Diagnostic and Interventional Endoscopy

Research Article

The Role of Intravenous Hydration in the Prevention of Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis

Gizem Kırmızıer[1], Serkan Yaras[1], Enver Üçbilek[1], Osman Özdoğan[1], Ibrahim Yilmaz[2], Fehmi Ates[1], Orhan Sezgin[1], Engin Altintas[1]

[1]Department of Gastroenterology, Mersin University, Faculty of Medicine, Mersin, Turkey
[2]Department of Gastroenterology, Hatay Public Hospital, Hatay, Turkey

Cite this article as: Kırmızıer G, Yaras S, Üçbilek E, *et al*. The role of intravenous hydration in the prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis. *Diagn Interv Endosc.* 2023;2(1):9-13.

This study was presented as an oral presentation at the 34th National Gastroenterology Week.

Corresponding author: Gizem Kırmızıer, e-mail: gizem_isguzar@hotmail.com

Received: January 23, 2023 **Accepted:** March 25, 2023 **Publication date:** March 28, 2023 **DOI:** 10.5152/DiagnIntervEndosc.2023.223655

Abstract

Objective: Pancreatitis is the most frequently observed complication after endoscopic retrograde cholangiopancreatography. Several preventive methods for post-endoscopic retrograde cholangiopancreatography pancreatitis have been developed. A pilot study was conducted to determine whether aggressive periprocedural hydration with lactated Ringer's solution reduces the incidence of post-endoscopic retrograde cholangiopancreatography pancreatitis.

Methods: The study included 32 patients who required endoscopic retrograde cholangiopancreatography for diagnostic or therapeutic purposes. Patients were randomized (1 : 1) to receive either aggressive hydration with lactated Ringer's solution (n=16) or standard hydration with the same solution (n=16). Oral intake was stopped after midnight and endoscopic retrograde cholangiopancreatography began at 10:00 AM. Hourly fluid requirements of patients in the aggressive hydration group were calculated based on the 4-2-1 formula (4 mL/kg/h for the first 10 kg, 2 mL/kg/h for the next 10 kg, and 1 mL/kg/h thereafter) and fluid requirements of 10 hours were met in 2 hours from 08:00 to 10:00 AM before endoscopic retrograde cholangiopancreatography. At the 4th and 24th hours following endoscopic retrograde cholangiopancreatography, serum amylase and lipase levels, volume overload, and other complications were assessed. Acute pancreatitis was defined and ranked in accordance with the 2012 Atlanta Classification criteria.

Results: Of all patients, 34% (11/32) developed pancreatitis after endoscopic retrograde cholangiopancreatography, compared with 12.5% (2/16) in the aggressive hydration group and 56.3% (9/16) in the standard hydration group. Pancreatitis was significantly less prevalent in the aggressive hydration group (P=.009). All observed cases of pancreatitis were mild.

Conclusion: According to this pilot study, aggressive hydration with lactated Ringer's solution reduces the risk of post-endoscopic retrograde cholangiopancreatography pancreatitis.

Keywords: Hydration, endoscopic retrograde cholangiopancreatography, pancreatitis

INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is a diagnostic and therapeutic procedure widely used for pancreatobiliary disorders such as stone removal and treatment of biliary obstruction. The ERCP has the highest risk of complications and mortality of all the mainstay endoscopic modalities, with post-ERCP pancreatitis (PEP) being the most common complication after sedation-related adverse events.[1] In low-risk patients, it occurs at a rate of 2%-4%, while in high-risk patients it occurs at a rate of 8%-40%.[2,3]

Abdominal discomfort after ERCP is common in the diagnosis of PEP. Clinical diagnosis, in conjunction with serum amylase and/or lipase, is required to distinguish between PEP and other complications. The PEP is managed similarly to acute pancreatitis, with intravenous fluid therapy being the most critical step.[4]

The degree of difficulty of ERCP, ampulla type, the number of attempts required to achieve selective biliary cannulation, biliary cannulation method, and the length of time required to complete the process are predictors of difficult ERCP and potential PEP.[5] Prevention strategies for PEP include pharmacologic prophylaxis and procedural techniques. The study aimed to evaluate the efficacy of aggressive hydration (AH) with lactated Ringer's solution (LRS) in preventing PEP at a single center.

