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Brief Report

Management of Malignant Rectal Pain and Tenesmus: A Systematic Review

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Abstract

Background: Malignant rectal pain (MRP) and tenesmus cause significant morbidity for cancer patients at all stages of disease. There is little evidence to guide management of these symptoms.
Objective: The objective of this review was to summarize the existing evidence base for palliative management of MRP and tenesmus outside of standard oncologic or surgical management.
Design: A systematic review of PubMed and Embase was conducted according to PRISMA guidelines using preselected search terms for publications between 1980 and January 2017.
Setting/Subjects: Studies that described management for patients with tenesmoid pain from malignant tumors of the rectum, anus, or perineum were identified.
Measurements: The primary outcome was response of pain to treatment.
Results: The search produced 1412 titles. Twenty articles met criteria for inclusion in the review, including 11 case series and 9 case reports. A variety of treatments were found with most patients receiving interventional procedures, but overall evidence to support any particular intervention is limited and of poor quality.
Conclusions: This review highlights the limited current evidence base for medical and interventional treatments for MRP and tenesmus. Further study is needed to clarify the best approach to managing these challenging symptoms.

Keywords: neoplams; pain management; rectum; review; tenesmus

Introduction

MALIGNANT RECTAL PAIN (MRP) and tenesmus are often distressing symptoms that can impact quality of life (QOL). They can present in multiple oncologic settings, including primary tumors of the rectum or anus, genitourinary malignancies with direct extension to the rectum or anus, or pelvic metastatic deposits involving the lower pelvic region. These symptoms are frequently difficult to manage given the complex anatomy and innervation of the anorectum.

The rectum travels caudally to the levator ani where it becomes the anal canal, composed of an external (skeletal muscle) and internal (smooth muscle) sphincter.[1–3] The pelvic plexus, located laterally and superiorly to the levator ani, innervates the rectum and internal sphincter. It is composed of sympathetic nerves cranially (branches of L1–L3) and parasympathetic nerves caudally (branches of S2–S5). Branches of the pudendal nerve and sacral nerve roots (S2–S5) supply the rectum, levator ani, and external sphincter.[2–4] Tumor invasion into this region can subsequently lead to combinations of nociceptive pain, neuropathic pain, and tenesmus (the painful sensation of persistent rectal fullness and incomplete defecation). Tenesmus is felt to be due to smooth muscle stretching and contraction.[5]

The complicated pathophysiology of MRP and tenesmus makes this syndrome challenging to manage. Standard cancer pain management strategies include opioids for nociceptive pain and adjuvants such as antidepressants and antiepilectics for neuropathic pain.[6] The purpose of this systematic review is to assess the available evidence for the management of MRP and tenesmus in patients with malignancies involving the anorectal region.

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Methods

Search strategy

This systematic review was conducted according to PRISMA guidelines.[7] A systematic search of Pubmed and Embase from 1980 to January 2017 (limited to English language publications) using Medical Subject Heading terms and keywords was compiled by a multidisciplinary team with experience managing MRP and tenesmus (Table 1). In addition, palliative care textbooks were screened for relevant trials and abstracts, as were the United States National Library of Medicine Clinical Trials registry and palliative care and oncology conference proceedings.[8] The bibliographies of included articles were screened for relevant articles.

Study selection

Studies involving patients with rectal or tenesmoid pain secondary to a pelvic malignancy in which the primary outcome was pain management were identified. Studies were first screened by title and then abstract by a single author. Inclusion and exclusion criteria, described in Table 2, were applied to selected articles. Disease-modifying treatments including chemotherapy, radiation, surgery, and tumor ablation were excluded as these treatments themselves can be associated with rectal pain.

Study assessment and synthesis

Relevant articles were independently graded by two authors using strength of recommendation taxonomy (SORT).[9] The following information was abstracted from each study: author, publication date, design, sample size, age, gender, histology, intervention, and outcome. Patients from each study were pooled according to similar palliative interventions (e.g., drug class and procedure) and discussed descriptively. Data could not be quantitatively pooled in a meta-analysis due to a limitation in study quality and number.

