3-5]. It has been shown that ECW is reduced in the presence of biliary obstruction when compared with healthy subjects [7-9]. In the present study, dopamine administration associated with i.v. fluid infusion prior to biliary drainage led to an improvement in renal function in selected patients with malignant OJ. This effect of dopamine was prolonged after endoscopic internal biliary drainage. These findings are relevant for the peri-drainage management of OJ patients, especially when some degree of renal dysfunction is detected.

Cholestatic patients showed a paradoxical increase of ANP plasma concentrations, and renin and aldosterone in the normal-high range suggesting a marginal reduction of plasma volume [6-13]. This reduction of plasma volume has been previously associated with hemodynamic changes [10, 24, 25]. Part of the volume depletion in obstructive jaundice is due to an increase in sodium taurocholate, which has a natriuretic property [26]. It may be speculated that this may limit ascites accumulation in patients with biliary cirrhosis in striking contrast to patients with alcoholic cirrhosis. The reduction of plasma volume is commonly associated with hypoalbuminemia in malignant OJ [14]. These changes cannot be ascribed to malnutrition [27], because in protein and fat nutritional deficiency a relative expansion, but not reduction of the ECW, is observed [28].

The administration of normal saline the day before biliary drainage improved the CrCl increased diuresis and corrected the ECW deficit. The infusion volume is related to the magnitude of ECW depletion in patients with two to three weeks of OJ duration [14]. Previous studies have attributed the preservation of renal function mostly to the benefits of a pre-procedural intravenous volume expansion [7, 21]. The renal functional improvement is transient and restricted to the duration of fluid infusion as a consequence of the lack of the beneficial effect on CrCl of the fluid expansion in a relevant proportion of patients (30%) either after drainage or post-operative recovery of renal function [18]. These data suggest that other sodium and water content regulatory hormones,

Table III. Comparison of different parameters during post-drainage in patients with and without dopamine associated with intravenous fluid therapy

	Pre-drainage	24 h	72 h	P* Intra group	Inter group
Bilirubin (mg/dl)					
Iv fluid	14±6.5	12±5.0[c]	7±3.0[b]	0.001	
Dopamine predrainage	18±5.0	13±3.5	6.5±3.5	0.001	NS
Dopamine pre-postdrainage	15±4.5	10±4.0[a]	6±2.8[b]	0.001	
CrCl (ml/min)					
Iv fluid	97±31	76±34[b]	98±38	NS	
Dopamine predrainage	103±37	116±39[b]	110±39	NS	0.045
Dopamine pre-postdrainage	108±34	117±37	111±40	NS	
Urine sodium excretion (mEq/L)					
Iv fluid	170±45	116±34[a]	106±37[b]	NS	
Dopamine pre-drainage	198±38	126±32	105±31[b]	<0.001	<0.05
Dopamine pre/post-drainage	187±40	166±33	121±24	NS	
ECW (%body weight)					
Iv fluid	24.7±2.8	23.2±4.5[a]	24.6±3.0[c]	NS	
Dopamine pre-drainage	22±3.4	23±3.5	24±3.0[b]	NS	
Dopamine pre/post-drainage	21±3.0	21±3.0	23±3.5	NS	
ANP (ng/L)					
Iv fluid	240±47	116±24[a]	95±27[b]	<0.001	
Dopamine pre-drainage	256±38	134±28	111±31[b]	<0.001	NS
Dopamine pre/post-drainage	261±4	182±22	127±24	<0.001	
Aldosterone (nmol/L)					
Iv fluid	2.4±0.6	1.4±0.4[b]	1.2±0.4[c]	<0.01	
Dopamine pre-drainage	2.2±0.8	1.6±0.7	1.4±0.6[b]	<0.01	NS
Dopamine pre/post-drainage	2.2±0.5	1.8±0.5	1.6±0.2[b]	<0.01	
Renin (µg/L)					
Iv fluid	0.022±0.010	0.009±0.03[b]	0.007±0.03[c]	0.01	
Dopamine pre-drainage	0.041±0.015	0.054±0.02	0.057±0.03	NS	0.01
Dopamine pre/post-drainage	0.042±0.020	0.048±0.01	0.054±0.01	NS	
ADH (ng/L)					
Iv fluid	15±2	15±5	15±6	NS	
Dopamine pre-drainage	12±2	17±6	17±4	NS	NS
Dopamine pre/post-drainage	14±4	15.5±5	14.5±4.5		
ET-1 (pg/ml)					
Iv fluid	15±1.3	12±1.4	9±2	0.03	
Dopamine pre-drainage	16.6±2	12.8±1.7[b]	9.8±1.5[c]	0.01	
Dopamine pre/post-drainage	17.4±1.6	13.2±1.6[b]	9±1.6[c]	0.01	
PGE_2 (pg/L)					
Iv fluid	19880±750	16714±672	15293±668	0.03	
Dopamine pre-drainage	15670±520	13212±501[b]	12613±480[c]	0.01	0.01
Dopamine pre/post-drainage	16110±563	11322±522[b]	9456±480[c]	0.01	