METHODS

The Clinical Research Ethics Committee of the MersinUniversity Faculty of Medicine approved the study (Date: 09/03/2017, No: 2017/58). All patients who took part in the study signed a consent form indicating their understanding of the study's purpose.

Patients

A total of 32 patients with diagnostic or therapeutic ERCP indications were included in the study. Patients with sepsis, who require severe intravenous hydration, were excluded. Patients with renal insufficiency (creatinine clearance < 40 mL/min), severe liver disease (albumin < 3 mg/dL), heart failure worse than New York Heart Association class 2, electrolyte imbalance, peripheral edema, pulmonary edema, or acid were excluded. Pregnant women, with an ERCP history or contrast allergy, and those under the age of 18 and over the age of 70 were also excluded.

Intervention

Patients were randomized (1 : 1) to receive either AH with LRS (n=16) or standard hydration (SH) with the same solution (n=16). Oral intake of all patients was stopped after midnight and ERCP started at 10:00 AM. The hourly fluid requirements of patients in the AH group were calculated based on the 4-2-1 formula (4 mL/kg/h for the first 10 kg, 2 mL/kg/h for the next 10 kg, and 1 mL/kg/h thereafter) and the 10-hour fluid requirement was met in 2 hours from 08:00 to 10:00 AM before ERCP. The SH group did not receive intravenous hydration after midnight until 10:00 AM. Standard hydration therapy was stated as 1.5 mL/kg/h. From ERCP initiation to oral intake, both groups received an 8-hour intravenous infusion of LRS at a rate of 1.5 mL/kg/h. İntravenous hydration was stopped in both groups as soon as patients tolerated a normal diet.

Endpoints

Post-ERCP pancreatitis was the primary endpoint. The definition and severity classification of acute pancreatitis was determined using the 2012 Atlanta Classification criteria.[6] This necessitates at least 2 of the 3 following diagnostic criteria: The condition is diagnosed by abdominal pain, a 3-fold increase in serum amylase or lipase levels, and imaging abnormalities consistent with acute pancreatitis. Mild disease is devoid of organ failure and local or systemic complications, moderate disease has temporary organ failure (<48 hours) or local/systemic complications, and severe disease has persistent single or multiple organ failure (>48 hours).[6] Secondary endpoints were isolated hyperamylasemia and/or hyperlipasemia that did not meet the criteria for acute pancreatitis. Serum amylase and lipase levels were measured 4th and 24th hours following the procedure.

Wire-guided cannulation technique was used in all patients. An experienced endoscopist (EA) performed all ERCP procedures. The operation's difficulty level was expressed as easy or difficult (cannulation period of > 10 min. expresses difficult cannulation). A physical examination for fluid overload and other ERCP complications was also performed on the 4th and 24th hours after the procedure. Patient demographics, procedure specifications, vital signs, and laboratory results were prospectively recorded.

Statistical Analysis

Repeated measurements will be taken at the 4th and 24th hours of the procedure in 2 groups, AH and SH. It was decided to include 32 patients in the study, with an effect size of 1, 0.05 type I error, 0.80 power, and 16 of the required sample size in each group.

The Shapiro–Wilk test was used to determine whether continuous measurement controls were normally distributed. Student's *t*-test was used to compare group differences in continuous variables. Descriptive statistics, the mean, and standard deviation values were provided. For differences between categorical variables, the Pearson chi-square test was utilized. As descriptive statistics, numbers and percentage data were provided. In addition, a 2-way analysis of variance in repeated measures was used to assess the differences between measurements made at different times in the groups. The Greenhouse–Geisser criterion was used to assess the sphericity assumption of the variance-covariance matrices. As descriptive statistics, the mean and standard deviation values were provided. $P < .05$ was taken as statistical significance.

RESULTS

Twelve of the 32 patients included in the study were male, and 20 of them were female. While the mean age of the 32 participants was 48.7 ± 15.2 years, the mean age of females was 50.8 ± 17.2 years and the mean age of males was 45.3 ± 11.2 years. Bile duct stone was diagnosed in 84.4% (n=27) of patients, and malignant biliary strictures in 15.6% (n=5) (See Table 1).

