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[Intervention Review]

Interventions for necrotising pancreatitis

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ABSTRACT

Background

Acute necrotising pancreatitis carries significant mortality, morbidity, and resource use. There is considerable uncertainty as to how people with necrotising pancreatitis should be treated.

Objectives

To assess the benefits and harms of different interventions in people with acute necrotising pancreatitis.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL, 2015, Issue 4), MEDLINE, EMBASE, Science Citation Index Expanded, and trials registers to April 2015 to identify randomised controlled trials (RCT). We also searched the references of included trials to identify further trials.

Selection criteria

We considered only RCTs performed in people with necrotising pancreatitis, irrespective of aetiology, presence of infection, language, blinding, or publication status for inclusion in the review.

Data collection and analysis

Two review authors independently identified trials and extracted data. We calculated the odds ratio (OR) and mean difference with 95% confidence intervals (CI) using Review Manager 5 based on an available-case analysis using fixed-effect and random-effects models. We planned a network meta-analysis using Bayesian methods, but due to sparse data and uncertainty about the transitivity assumption, performed only indirect comparisons and used Frequentist methods.

Main results

We included eight RCTs with 311 participants in this review. After exclusion of five participants, we included 306 participants in one or more outcomes. Five trials (240 participants) investigated the three main treatments: open necrosectomy (121 participants), minimally invasive step-up approach (80 participants), and peritoneal lavage (39 participants) and were included in the network meta-analysis. Three trials (66 participants) investigated the variations in the main treatments: early open necrosectomy (25 participants), delayed open necrosectomy (11 participants), video-assisted minimally invasive step-up approach (12 participants), endoscopic minimally invasive

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step-up approach (10 participants), minimally invasive step-up approach (planned surgery) (four participants), and minimally invasive step-up approach (continued percutaneous drainage) (four participants). The trials included infected or sterile necrotising pancreatitis of varied aetiology.

All the trials were at unclear or high risk of bias and the overall quality of evidence was low or very low for all the outcomes. Overall, short-term mortality was 30% and serious adverse events rate was 139 serious adverse events per 100 participants. The differences in short-term mortality and proportion of people with serious adverse events were imprecise in all the comparisons. The number of serious adverse events and adverse events were fewer in the minimally invasive step-up approach compared to open necrosectomy (serious adverse events: rate ratio 0.41, 95% CI 0.25 to 0.68; 88 participants; 1 study; adverse events: rate ratio 0.41, 95% CI 0.25 to 0.68; 88 participants; 1 study). The proportion of people with organ failure and the mean costs were lower in the minimally invasive step-up approach compared to open necrosectomy (organ failure: OR 0.20, 95% CI 0.07 to 0.60; 88 participants; 1 study; mean difference in costs: USD -11,922; P value < 0.05; 88 participants; 1 studies). There were more adverse events with video-assisted minimally invasive step-up approach group compared to endoscopic-assisted minimally invasive step-up approach group (rate ratio 11.70, 95% CI 1.52 to 89.87; 22 participants; 1 study), but the number of interventions per participant was less with video-assisted minimally invasive step-up approach group compared to endoscopic minimally invasive step-up approach group (difference in medians: 2 procedures; P value < 0.05; 20 participants; 1 study). The differences in any of the other comparisons for number of serious adverse events, proportion of people with organ failure, number of adverse events, length of hospital stay, and intensive therapy unit stay were either imprecise or were not consistent. None of the trials reported long-term mortality, infected pancreatic necrosis (trials that included participants with sterile necrosis), health-related quality of life at any time frame, proportion of people with adverse events, requirement for additional invasive intervention, time to return to normal activity, and time to return to work.

Authors' conclusions

Low to very low quality evidence suggested that the minimally invasive step-up approach resulted in fewer adverse events, serious adverse events, less organ failure, and lower costs compared to open necrosectomy. Very low quality evidence suggested that the endoscopic minimally invasive step-up approach resulted in fewer adverse events than the video-assisted minimally invasive step-up approach but increased the number of procedures required for treatment. There is currently no evidence to suggest that early open necrosectomy is superior or inferior to peritoneal lavage or delayed open necrosectomy. However, the CIs were wide and significant benefits or harms of different treatments cannot be ruled out. The TENSION trial currently underway in Netherlands is assessing the optimal way to perform the minimally invasive step-up approach (endoscopic drainage followed by endoscopic necrosectomy if necessary versus percutaneous drainage followed by video-assisted necrosectomy if necessary) and is assessing important clinical outcomes of interest for this review. Implications for further research on this topic will be determined after the results of this RCT are available.