NS: not significant. Newman-Keuls test: a:p<0.05 with pre-drainage, b:p<0.01 with pre-drainage; c:p<0.001 with pre-drainage; ANP: atrial natriuretic peptide; ADH: antidiuretic hormone; ET-1: endothelin-1; PGE2: prostaglandin E2; CrCL: creatinine clearance; ECW: extracellular

such as endothelin-1 (ET-1) [17] also play a role as a final mediator of perioperative renal failure. When volume depletion is observed, as occurs in obstructed patients, the increase of ET-1 activity is often detected associated with renal vasoconstriction and reduced glomerular filtration rate. This situation is compatible with the compensatory elevation of PGE2 in urine [19]. The release of dopamine induces renal vasodilatation that may counteract the renal vasoconstriction associated with ET-1. This has been demonstrated in experimental models of long term OJ [20]. The present study showed that patients receiving dopamine with fluid pre-drainage administration demonstrated a significant improvement in CrCl accompanied by an increase of urinary sodium excretion and a decrease in PGE2 concentration in urine, indicating an inhibition of prostaglandin secretion. The group treated only with fluid administration did not show any evidence of an increase in ECW and diuretic response.

It has been previously observed that the administration of dopamine during the perioperative period failed to improve renal function in patients with OJ [7, 21]. These studies, however, were performed only during the postoperative period in a small series of patients with significant dispersion

Table IV. Stepwise multiple regression analysis of variables influencing Creatinine Clearance (CrCl) after dopamine administration in patients with obstructive jaundice.

	Coefficient	S.E.	Wald
Intercept	0.31	0.1	
Bilirubin (mg/dl)	0.90	0.21	2.8
Urinary Na excretion (mEq/L)	-0.04	0.05	- 0.4

S.E.: Standard error; Wald: statistic which tests the null hypothesis that a coefficient in a logistic regression model is zero; Increased CrCl (%) following dopamine administration: 0.31 +0.90 (bilirubin) - 0.04 (urinary sodium)

of data. In the present study, patients under fluid therapy alone presented a transient decrease in CrCl 24 hours after biliary drainage. This impairment was not found in the dopamine-treated group. This may be related to better pre-drainage recovery of glomerular filtration, facilitated by the administration of dopamine, counteracting the effects of potential release of late kidney damaging mediators. Moreover, the percentage of CrCl determinations which improved by 10% or more after the restoration of duodenal bile flow compared to baseline, was higher in patients with dopamine administration.

In order to select patients which would benefit from the administration of dopamine associated with volume replacement, a multivariate analysis was performed that showed that dopamine would be especially useful in patients with higher serum bilirubin levels and lower urinary sodium excretion. This assumption would support the hypothesis that dopamine is more beneficial in patients with increased activity of ET-1 in whom urinary sodium elimination is markedly reduced.

Conclusion

The administration of dopamine associated with appropriate fluid infusion may be included in the management of renal dysfunction of selected patients with malignant OJ under endoscopic biliary drainage, especially during the pre-drainage period.

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Conflicts of interest

None to declare.