The operation was easy in 21 patients (65.6%), it was difficult in 5 patients (15.6%), and unsuccessful in 6 patients (18.7%). While

Table 1. Features, Diagnoses, and Laboratory Findings of the Patients

	Aggressive Hydration (n=16)	Standard Hydration (n=16)	Statistics
			P
Age	47.5 ± 15.3	49.9 ± 15.6	.659
Gender (female/male)	12/4	8/8	.144
Indication (stone/malignant)	12/4	14/2	.674
Urea	26 ± 9.70	26 ± 9.21	1.000
Creatinine	0.65 ± 0.16	0.67 ± 0.15	.683
Hematocrit	36.98 ± 4.01	36.51 ± 5.22	.781

Table 2. Features of the Operation

	Aggressive Hydration (n=16)	Standard Hydration (n=16)	Statistics
			P
Difficulty (easy/uneasy)	9/3	12/2	.589
Unsuccessful	4	2	.500
Precut	9	9	1.000
Pancreatic cannulation	3	7	.127
Number of pancreatic cannulations	2.33 ± 2.31	3.57 ± 2.37	.468
Pancreas opaque	2	1	1.000
Duodenal diverticulum	2	0	.484

MAIN POINTS

- Pancreatitis following endoscopic retrograde cholangiopancreatography (ERCP) is a common complication that can be avoided by intravenous hydration.
- There have been numerous strategies developed to prevent post-ERCP pancreatitis (PEP).
- In comparison to other PEP prevention strategies, this strategy is safe, inexpensive, and easy to administer.
- Further studies in high-risk patients are required to optimize the procedure

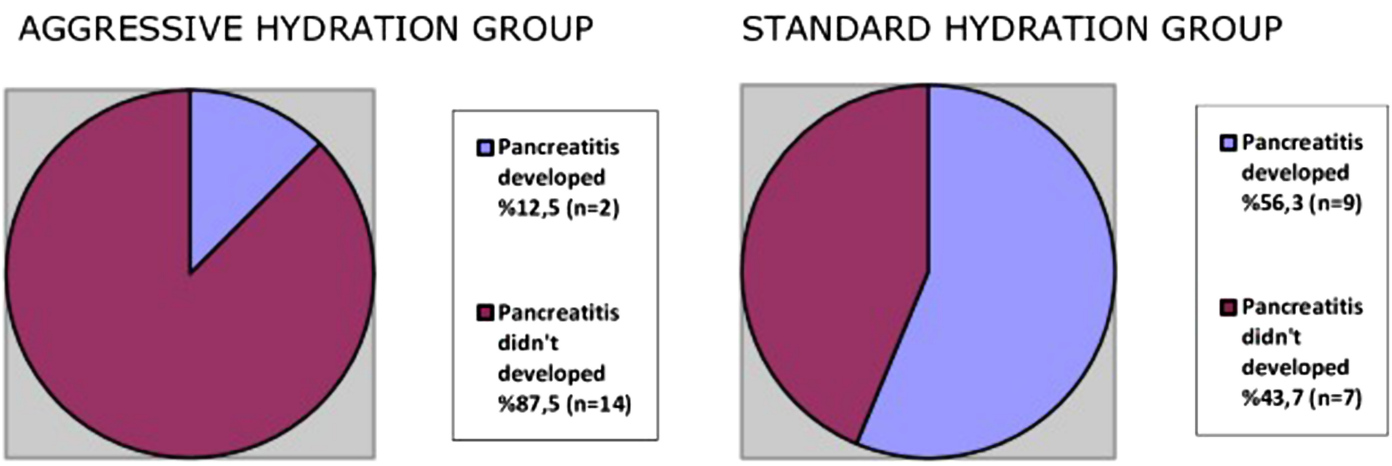

Figure 1. Pancreatitis rates in groups.

pancreatic cannulation was used an average of 2.33 ± 2.31 times in 3 patients in the AH group, it was used an average of 3.57 ± 2.37 times in 7 patients in the SH group. In addition, although cannulation of the pancreas was more frequent in the SH group compared to the AH group, there was no statistically significant difference (P=.127 and P=.468, respectively) (See Table 2).

Eleven (34.3%) of the 32 patients developed pancreatitis. There was a statistically significant difference between the groups in the incidence of pancreatitis (P=.009). Two (12.5%) patients in the AH group developed PEP, compared with 9 (56.3%) patients in the SH group (See Figure 1).