Table 2. Inclusion and Exclusion Criteria

Inclusion criteria	*Exclusion criteria*
Adult patients with cancer	Patients with acute surgery related pain
Studies that focus on palliative management of rectal/anal pain and tenesmus	Patients with pain secondary to treatment with chemotherapy or radiation (e.g., radiation proctitis)
Articles published 1980–2016	Patients with bony metastasis as the cause of pain
Conference abstracts published 2012–2016	Management strategies that aim to reduce tumor burden (chemotherapy, radiation, surgical, and ablation procedures)
Unpublished or ongoing clinical trials	Pain management not a primary outcome of study
Published in English	

Results

The literature search results are shown in Figure 1. Twenty articles met the inclusion criteria (11 case series and 9 case reports). All were graded as SORT Level 3: other evidence of

Table 1. Search Terms

	Population	*Intervention*	*Outcome*
MeSH headings	Pain Neuralgia Rectum Anal canal Perineum Pelvis Painful defecation Neoplasms Pelvic neoplasms Rectal neoplasm Anus neoplasm	Analgesics, opioid Methadone Calcium channel blockers Diltiazem Nifedipine Anti-inflammatory agents Suppositories Nitroglycerin Lidocaine Bupivacaine Clonidine Nerve block Albuterol Steroids Vasodilator agents Loop ileostomy Antidepressants Anticonvulsants Cannabinoids Cannabis	Pain management Analgesia
Keywords	Tenesmus Tenesmoid Cancer Malignant/malignancy Rectal Anal Perineal Pelvic	Opium Belladonna Alpha agonists Botox/botulinum Diverting colostomy Marijuana/Marihuana	

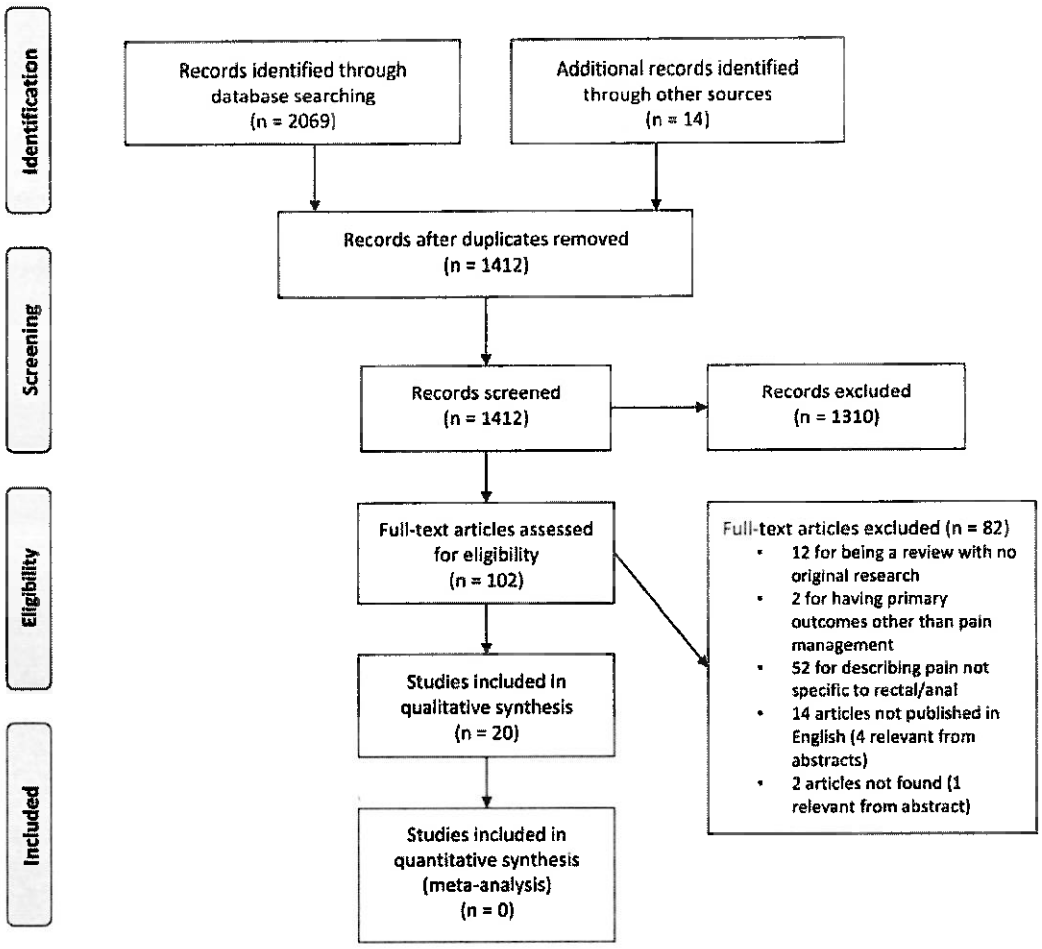

FIG. 1. PRISMA flow diagram.