References

1. Clairmont P, Von Haberer H. Ueber Anurie nach Gallensteinoperatoinen. Mitteilunger aus den Grenzgebieten der Medizen und Chirurgie 1910; 22: 159-172.
2. Fogarty BJ, Parks RW, Rowlands BJ, Diamond T. Renal dysfunction in obstructive jaundice. Br J Surg 1995; 82: 877-884.
3. Williams RD, Elliot DW, Zollinger RM. The effect of hypotension in obstructive jaundice. Arch Surg 1960; 81: 334-340.
4. Gillett DJ. The effect of obstructive jaundice on the blood volume in rats. J Surg Res 1971; 11: 447-449.
5. Sitges-Serra A. Renal failure in obstructive jaundice. In: Arroyo V, Ginés P, Schrier P, Rodés J (eds). Liver and Kidney. Blackwell Publishers, 1999: 79-98.
6. Sitges-Serra A, Carulla X, Piera C, et al. Body water compartments in patients with obstructive jaundice. Br J Surg 1992; 79: 553-556.
7. Parks RW, Diamond T, McCrory DC, Johnston GW, Rowlands BJ. Prospective study of postoperative renal function in obstructive jaundice and the effect of perioperative dopamine. Br J Surg 1994; 81: 437-439.
8. Padillo FJ, Rodriguez M, Gallardo JM, et al. Preoperative assessment of body fluid disturbances in patients with obstructive jaundice. World J Surg 1999; 23: 681-687.
9. Green J, Beyar R, Sideman S, Mordechovitz D, Better OS. The "jaundiced heart": A possible explanation for postoperative shock in obstructive jaundice. Surgery 1986; 100:14-20.
10. Padillo J, Puente J, Gómez M, et al. Improved cardiac function in patients with obstructive jaundice after internal biliary drainage: hemodynamic and hormonal assessment. Ann Surg 2001; 234: 652-656.
11. Oms L, Martínez-Ródenas F, Valverde J, Jiménez W, Sitges-Serra A. Reduced water and sodium intakes associated with high levels of natriuretic factor following common bile duct ligation in the rabbit. Br J Surg 1990; 77: 752-755.
12. Valverde J, Martínez-Ródenas F, Pereira JA, et al. Rapid increase in plasma levels of atrial natriuretic peptide after common bile duct ligation in rabbit. Ann Surg 1992; 216: 554-559.
13. Gallardo JM, Padillo J, Martín-Malo A, Miño G, Pera C, Sitges-Serra A. Increased plasma levels of atrial natriuretic peptide and endocrine markers of volume depletion in patients with obstructive jaundice. Br J Surg 1998; 85: 28-31.
14. Padillo FJ, Rodriguez M, Gallardo JM, et al. Changes in the pattern of visceral proteins after internal biliary drainage in patients with obstructive jaundice. Eur J Surg 1999; 165: 550-555.
15. Martínez-Ródenas F, Pereira JA, Jiménez W, Gubern JM, Sitges-Serra A. Circulating bile is the main factor responsible for atrial natriuretic peptide release in experimental obstructive jaundice. Br J Surg 1998; 85: 480-484.
16. Padillo FJ, Briceño J, Cruz A, et al. Randomized clinical trial of the effect of intravenous fluid administration in patients with obstructive jaundice undergoing endoscopic drainage. Br J Surg 2005; 92: 39-43.
17. Sarac AM, Aktan AO, Moini H, Bilsel S, Scapa E. Role of endothelin in obstructive jaundice. Dig Dis Sci 1999; 44: 356-363.
18. Padillo FJ, Cruz A, Briceño J, Martin-Malo A, Pera-Madrazo C, Sitges-Serra A. Multivariate analysis of factors associated with renal dysfunction in patients with obstructive jaundice. Br J Surg 2005; 92: 1388-1392.
19. Uemura M, Tsujii T, Fukui H, et al. Urinary prostaglandins and renal function in obstructive jaundice. Scand J Gastroenterol 1989; 24:705-715.
20. Benko H, Mostbeck A, Peschl L, Schüller J, Neumayr A. The effect of dopamine on the renal function in dogs with chronic ligation of the common bile duct. Wien Klin Wochenschr 1977; 89: 562-566.
21. Wahbah AM, el-Hefny MO, Wafa EM, et al. Perioperative renal protection in patients with obstructive jaundice using drug combinations. HepatoGastroenterology 2000; 47: 1691-1694.

22. Levey AS, Coresh J, Greene T, et al; Chronic Kidney Disease Epidemiology Collaboration. Expressing the modification of diet in renal disease study equation for estimating glomerular filtration rate with standardized serum creatinine values. Clin Chem 2007; 53: 766-772.
23. Lukaski HC, Bolonchuk WW. Estimation of body fluid volumes using tetrapolar bioelectrical impedance measurements. Aviat Space Environ Med 1988; 59: 1163-1169.
24. Lumlertgul D, Boonyaprapa S, Bunnachak D, et al. The jaundiced heart: evidence of blunted response to positive inotropic stimulation. Ren Fail 1991; 13: 15-22.
25. Green J, Better OS. Systemic hypotension and renal failure in obstructive jaundice-mechanistic and therapeutic aspects. J Am Soc Nephrol 1995; 5: 1853-1871.
26. Better OS, Guckian V, Giebisch G, Green R. The effect of sodium taurocholate on proximal tubular reabsorption in the rat kidney. Clin Sci (Lond) 1987; 72: 139-141.
27. Padillo FJ, Andicoberry B, Muntane J, et al. Factors predicting nutritional derangements in patients with obstructive jaundice: A multivariate analysis. World J Surg 2001; 25: 413-418.
28. Sitges-Serra A, Franch G. Nutrition Assessment. In: Payne-James J, Grimble G, Silk D. (eds). *Artificial Nutritional Support in Clinical Practice*. Blackwell (2nd Edition). London, 2001: 165-176.