Administration of contrast material to the pancreas and pancreatic cannulation has been associated with the occurrence of PEP. It was found to be unrelated to the difficulty of the operation, as well as age, gender, diagnosis, precut, and the presence of a diverticulum. With the exception of pancreatitis, none of the patients experienced either fluid overload or other complications. Pancreatitis was present in all of the patients in a mild form. The patients were discharged from the hospital within 48-72 hours.

In terms of hyperamylasemia and hyperlipasemia, there was a significant difference between the AH and the SH groups. Hyperamylasemia occurred in half of the AH group and in 93.8 % of the SH group (P=.015), whereas hyperlipasemia occurred in 25% of the AH group and in 81.3 % of the SH group (P=.001) (See Table 3).

When lipase results were analyzed, it was found that only the SH group had statistically significant differences between repeated measurements (P=.039). Only the initial measurement values in the SH group were found to be significantly lower than the measurement values at the 4th and 24th hours (P=.007 and P=.017, respectively).

Table 3. Complications Relevant to the Operation

	Aggressive Hydration (n=16)	Standard Hydration (n=16)	Statistics
			P
Fluid overload	0	0	1.000
Pancreatitis	2	9	.009
Hyperlipasemia	4	13	.001
Hyperamylasemia	8	15	.015
Other	0	0	1.000

Although the initial measurements were higher in the SH group than in the AH group, the difference was thought to be coincidental when the variations in lipase measurements at different time points in the groups were examined. However, the measurement values of the SH group were higher at the 4th and 24th-hour measurements, and the differences were statistically significant (P=.016 and P=.09, respectively) (see Figure 2).

When the amylase findings were analyzed, it was found that there were statistically significant differences between the repeated measurements of the 2 groups (P=.001 and P=.001, respectively). When the difference in amylase levels between the groups was compared at different times, it was found that while the measurement values in the SH group were lower than those in the AH group at first, they were higher in the

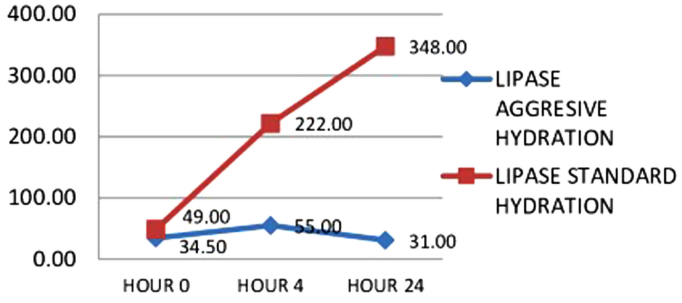

Figure 2. Distribution between groups of repeated lipase measurements.

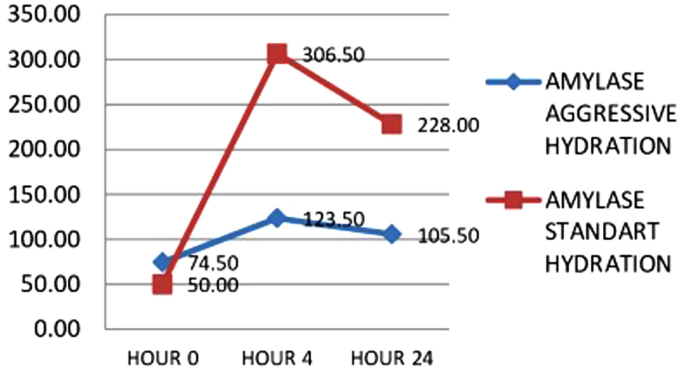

Figure 3. Distribution between groups of repeated amylase measurements.

SH group at the 4th and 24th hours ($P = .009$ and $P = .003$, respectively) (See Figure 3).

DISCUSSION

The most common complication of ERCP is acute pancreatitis.[2] The PEP is treated similarly to acute pancreatitis, with intravenous fluid therapy being the most crucial step in the treatment of acute pancreatitis.[4] To avoid PEP, numerous preventive strategies have been devised. This randomized, controlled study demonstrates that AH with LRS before ERCP decreases the incidence and severity of PEP.