lower quality. These 20 articles described 40 patients: 13 received medication and 27 received an interventional procedure. The median age was 64 (range 34–83) years. Twenty-two were male, 17 female, and one unknown gender. Twenty-five patients had a gastrointestinal primary tumor, the other 14 had metastatic disease from another primary. One patient was missing data describing the tumor site. Detailed results for patient symptoms, management, response, and potential confounding factors are summarized in Tables 3 and 4.

Opioids

Opioids were effective for tenesmus in two patients.[10,11] One patient experienced significant pain relief with an opioid rotation from morphine to methadone. A second patient had tenesmus resolution and decreased systemic opioid requirements after the addition of morphine gel per rectum.

Vasodilators

Eight patients received a vasodilator for MRP with or without tenesmus.[12–14] Three of four experienced significant relief of tenesmus with nifedipine.[12] Two patients had reduced pain, tenesmus, and opioid requirements with diltiazem.[13] This approach was well tolerated but confounded by the use of other analgesics. Lastly, two patients with anal pain experienced relief with intravenous phentolamine.[14] Of the eight patients in these case series, half experienced hypotension (one requiring ephedrine) and one had a transient arrhythmia.

Local anesthetics

One patient on opioids for a protruding rectal cancer experienced immediate and sustained analgesia after the application of topical lidocaine and prilocaine.[15] Another patient with rectal pain and tenesmus refractory to opioids, ketamine, and midazolam was treated with bupivacaine per rectum.[16] Pain response was achieved within 15 minutes. A higher dose provided 11 hours of pain relief without side effects.

Ketamine

The N-methyl-D-aspartate (NMDA) antagonist, ketamine, was used to treat nociceptive and neuropathic anal and perineal pain in a single patient.[17] The patient's pain improved, but she still needed a saddle block for pain while sitting.

Sympathetic neurolysis

Eighteen patients received sympathetic neurolytic procedures for MRP with or without tenesmus. Twelve received lumbar sympathectomy, with 10 experiencing complete