PLAIN LANGUAGE SUMMARY

Treatment methods for people with necrotising pancreatitis (pancreatic destruction due to inflammation of pancreas)

Review question

How should people with necrotising pancreatitis be treated?

Background

The pancreas is an organ in the abdomen (tummy) that secretes several digestive enzymes (substances that enable and speed up chemical reactions in the body) into the pancreatic ductal system, which empties into the small bowel. It also contains the Islets of Langerhans, which secrete several hormones including insulin (helps regulate blood sugar). Acute pancreatitis is sudden inflammation of the pancreas and can lead to destruction of the pancreas (pancreatic necrosis). Pancreatic necrosis can be infected or non-infected (sterile). Pancreatic necrosis can lead to failure of other organs, such as the lungs and kidneys, and is a life-threatening illness. The main treatments for pancreatic necrosis include removal of the dead tissue (debridement or necrosectomy), peritoneal lavage (washing dead tissue out of the abdomen, drainage (inserting a tube or 'drain' to drain out the fluid collection around the pancreas), or initial drainage followed by necrosectomy if necessary (called the minimally invasive 'step-up' approach). The minimally invasive step-up approach can be performed in different ways. For example, in video-assisted minimally invasive step-up approach, necrosectomy is performed after a period of drainage through a key-hole operation; in the endoscopic minimally invasive step-up approach, necrosectomy is performed with the help of an endoscope (instrument used to look inside the abdomen).

The best way to treat people with necrotising pancreatitis is not clear. We sought to resolve this issue by searching for existing studies on the topic. We included all randomised controlled trials (clinical studies where people are randomly put into one of two or more treatment groups) whose results were reported to 7 April 2015.

Study characteristics

Eight trials including 311 participants met the inclusion criteria for the review, of whom 306 participants were included in various comparisons. The treatments compared in five trials included necrosectomy, peritoneal lavage, and the step-up approach. Three other trials compared variations in timing of necrosectomy and methods of step-up approach. The participants in the trials had infected or sterile pancreatic necrosis resulting from varying causes.

Key results

Overall, the short-term death rate (mortality over a short time) was 30% and serious adverse events (side effects or complications) rate was 139 per 100 participants. The differences in short-term mortality and percentage of people with serious adverse events were imprecise in all the comparisons. The number of serious adverse events and adverse events were fewer in the minimally invasive step-up approach compared to open necrosectomy. The complications resulting from the disease and treatment included heart failure (heart does not pump enough blood around the body at the correct pressure), lung failure (lungs do not remove waste products from the blood), kidney failure (kidneys do not remove waste products from the blood), and blood poisoning (micro-organisms and their poisons are in the blood). The percentage of people with organ failure and the average costs were lower in the minimally invasive step-up approach compared to open necrosectomy. The number of adverse events were more with the video-assisted minimally invasive step-up approach compared to the endoscopic-assisted minimally invasive step-up approach but the total numbers of procedures performed were less with the video-assisted minimally invasive step-up approach compared to the endoscopic minimally invasive step-up approach. The differences in any of the other comparisons for number of serious adverse events, percentage of people with organ failure, number of adverse events, length of hospital stay, and intensive therapy unit stay were either imprecise or were not consistent. None of the trials reported long-term mortality, infected pancreatic necrosis (in trials that included participants with sterile necrosis), health-related quality of life (which measures physical, mental, emotional, and social functioning), percentage of people with adverse events, requirement for additional invasive intervention, time to return to normal activity, and time to return to work.

Quality of the evidence

The overall quality of evidence was low or very low for all the measurement because the trials were at high risk of bias (e.g. prejudice of people who conducted the trial and trial participants who prefer one treatment over another) and were small trials. As a result, further studies are required on this topic.