Ischemia and reperfusion damage is caused by impaired microcirculation, which is the fundamental mechanism underlying pancreatitis pathogenesis. The release of cytokines and inflammatory mediators causes increased capillary permeability, which leads to a decrease in intravascular volume, altered microcirculation, and hemodynamic dysfunction. Fluid resuscitation has been proposed to maintain hemodynamics in patients with acute pancreatitis, and it reduces mortality and sequelae including pancreatic necrosis, organ damage, and systemic inflammatory response syndrome (SIRS).[7,8] When compared with the SH protocol, the AH protocol may be more effective in reducing SIRS rates, increasing clinical improvement rates, decreasing hemoconcentration, and shortening the length of hospital stays in patients with acute pancreatitis.[8,9]

In the treatment of acute pancreatitis, LRS is superior to normal saline (NS) in the following ways: NS may cause a high chloride load, which may cause kidney damage.[10] Acidosis caused by NS may promote inflammation, which can lead to trypsinogen activation due to the acidic environment.[11,12] Lactate has been shown to suppress inflammation by negatively regulating TLR induction of the NLRP3 inflammasome and IL1 production via ARRB2 and GPR81.[13]

Comparing LRS with NS for fluid resuscitation has been the subject of several research. In the SMART trial, Semler et al[14] found that IV fluid administration with LRS in critically ill patients resulted in a lower composite mortality rate from any cause, supplemental renal replacement therapy when compared to NS. Several small randomized controlled trials comparing LRS and NS in patients with acute pancreatitis have yielded contradictory outcomes. As opposed to de-Madaria et al.[15] Wu et al[16] found higher SIRS reduction at 24 hours; in both studies, LRS was linked to lower C-reactive protein levels. In recent meta-analyses, SIRS rates did not differ between LRS and NS patients; however, LRS patients had reduced hospital stay, lower rates of intensive care admission and local complications than NS patients.[17-20]

While hydration is the cornerstone of acute pancreatitis treatment, the current study adds to the evidence that AH with LRS may be an effective PEP-preventative approach. Numerous studies and meta-analyses have demonstrated the importance of hydration in preventing PEP.[21-27] Buxbaum et al[21] conducted the first randomized trial of AH to reduce the risk of PEP and discovered that AH with LRS decreased the risk of PEP (95% confidence interval (CI): 5.8%-35.9%; $P = .016$). The statistical significance of this difference is consistent with our findings. In contrast to Buxbaum et al.[21] amylase and lipase levels were statistically lower in the AH group at the 4th and 24th hours in the current study. Wu et al[26] conducted a meta-analysis on 10 randomized controlled trials involving 2200 patients. According to this meta-analysis, AH decreases the frequency of PEP and hyperamylasemia compared to SH.

Several strategies for PEP prevention have been researched. Meta-analyses indicate that prophylactic pancreatic duct stenting reduces the incidence of PEP by approximately 60%.[28,29] However, the success rate depends on the operator's ability to perform rapid pancreatic duct cannulation and the pancreas's ductal anatomy. In addition, it may not be cost-effective when used in conjunction with stents. To prevent the development of PEP, it is appropriate to prefer non-invasive techniques. The effectiveness of nonsteroidal anti-inflammatory drugs has also been demonstrated. According to a recent meta-analysis, the combination of LRS and indomethacin is 94% more effective than monotherapy.[30] Lactated Ringer's is effective on its own, but its effectiveness is enhanced when combined with other preventive measures. However, the cost is a limitation.

There are some limitations to the current study. To ensure the patients' safety after AH, they were selected according to rather strict inclusion criteria. Consequently, patients with significant comorbid diseases were excluded, limiting the generalizability of the findings. This circumstance prevented us from assessing the safety of AH therapy in high-risk patients. Compared with current studies, pancreatitis rates are higher in our study. We believe that the higher frequency of PEP in our study than in the literature is due to the use of frequent precuts, a quite high number of pancreatic cannulations, and the 2012 Atlanta Classification criteria for defining pancreatitis. Furthermore, we believe that the small sample size of our study increases heterogeneity.

CONCLUSION

Randomized controlled trials and meta-analyses indicate that aggressive periprocedural hydration with lactated Ringer's solution reduces the risk of PEP. Compared with other prevention strategies, this technique is safe, inexpensive, and easy to implement. To evaluate the method's efficacy and modify the fluid treatment's dosage and duration, larger and better-designed studies are necessary.