Table 3. Summary of Patients and Studies Receiving Medical Management

Study (design)	*Clinical scenario*	*Intervention*	*Response*	*Notes*
Krajnik et al.[10] (case series 1999)	56M metastatic rectal Ca: sacral pain and tenesmus.	Opioids: morphine gel 0.03% rectally: doses ranging from 7 mL BID to TID.	Pain fully relieved and one-third systemic opioid (Fentanyl patch) reduction for 14 weeks until death.	
Mercadante et al.[11] (case report 2001)	68M metastatic rectal Ca: rectal–perineal pain and tenesmus refractory to opioids, amitriptyline.	Opioids: morphine to methadone rotation 10 mg TID.	Pain reduced from 10/10 to 2/10.	Addition of amitriptyline a potential confounder. Duration of effect not reported.
McLoughlin and McQuillan[12] (case series 1997)	73M rectal Ca: rectal pain and tenesmus.	Vasodilators: nifedipine 20 mg PO BID.	>75% reduction in tenesmus for 3 weeks until death.	Concurrent or previous medications not described for any patient.
	72F metastatic breast Ca: rectal pain and tenesmus.	Vasodilators: nifedipine 10 mg PO BID.	Pain fully relieved for 2 weeks until death.	
	?F metastatic melanoma: rectal pain.	Vasodilators: nifedipine 20 mg PO BID.	No response: treatment discontinued after 5 days.	
	60F colon Ca: tenesmus.	Vasodilators: nifedipine 20 mg PO BID.	>80% reduction for 9 days until death.	
Stowers et al.[13] (case series 2014)	70M metastatic urothelial Ca: perineal pain and tenesmus refractory to opioids, gabapentin, and three ganglion impar blocks.	Vasodilators: diltiazem 120 mg/day.	>2/3 reduction in pain with no adverse effects for 1 month. >85% reduction in opioid requirements.	Increase in gabapentin and addition of methadone potential confounders.
	64F rectal Ca: rectal pain and tenesmus refractory to opioids.	Vasodilators: diltiazem 120 mg/day.	≥85% reduction in pain and systemic opioid use. No adverse effects for 1 month.	
Yasukawa et al.[14] (consecutive case series 2007)	79F metastatic rectal Ca: abdominal and anal pain refractory to opioids.	Vasodilators: IV infusion of 80 mg/day phentolamine × 2 days.	Pain free for 96 days.	Case series included eight patients but only two had relevant pain. Four patients had hypotension, two requiring ephedrine. One patient had transient arrhythmia.
	68M hepatocellular Ca: abdominal/anal pain refractory to opioids.	Vasodilators: IV infusion of 80 mg/day phentolamine × 2 days. Repeated a second time due to recurrence of pain.	>85% pain reduction for 62 days.	
Zaporowska-Stachowiak et al.[16] (case series 2014)	83F metastatic ovarian Ca: rectal pain and tenesmus unresponsive to morphine, ketamine, midazolam, and gabapentin.	Local anesthetics: 100 mL of 0.1% bupivacaine rectally.	>70% pain reduction for 11 hours.	
Stegman and Stoukides[15] (case report 1996)	69F colorectal Ca: rectal pain.	Local anesthetics: topical lidocaine 2.5% and prilocaine 2.5% q8h	Pain free despite tumor growth for 4 weeks until patient death. >25% reduction in opioid requirements.	Confounded by addition of rectal dexamethasone 4 mg BID.
Tarumi et al.[17] (case report 2000)	45F recurrent rectal Ca: somatic and neuropathic anal and perineal pain refractory to opioid and lidocaine infusions.	Ketamine: 50 mg IV over 30 minutes at bedtime	Partial response: patient still needed saddle block. No side effects. Change in opioid requirements not described.	

BID, twice daily; Ca, cancer; F, female; IV, intravenous; M, male; TID, three times daily; ?, unknown.

TABLE 4. SUMMARY OF PATIENTS AND STUDIES RECEIVING INTERVENTIONAL MANAGEMENT

Study (design)	*Clinical scenario*	*Intervention*	*Response*	*Notes*
Bristow and Foster[18] (prospective consecutive case series 1988)	All patients with tenesmus refractory to opioids and chlorpromazine, diazepam, or antidepressant. 1. 66F leiomyosarcoma of ilieum. 2. 81F anorectal Ca 3. 72M prostate Ca 4. 44F colon Ca 5. 73M prostate Ca 6. 50M rectal Ca 7. 70M sigmoid Ca 8. 49F cervical Ca 9. 49F ovarian Ca 10. 64M colonic Ca 11. 57M rectal Ca 12. No data	Sympathetic neurolysis: lumbar sympathectomy with phenol.	Complete response: 10/12 patients until most recent follow-up (ranging 3 days to 7 months, mean of 53 days). Partial response: 1/12. No response: 1/12. One patient was hypotensive for 8 hours postblock responding to IV fluid.	Results generalized for all patients (nonresponders not identified) with limited individual patient data. Data for one patient not included in demographic table. Details of pain severity not included.
Turker et al.[19] (case series 2005)	63M metastatic rectal Ca: pelvic pain and tenesmus despite intrathecal morphine, gabapentin, amitriptyline.	Sympathetic neurolysis: superior hypogastric block.	>75% pain reduction for 6 months until death. Stopped gabapentin. Required two-third less intrathecal morphine.	
	66F metastatic cervical Ca: right lower quadrant abdominal pain and tenesmus despite opioids, amitriptyline.		Pain and tenesmus disappeared for 12 months and morphine reduced by two-third. Upon pain recurrence, block repeated with 6 months good pain relief until death.	
	48M metastatic rectal Ca: pelvic pain and tenesmus despite NSAID, opioids, amitriptyline.		>75% reduction in pain and tenesmus for 8 months until death. 75% reduction in Fentanyl requirements.	
Wilsey et al.[20] (case series 2002)	72M recurrent anal Ca: rectal and perineal pain despite opioids, tramadol, dothiepin, and gabapentin.	Sympathetic neurolysis: superior hypogastric block.	40% reduction in pain for 1 week but patient suffered rapid general decline and required more opioids until death a few weeks later.	Only one of two cases in this series relevant and included in this review.
Hong and Jang[21] (case report 2006)	67M recurrent rectal Ca: perianal and scrotal pain.	Sympathetic neurolysis: ganglion impar block through chemical neurolysis.	Immediate complete relief postblock for one month. Soreness at injection site at one week.	No details of previous medication use or pain severity.
Gurses[22] (case report 2014)	75M colon Ca: severe perineal pain. Pain refractory to fentanyl 300 μg/h patch, pregabalin, tramadol, and NSAIDs.	Sympathetic neurolysis: ganglion impar block through radiofrequency ablation.	Two-third pain reduction at one month follow-up. Discontinued all medications except tramadol.	Limited follow-up and discussion of etiology of pain.

