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Acute colonic pseudo-obstruction (ACPO) or Ogilvie syndrome is an idiopathic syndrome of dilation of the colon without mechanical obstruction that develops in hospitalized patients usually in the setting of significant medical and surgical conditions. Standard care therapy includes colonoscopic decompression or neostigmine. The latter is not Food and Drug Administration-approved for this indication but has been the recent intervention of choice. A patient with ACPO failed 2 injections of neostigmine. A clinical trial of subcutaneous methylnaltrexone was administered because she was on opioid therapy. There was a brisk response to methylnaltrexone, a  $\mu$ -opioid-receptor antagonist which does not cross the bloodbrain barrier. This is the first case report in the literature and in the pharmaceutical company's data bank that illustrates a potential role for methylnaltrexone in ACPO. Prospective, larger studies to determine the role of methylnaltrexone in ACPO are warranted.