



Combined Extracorporeal Shock Wave Lithotripsy and Endoscopic Retrograde Pancreatography for Painful Chronic Pancreatitis: Is It Effective?

Harshavardhan Telaprolu¹  Surinder Singh Rana¹

¹Department of Gastroenterology, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

J Digest Endosc 2024;15:208–210.

Address for correspondence Dr. Surinder Singh Rana, MD, DM, FASGE, AGAF, Master ISG, Department of Gastroenterology, Postgraduate Institute of Medical Education and Research (PGIMER), Sector 12, Chandigarh 160 012, India (e-mail: drsurinderrana@gmail.com).

Abstract

Management of pain in chronic pancreatitis (CP) is challenging, and surgery used to be the intervention of choice in patients having pain refractory to medical therapy. Advancement in minimally invasive interventions resulted in a paradigm shift in the management of pain in CP. Pancreatic endotherapy is currently considered the intervention of choice for the management of ductal hypertension in CP. However, multiple mechanisms including ductal hypertension and neurogenic as well as psychological factors contribute to the causation of pain in CP and therefore no single intervention is effective in all patients. The precise role of interventional procedure in a complex disease like CP with multiple pathogenic mechanisms requires a prospective comparative study with a sham group and there are no such comparative studies in the literature. In this news and views, we discuss a recently published sham-controlled randomized trial (Combined extracorporeal shock wave lithotripsy and endoscopic treatment for pain in chronic pancreatitis (SCHOKE) trial) that examined the efficacy of extracorporeal shock wave lithotripsy (ESWL) and endoscopic retrograde pancreatography (ERP) compared with the sham procedure.

Keywords

- ▶ chronic pancreatitis
- ▶ endotherapy
- ▶ stent

Chronic pancreatitis (CP) results in prolonged inflammation of the pancreatic tissue resulting in ductal abnormalities and pancreatic fibrosis.^{1,2} These changes contribute to the development of chronic pain through different mechanisms. In patients of CP, pain is the most dominant symptom and impacts their quality of life.³ Because of multiple mechanisms and the contribution of psychosocial factors, the management of pain in CP is challenging. In addition to structural causes of pain, central sensitization, along with psychosocial factors, also contributes to pain. Medical and psychosocial management often needs to be supplemented with structural interventions. Structural interventions target intraductal hypertension and these may be endoscopic, interventional, or surgical.^{4,5}

Extracorporeal shock wave lithotripsy (ESWL) fragments the intraductal calculi and is useful in clearing of larger main duct calculi and the consequent duct obstruction. Excellent results and minimum adverse effects with ESWL have been reported in multiple observational studies and comparative randomized controlled trials (RCTs).^{6–9} The precise role of interventional procedure in a complex disease like CP with multiple pathogenic mechanisms requires a prospective comparative study with a sham group and there are no such comparative studies in the literature. A recently published sham-controlled randomized trial (SCHOKE trial) examined the efficacy of ESWL and endoscopic retrograde pancreatography (ERP) compared with the sham procedure.¹⁰ This study is notable for its inclusion of a sham comparison.

article published online
August 20, 2024

DOI <https://doi.org/10.1055/s-0044-1789009>.
ISSN 0976-5042.

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The study was conducted at a single tertiary care center, involving 106 patients of CP with chronic pain. Patients with previous interventions and with contraindications to endotherapy and ESWL were excluded. They were randomly assigned to the ESWL and ERP group ($n=52$) or the sham group ($n=54$), and three patients each were excluded from both groups. In the ESWL group, complete stone fragmentation was achieved with the initial ESWL session in 32/52 (62%) patients and in 17/52 (33%) patients by the second session. None of the studied patients required more than three sessions. This clearance was followed by a single ERP procedure where 46/52 (88%) patients achieved complete ductal clearance. Pancreatic duct stenting was done in all these patients after ERP. No intervention was done in the sham group and these patients continued their usual medical treatment, including antioxidants and pancreatic enzyme supplements.

When followed up after 12 weeks, patients in the ESWL/ERP group had better pain relief as compared with the sham group (mean difference in change, -0.7 [95% confidence interval (CI), -1.3 to 0] on the visual analog scale [VAS]; $P=0.039$). However, the difference between the two groups was not sustained at the 24-week follow-up, and no differences were seen for 30% pain relief at the 12- or 24-week follow-up. This improvement in pain score was accompanied by a decrease in the requirement of opioid-based analgesics, lower frequency of depression, and overall better-perceived health status after the 12-week follow-up. However, the difference between groups was not sustained at the 24-week follow-up. The average change in pain-diary score (VAS) at the 12-week follow-up was -5.0 (95% CI, -5.4 to -4.5) in the ESWL/ERP group and -4.3 (CI, -4.7 to -3.8) in the sham group, with a mean difference of -0.7 (CI, -1.3 to 0 ; $p=0.039$), suggesting a modest pain relief with intervention. The adverse effects were similar between the two groups. Importantly, significant pain reduction was seen in both treatment groups, with significant and long-lasting pain relief in the sham group. The authors concluded that compared with a sham procedure, pancreatic ductal clearance using combined ESWL/ERP provided modest short-term pain relief in patients with CP and intraductal stones.