(*continued*)

TABLE 4. (CONTINUED)

Study (design)	*Clinical scenario*	*Intervention*	*Response*	*Notes*
Slatkin and Rhiner[23] (case series 2003)	52F metastatic colorectal Ca: intractable vaginal and rectal pain despite PCA with opioids and adjuvants. Patient had ileostomy and nephrostomy.	Intrathecal neurolysis: phenol saddle block (0.75 mL of 10% phenol).	>55% pain reduction for three months until death. 94% reduction in opioid requirements. Mild weakness of legs after injection resolved after two hours.	Case series of four patients with only one included in review.
Hellendoorn-Smit and Overweg-van Kints[24] (case report 1988)	61M recurrent rectal Ca: perineal pain despite opioids.	Intrathecal neurolysis: three successive phenol blocks at L5-S1 with increasing doses. Dosing and frequency of blocks based on pain response.	Complete relief × 1 week after first block. Complete relief × 6 weeks and opioid discontinuation after second block. Then required intrathecal opioids before receiving third block that gave complete relief × 8 months until death with side effects of right foot paresthesia and later left leg pain.	
Turconi and Papa[25] (case report 2012)	64M rectal Ca: rectal pain with tenesmus despite opioids and adjuvants.	Intrathecal neurolysis: phenol block at L5-S1.	>60% pain reduction lasting for four days of follow-up. Morphine reduced by 75%.	Conference abstract from a conference with very short follow-up.
Finnegan et al.[26] (case series 2008)	63M locally recurrent advanced rectal Ca with perianal abscess: perianal pain despite epidural morphine, bupivacaine, and clonidine.	Epidural neurolysis: injection of 10 mL of 6% phenol through epidural catheter.	"Excellent pain relief" for nine days until death with only transient burning sensation in back and legs immediately after injection of phenol.	Case series with one of two patients included in review. No details of pain severity of quantity of effect.
Harrison[27] (case report 1999)	34F cervical Ca metastatic to rectum: lumbosacral pain, tenesmus, and painful defecation despite morphine, diclofenac, and amitriptyline.	Epidural analgesia: epidural infusion with diamorphine and bupivacaine but switched to ropivacaine at higher than standard doses.	Improved analgesia and QOL until death. Improvement in motor blockade after switching to bupivacaine.	Focuses on the use of high-dose ropivacaine. Limited patient outcome details.
Goucke[28] (case report 1993)	60M ulcerating anal Ca: perianal and buttock pain, painful defecation. Short duration of response to epidural analgesia, epidural neurolysis, and diverting colostomy.	Intrathecal analgesia: with morphine and bupivacaine boluses. Implantable pump installed and bolus dosing adjusted based on pain response.	Improved pain control and QOL until death 345 days later.	Limited details on pain severity.
Nauta et al.[29] (Prospective consecutive case series 2000)	51F recurrent metastatic colorectal Ca: rectal pain despite oral opioids and PCA. 49M metastatic lung Ca: perianal and coccygeal pain worse with defecation and urination. Refractory to opioids. 49M presacral small cell Ca: rectal pain worse with defecation refractory to opioids.	Punctate midline myelotomy.	"Satisfactory-to-excellent" pain control at one month. Stopped most opioids. Pain recurrence by two months. Had transient urinary retention. Initial relief, but required reinitiation of opioids. Complete pain relief × 11 months without need for opioids before tumor increased and pain recurred.	Case series of six patients with only three included. Details of opioid requirements and pain severity for each patient not described.