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of Mersin University Faculty of Medicine (Date: March 9, 2017 No: 2017/58).

Informed Consent: All patients included in this study had signed an informed consent form.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – E.A.; Design – E.A.; Supervision – E.A.; Resources – E.A., S.Y., E.Ü., F.A., O.S.; Materials – E.A., S.Y., E.Ü., O.Ö., F.A., O.S.; Data Collection and/or Processing – G.K., İ.Y.; Analysis and/or Interpretation – G.K., E.A., O.S.; Literature Search – G.K.; Writing Manuscript – G.K., E.A., O.S.; Critical Review – E.A., O.S.

Declaration of Interests: The authors declare that they have no competing interests.

Funding: The authors declared that this study has received no financial support.

REFERENCES

1. Dumonceau JM, Kapral C, Aabakken L, et al. ERCP-related adverse events: European Society of Gastrointestinal Endoscopy (ESGE) guideline. *Endoscopy*. 2020;52(2):127-149. [CrossRef]
2. Thaker AM, Mosko JD, Berzin TM. Post-endoscopic retrograde chola ngiopancreatography pancreatitis. *Gastroenterol Rep (Oxf)*. 2015;3(1):32-40. [CrossRef]
3. Kochar B, Akshintala VS, Afghani E, et al. Incidence, severity, and mortality of post-ERCP pancreatitis: a systematic review by using randomized, controlled trials. *Gastrointest Endosc*. 2015;81(1):143-149.e9. [CrossRef]
4. James TW, Crockett SD. Management of acute pancreatitis in the first 72 hours. *Curr Opin Gastroenterol*. 2018;34(5):330-335. [CrossRef]

