Original Article

Neurolytic Sympathectomy in the Management of Cancer Pain—Time Effect: A Prospective, Randomized Multicenter Study

Yasser M. Amr, MD, and Mohamed Y. Makharita, MD

Departments of Anesthesiology and Surgical Intensive Care (Y.M.A.), Faculty of Medicine, Tanta University, Tanta; and Departments of Anesthesiology and Surgical Intensive Care (M.Y.M.), Faculty of Medicine, Mansoura University, Mansoura City, Egypt

Abstract

Context. Sympathectomy is currently used as the fourth step of the modified World Health Organization (WHO) analgesic ladder. Sympathectomy can be performed early, before the second step on the ladder.

Objectives. We hypothesized that early sympathectomy would reduce pain and opioid consumption and improve quality of life.

Methods. One hundred nine patients, with inoperable abdominal or pelvic cancer, reporting visceral pain of 40—70 on a visual analogue scale and taking nonopioid analgesics were allocated randomly into two groups: either blocks were performed before Step 2 of the WHO ladder, then analgesics were managed according to the ladder (Group I) or analgesics were given according to the WHO ladder, and blocks were performed as the fourth step after failure of strong opioids to control pain (Group II). Visual analogue scale scores, responder analysis, daily opioid consumption, related side effects, and quality of life were assessed.

Results. Responders were significantly higher in Group I ($P < 0.0001$), and partial responders and nonresponders significantly increased in Group II ($P < 0.0001$ and 0.006, respectively). Opioid consumption significantly decreased in Group I ($P < 0.0001$ during first 12 months and 0.007 at the last assessment time), with concomitant significant reduction in related side effects. The number of patients who had a good analgesic response on tramadol significantly increased in Group I during the first five months ($P < 0.05$). European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 global quality-of-life subscale scores revealed significant improvement until the fifth month in Group I ($P < 0.05$).

Conclusion. Sympathectomy before Step 2 on the WHO analgesic ladder seems to lead to better pain control, less opioid consumption, and better quality of life in cancer patients. J Pain Symptom Manage 2014;48:944—956.

Address correspondence to: Yasser M. Amr, MD, Departments of Anesthesiology and Surgical Intensive Care, Tanta University Hospital, Tanta 31527, Egypt. E-mail: yasser.amr@gmail.com

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Key Words
Early sympathectomy, cancer pain, WHO analgesic ladder

Introduction

Pain associated with cancer affects quality of life and restricts patients' activity.[1] Pain control is the principal aim of management of patients with inoperable cancer. World Health Organization (WHO) guidelines recommend oral administration of drugs, starting, if the patient is not in severe pain, with nonopioid analgesics and adjuvant medications. Then, if complete pain relief is not achieved, a weak opioid such as tramadol is added to the existing nonopioid analgesics as the second step. If this is insufficient, the weak opioid is replaced by a stronger one, such as morphine, fentanyl, or hydromorphone as the third step on the analgesic ladder, while continuing the nonopioid medications, escalating the opioid dose until the patient is pain free or at the maximum pain relief with tolerable side effects.[2]

Sensory afferent fibers supplying abdominal and pelvic organs pass without relay in the sympathetic ganglia, thus justifying the role of destruction of the sympathetic chain at the ganglion level to treat chronic pain of different causes including cancer.[3,4] It is not the sympathectomy per se, that is, beneficial, but rather the neurolysis of the visceral afferent nerves that run with the sympathetic fibers. Tumors originating from upper abdominal viscera cause severe abdominal pain that may respond to celiac plexus or splanchnic nerve blocks.[5] Superior hypogastric plexus block has been used for the treatment of cancer-related pelvic pain.[6]

Neurolytic sympathetic block has been used as the fourth step on the WHO ladder. But nowadays, reserving it as a "last step" is a matter of debate.[7] This study investigates the degree of pain relief, opioid consumption, and quality of life provided by using sympathectomy before the second step on the WHO pain management ladder vs. its performance as the fourth step.

Methods

The study was conducted from June 2011 to July 2013 in the pain relief units of two university teaching hospitals and one oncology center after approval of the institutional ethics committee and written informed consent from the patients. The study was registered in the Pan African Clinical Trial Registry (identification number PACTR201311000619168).

Inclusion Criteria

Patients were included if 1) they were suffering from visceral pain originating from inoperable abdominal or pelvic cancer, 2) they reported a visual analogue scale (VAS) score from 40 to 70 after failure of nonopioid analgesics (first step of the WHO analgesic ladder), 3) the diagnosis was histologically and radiologically proven, and 4) their pain was localized to the upper abdomen or pelvic region and described by patients as deep not superficial.

Exclusion Criteria

Patients were excluded if they had 1) international normalized ratio (INR) >1.5 or platelet count <50,000, 2) infection at the site of needle entry, 3) persistent hypotension, 4) ascites, 5) received a previous neurolytic block, or 6) had a psychiatric illness.

One hundred nine patients were randomly allocated into two groups (Fig. 1): In Group I, celiac, splanchnic, or superior hypogastric blocks were performed before the second step on the WHO ladder after nonopioid medications failed to relieve their pain; analgesic requirements subsequently were managed according to the severity of pain and the WHO analgesic ladder. In Group II, analgesics were given according to the WHO analgesic ladder, and blocks were performed as the fourth step on the ladder after failure of pain control with high doses of strong opioids such as morphine sulfate and hydromorphone tablets or transdermal fentanyl patches; analgesic requirements subsequently were managed according to the severity of pain.

WHO guidelines include nonopioid analgesics as the first step (nonsteroidal anti-inflammatory drugs plus adjuvant medications). Tramal® 50 mg and tramadol 100 mg sustained