Commentary

Interventional therapy for the relief of ductal hypertension has been shown to be an efficacious management option for painful CP.^{1,11,12} ESWL is an accepted interventional option, especially recommended for larger pancreatic duct stones, by various guidelines.^{13,14} However, the SCHOKE trial has raised questions on the efficacy of pancreatic endotherapy for the relief of pain in CP. It showed a modest improvement in pain, which, importantly, was not sustained at 6 months of follow-up. An interesting observation was significant pain relief seen in patients randomized to the sham procedure group (91% of patients). The study is commendable for the use of a sham procedure for comparison with ESWL/ERP as intervention procedures have been shown to have significant sham effects.¹⁵ This study reiterates that management of pain in CP requires both plumbing to correct the anatomical abnormality and management of neurogenic component of pain by

altering the wiring problem. This study also underscores the importance of a sham group in studies evaluating the efficacy of interventions in complex multifactorial diseases like CP.

Does this sham-controlled randomized study suggest that endotherapy has a limited role in the management of painful CP? CP is an enigmatic disease with a poorly understood pathogenesis of pain and therefore a short-term follow-up of 6 months cannot assess the complete spectrum of efficacy of any intervention. Further follow-up of the studied patients may provide more insights into the long-term effects of tackling ductal hypertension. Moreover, the mean score of pain in the included patients was 5 and it is possible that the difference in the efficacy between endotherapy and sham might have been greater if patients with severe pain were included. Also, the authors studied only the intensity of pain as the outcome measure, whereas pain is a composite measure of affective and cognitive components, and instruments/scores including these measures provide a more composite assessment of pain. Moreover, patients in the sham group continued with medical therapy including analgesics, antioxidants, and pancreatic enzyme supplements, and this could have contributed to pain relief in the sham group.

In conclusion, endotherapy is an important component of the comprehensive management of pain in CP, and studies evaluating the efficacy of interventions/drugs in pain in CP should have a sham comparator group.

Funding

None.

Conflict of Interest

None declared.

References

- Sharma V, Rana SS, Bhasin DK. Medical management of pain in chronic pancreatitis. *Trop Gastroenterol* 2014;35(04):205–211
- Singh VK, Yadav D, Garg PK. Diagnosis and management of chronic pancreatitis: a review. *JAMA* 2019;322(24):2422–2434
- de Rijk FEM, van Veldhuisen CL, Kempeneers MA, et al; Dutch Pancreatitis Study Group. Quality of life in patients with definite chronic pancreatitis: a nationwide longitudinal cohort study. *Am J Gastroenterol* 2023;118(08):1428–1438
- Bhasin DK, Rana SS, Sidhu RS, et al. Clinical presentation and outcome of endoscopic therapy in patients with symptomatic chronic pancreatitis associated with pancreas divisum. *JOP* 2013;14(01):50–56
- Bhasin DK, Rana SS. Extracorporeal shock wave lithotripsy (ESWL) for large pancreatic stones: are these shocks worth while? *Indian J Gastroenterol* 2010;29(04):133–136
- Korpela T, Udd M, Tenca A, et al. Long-term results of combined ESWL and ERCP treatment of chronic calcific pancreatitis. *Scand J Gastroenterol* 2016;51(07):866–871
- Geusens D, van Malenstein H. The role of extracorporeal shock wave lithotripsy in the treatment of chronic pancreatitis. *Acta Gastroenterol Belg* 2021;84(04):620–626
- Dumonceau JM, Costamagna G, Tringali A, et al. Treatment for painful calcified chronic pancreatitis: extracorporeal shock wave lithotripsy versus endoscopic treatment: a randomised controlled trial. *Gut* 2007;56(04):545–552
- Tandan M, Reddy DN, Talukdar R, et al. Long-term clinical outcomes of extracorporeal shockwave lithotripsy in painful chronic calcific pancreatitis. *Gastrointest Endosc* 2013;78(05):726–733

- 10 Talukdar R, Olesen SS, Unnisa M, et al. Extracorporeal shock-wave lithotripsy and endoscopy for the treatment of pain in chronic pancreatitis : a sham-controlled, randomized trial. *Ann Intern Med* 2024;177(06):749–758
- 11 Rana SS, Shah J, Bush N, Sharma R, Dhalaria L, Gupta R. Endoscopic dilatation of tight difficult pancreatic duct strictures: Soehendra stent retriever or wire guided cystotome. *Pancreatology* 2021;21(02):498–499
- 12 Bhasin DK, Rana SS, Chandail VS, et al. Clinical profile of calcific and noncalcific chronic pancreatitis in north India. *J Clin Gastroenterol* 2011;45(06):546–550
- 13 Löhr JM, Dominguez-Munoz E, Rosendahl J, et al; HaPanEU/UEG Working Group. United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). *United European Gastroenterol J* 2017;5(02):153–199
- 14 Shimizu K, Ito T, Irisawa A, et al. Evidence-based clinical practice guidelines for chronic pancreatitis 2021. *J Gastroenterol* 2022;57(10):709–724
- 15 Jonas WB, Crawford C, Colloca L, et al. To what extent are surgery and invasive procedures effective beyond a placebo response? A systematic review with meta-analysis of randomised, sham controlled trials. *BMJ Open* 2015;5(12):e009655