NSAID, nonsteroidal anti-inflammatory drug; QOL, quality of life; PCA, patient controlled analgesia.

relief of tenesmus.[18] Four patients received a superior hypogastric block resulting in improved MRP and tenesmus in all and significant opioid reduction in three patients.[19,20] Two patients received a ganglion impar block.[21,22] One had immediate and sustained analgesia for a month.[21] Another patient with severe pain with defecation experienced a significant pain reduction and discontinued multiple analgesics.[22]

Neuraxial blockade

Three patients received intrathecal neurolysis.[23–25] One patient had complete pain relief with three consecutive blocks lasting ~10 months until death.[24] The other two patients had >50% reduction in pain and >70% reduction in opioid requirements.[23,25] Among the three patients, one experienced transient mild leg weakness[23] and one developed right foot paresthesia and left leg pain.[24]

One patient received an epidural phenol neurolysis, resulting in "excellent pain relief" for nine days until death.[26] Another patient received epidural ropivacaine resulting in reversal of motor blockade secondary to bupivacaine. Pain control and QOL improved (described in limited details) for two months until death.[27] An intrathecal morphine and bupivacaine infusion titrated according to pain level were administered in boluses by a pump to another patient.[28] Pain was managed for nearly a year.

Three patients from a prospective consecutive case series had abdominal visceral pain, rectal pain, and tenesmus.[29] After receiving punctate midline myelotomy—cordotomy of the dorsomedial spinal column visceral pain pathway[30]—pain response allowing for opioid reduction varied from transient to 11 months in duration. The only adverse effect was transient urinary retention in one patient.

Conclusions

This systematic review highlights the challenges associated with management of MRP and tenesmus and the limited evidence available to guide treatment decisions. Twenty articles describing 40 patients identified interventions ranging from medications to targeted neurolytic procedures. Although no particular strategy has sufficient evidence to support widespread use, it is useful to consider the reported interventions in the context of their mechanism of action and pathophysiology of MRP and tenesmus. The most commonly reported interventions (18/40 patients) comprised sympathetic neurolytic procedures targeting various levels of the sympathetic nerve supply of the pelvis. These procedures are thought to block the visceral afferents transmitting localized pain and interrupt the sympathetic afferents perpetuating complex sympathetic maintained pain. Vasodilators were the most commonly reported medical intervention (eight patients). Calcium channel blockers (e.g., nifedipine and diltiazem) reduce smooth muscle contraction in the gastrointestinal tract.[31] Phentolamine, an α-adrenergic antagonist, also relaxes smooth muscle and mimics the effect of sympathetic neurolysis in interrupting sympathetic maintained pain.[32] Interestingly, only two patients were successfully palliated with opioids alone. At least 34 patients had symptoms refractory to opioids and at least 25 had no relief with common adjuvants including antidepressants and antiepileptics. These findings would suggest that the standard WHO analgesic ladder alone may not be sufficient for management of MRP and tenesmus.[6]

A major limitation of our search strategy was the inability to identify patients with MRP and tenesmus who were enrolled in studies exploring the impact of an intervention on cancer pain. For example, several high-quality studies were excluded for pooling patients into nonspecific pain syndromes such as "pelvic pain." All studies in this review are case reports or case series at high risk for bias. Some reports have very limited descriptions of the clinical setting, pain etiology and character, and patient demographics. Most do not describe the methodology used to select cases for presentation and were assumed to be retrospective and nonconsecutive in nature, allowing for selection bias. This review highlights the paucity of readily accessible high-quality literature to guide clinicians in the management of MRP and tenesmus.

The complex pathophysiology of MRP and tenesmus combined with the findings of our review may suggest that standard approaches for managing cancer pain alone are insufficient.[6] A combination of interventions that target smooth muscle and autonomic pathways in addition to opioids may be the most logical approach while considering the patient's extent of disease and goals of care.

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