5. Cahyadi O, Tehami N, de-Madaria E, Siau K. Post-ERCP pancreatitis: prevention, diagnosis and management. *Medicina (Kaunas)*. 2022;58(9): 1261. [CrossRef]
6. Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. *Gut*. 2013;62(1):102-111. [CrossRef]
7. Di Martino M, Van Laarhoven S, Ielpo B, et al. Systematic review and meta-analysis of fluid therapy protocols in acute pancreatitis: type, rate and route. *HPB (Oxford)*. 2021;23(11):1629-1638. [CrossRef]
8. Wu F, She D, Ao Q, Zhang S, Li J. Aggressive intravenous hydration protocol of Lactated Ringer's solution benefits patients with mild acute pancreatitis: a meta-analysis of 5 randomized controlled trials. *Front Med (Lausanne)*. 2022;9:966824. [CrossRef]
9. Buxbaum JL, Quezada M, Da B, et al. Early aggressive hydration hastens clinical improvement in mild acute pancreatitis. *Am J Gastroenterol*. 2017;112(5):797-803. [CrossRef]
10. Gad MM, Simons-Linares CR. Is aggressive intravenous fluid resuscitation beneficial in acute pancreatitis? A meta-analysis of randomized control trials and cohort studies. *World J Gastroenterol*. 2020;26(10):1098-1106. [CrossRef]
11. Rajamäki K, Nordström T, Nurmi K, et al. Extracellular acidosis is a novel danger signal alerting innate immunity via the NLRP3 inflammasome. *J Biol Chem*. 2013;288(19):13410-13419. [CrossRef]
12. Saluja A, Dudeja V, Dawra R, Sah RP. Early intra-acinar events in pathogenesis of pancreatitis. *Gastroenterology*. 2019;156(7):1979-1993. [CrossRef]
13. Hoque R, Farooq A, Ghani A, Gorelick F, Mehal WZ. Lactate reduces liver and pancreatic injury in toll-like receptor- and inflammasome-mediated inflammation via GPR81-mediated suppression of innate immunity. *Gastroenterology*. 2014;146(7):1763-1774. [CrossRef]
14. Semler MW, Self WH, Wanderer JP, et al. Balanced crystalloids versus saline in critically ill adults. *N Engl J Med*. 2018;378(9):829-839. [CrossRef]
15. De-Madaria E, Herrera-Marante I, González-Camacho V, et al. Fluid resuscitation with Lactated Ringer's solution vs normal saline in acute pancreatitis: a triple-blind, randomized, controlled trial. *U Eur Gastroenterol J*. 2018;6(1):63-72. [CrossRef]
16. Wu BU, Hwang JQ, Gardner TH, et al. Lactated Ringer's solution reduces systemic inflammation compared with saline in patients with acute pancreatitis. *Clin Gastroenterol Hepatol*. 2011;9(8):710-717.e1. [CrossRef]
17. Lee A, Ko C, Buitrago C, et al. Lactated Ringers vs normal saline resuscitation for mild acute pancreatitis: a randomized trial. *Gastroenterology*. 2021;160(3):955-957.e4. [CrossRef]
18. Chen H, Lu X, Xu B, Meng C, Xie D. Lactated Ringer solution is superior to normal saline solution in managing acute pancreatitis: an updated meta-analysis of randomized controlled trials. *J Clin Gastroenterol*. 2022;56(2): e114-e120. [CrossRef]
19. Guzmán-Calderón E, Diaz-Arocutipa C, Monge E. Lactate Ringer's versus normal saline in the management of acute pancreatitis: a systematic review and meta-analysis of randomized controlled trials. *Dig Dis Sci*. 2022;67(8):4131-4139. [CrossRef]
20. Kow CS, Burud IAS, Hasan SS. Fluid resuscitation with Lactated Ringer's solution versus normal saline in acute pancreatitis: a systematic review and meta-analysis of randomized trials. *Pancreas*. 2022;51(7):752-755. [CrossRef]
21. Buxbaum J, Yan A, Yeh K, Lane C, Nguyen N, Laine L. Aggressive hydration with Lactated Ringer's solution reduces pancreatitis after endoscopic retrograde cholangiopancreatography. *Clin Gastroenterol Hepatol*. 2014;12(2):303-7.e1. [CrossRef]
22. Choi JH, Kim HJ, Lee BU, Kim TH, Song IH. Vigorous periprocedural hydration with Lactated Ringer's solution reduces the risk of pancreatitis after retrograde cholangiopancreatography in hospitalized patients. *Clin Gastroenterol Hepatol*. 2017;15(1):86-92.e1. [CrossRef]
23. Ghaderi R, Ghojazadeh M, Khoshbaten M, Faravan A. Effect of aggressive fluid therapy on outcomes after endoscopic retrograde cholangiop ancreatography: a randomized controlled clinical trial. *Middle East J Dig Dis*. 2019;11(2):76-83. [CrossRef]
24. Park CH, Paik WH, Park ET, et al. Aggressive intravenous hydration with Lactated Ringer's solution for prevention of post-ERCP pancreatitis: a prospective randomized multicenter clinical trial. *Endoscopy*. 2018;50(4): 378-385. [CrossRef]
25. Wang RC, Jiang ZK, Xie YK, Chen JS. Aggressive hydration compared to standard hydration with Lactated Ringer's solution for prevention of post endoscopic retrograde cholangiopancreatography pancreatitis. *Surg Endosc*. 2021;35(3):1126-1137. [CrossRef]
26. Wu M, Jiang S, Lu X, et al. Aggressive hydration with lactated Ringer solution in prevention of post-endoscopic retrograde cholangiopancreatogr aphy pancreatitis: a systematic review and meta-analysis. *Med (Baltim)*. 2021;100(16):e25598. [CrossRef]
27. Radadiya D, Devani K, Arora S, et al. Peri-procedural aggressive hydration for post endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis prophylaxsis: meta-analysis of randomized controlled trials. *Pancreatology*. 2019;19(6):819-827. [CrossRef]
28. Choudhary A, Bechtold ML, Arif M, et al. Pancreatic stents for prophylaxis against post-ERCP pancreatitis: a meta-analysis and systematic review. *Gastrointest Endosc*. 2011;73(2):275-282. [CrossRef]
29. Mazaki T, Mado K, Masuda H, Shiono M. Prophylactic pancreatic stent placement and post-ERCP pancreatitis: an updated meta-analysis. *J Gastroenterol*. 2014;49(2):343-355. [CrossRef]
30. Márta K, Gede N, Szakács Z, et al. Combined use of indomethacin and hydration is the best conservative approach for post-ERCP pancreatitis prevention: a network meta-analysis. *Pancreatology*. 2021;21(7):1247-1255. [CrossRef]