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Tapentadol IR Versus Oxycodone IR Show Gastrointestinal and Central Nervous System Tolerability Compared With Oxycodone

Mohammed Shawagfeh[1]*, Rakan Al-Lwzi[2], Ahmed Al-Zobi[3], Mohammed Kderatmd[4], Thani Al-Awamreh[5], Mohmud Al-Zobi Farm[6]

*Consultant[1], Department of Anesthesia[1], Department of Neurosurgery[2], Department of Orthopaedics[3], Internal medicine and ICY[4], Department of Anesthesia[5], Department of Clinical Pharmacology[6], Royal Medical Services, Jordan.

Abstract

Objectives of the study is to compare the tolerability of exposure to tapentadol IR and oxycodone IR in patients with low back pain or pain from osteoarthritis of the knee or hip, cancer pain. This is a randomized, double-blind, controlled study of 100 patients with low back pain or pain from osteoarthritis of the knee or hip, cancer pain, were treated with a flexible dose of tapentadol IR, or a flexible dose oxycodone IR, during a period of 6 months at Hospital Virgen de las Nieves Pain Unit and Palliative Care (Department Of Anesthesia) Granada, Spain. The percentage of patients with treatment-emergent adverse events in the tapentadol IR group was lower than in the oxycodone IR. While the incidence of gastrointestinal symptoms were significantly lower in the tapentadol IR treated groups compared to the Oxycodone IR groups, the incidences of central nervous symptoms were not significantly different between the treatment groups. Tapentadol IR was safe and effective for the relief of pain, and its significantly improved gastrointestinal tolerability profile in comparison to Oxycodone IR.

Key words: Tapentadol IR, Oxycodone IR, tolerability.

*Corresponding Author: Dr. Mohammed Shawagfeh, MD, Pain Unit and Palliative Care, Department Of Anesthesia, KHMC, Jordan. Email: MdShawagfeh@yahoo.com

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Introduction

Appropriate management of acute pain remains a considerable challenge for health care providers, while insufficient management of acute pain may lead to poor patient outcomes and potentially life-threatening complications [1]. Opioids provide relief of moderate to severe acute pain; however, therapy with pure μ-opioid agonists is often limited by the prevalence of bothersome side effects. These can include nausea and vomiting with short-term use, and constipation with longer, chronic use [2]. Such symptoms can lead patients to discontinue treatment, adding additional complications to pain management for physicians [3].

The novel investigational medication tapentadol, a centrally acting oral analgesic with 2 mechanisms of action, μ-opioid receptor agonism and norepinephrine reuptake inhibition, provided pain relief for patients with fewer gastrointestinal and CNS side effects than those treated with an opioids prescription pain reliever [4]. Previous trials in patients with various types of moderate to severe acute pain have shown that tapentadol immediate release (IR) provides analgesia comparable to that provided by the pure μ-opioid agonist comparator, oxycodone IR, with a lower incidence of nausea, vomiting, and constipation. Findings suggest tapentadol may represent an improved treatment option for acute pain [5].

Here we present a series of 100 patients with low back pain or pain from osteoarthritis of the knee or hip, cancer pain, in patients attending this hospital in the Granada Spain, randomly received a flexible

dose of tapentadol IR, or a flexible dose of oxycodone IR.

Methods

This is a randomized, double-blind, controlled study which was achieved for six months of a trial of 100 patients with low back pain or pain from osteoarthritis of the knee or hip, cancer pain. The study was conducted between the 1st of July 2011 and the end of Janeuary 2012 at Hospital Virgen de las Nieves of Pain Unit and Palliative Care (Department Of Anesthesia) Granada. Spain.

Patients were randomly assigned to a flexible dose of 50 mg or 100 mg of tapentadol IR every four to six hours, up to a maximum of 600 mg/day, or a flexible dose of 10 mg or 15 mg of oxycodone IR every four to six hours, up to a maximum of 90 mg/day; patients were treated for up to 60 days. Treatment-emergent adverse events and study discontinuations were recorded.

The impact of these equianalgesic doses of tapentadol and oxycodone on gastrointestinal and central nervous system tolerability was then directly assessed in the current study, using a validated bowel function diary to comprehensively assess opioid-induced constipation symptoms and outcomes.

Results

While both tapentadol IR and oxycodone IR offered pain relief, the tapentadol IR treatment group experienced a statistically significantly lower incidence of nausea, vomiting, constipation and composite nausea/vomiting ($P<0.001$) for all treatment comparisons. Overall, the percentage of patients with treatment-emergent adverse events in the tapentadol IR group was lower than in the oxycodone IR.

The most common treatment emergent adverse events for both groups were nausea, vomiting, dizziness, constipation, headache, and somnolence (drowsiness). While the incidence of nausea, vomiting, constipation and the composite nausea and vomiting were significantly lower in the tapentadol IR treated groups compared to the oxycodone IR groups, the incidences of dizziness and somnolence (drowsiness) were not significantly different between the treatment groups as shown in table 1.

Adverse Event	Tapentadol Extended Release (%)	Oxycodone Controlled Release (%)
Gastrointestinal	**52.0**	**64.1**
- Constipation	15.8	33.5
- Nausea	21.2	36.5
- Vomiting	8.5	22.1
Nervous system	**45.4**	**39.9**
- Somnolence	11.8	17.2
- Dizziness	16.4	21.2
- Headache	0.6	2.1

Table 1: Treatment-Emergent Adverse Events of Patients

Both treatment groups indicated a comparable analgesic effect at the specified doses. The incidences of nausea, vomiting, constipation and the composite of nausea and/or vomiting in the tapentadol IR group were significantly lower than oxycodone.

Discussion

The under treatment of acute pain is common in many health care settings. The psychologic and physiologic effects of uncontrolled acute pain can result in longer hospital stays and unscheduled readmissions following surgery [6]. In addition, prolonged acute pain can cause sensitization of the central and peripheral nervous systems, leading to the development of chronic pain, which is often difficult and costly to treat [7].

Current treatment options for the management of acute pain include opioid analgesics (Eg: morphine, hydromorphone, and oxycodone) and nonopioid analgesics (Eg: acetaminophen, acetylsalicylic acid, and nonsteroidal anti-inflammatory drugs) [8]. Opioids are typically used for the management of moderate to severe acute pain,

but opioid use is limited by the occurrence of a range of side effects [9].

Tapentadol is a next generation centrally-acting analgesic, synthetic, oral mu-opioid receptor agonist which also inhibits norepinephrine and serotonin reuptake within the CNS. It is structurally and pharmacologically similar to tramadol, which is currently being developed for the relief of moderate to severe pain. It demonstrates an efficacy comparable to classical strong opioids, like oxycodone or morphine, and an improved tolerability profile, especially in regard to gastro-intestinal side effects like nausea, vomiting, and constipation [10]. Tapentadol is being developed as immediate-release formulation for acute pain and prolonged-release formulation for chronic pain; once approved, it will be used in hospital and outpatient settings [11].

The use of strong analgesics such as opioids chronic pain conditions is expanding. However, a substantial number of patients receiving pain therapy do not feel satisfied with their treatment and stop their opioid therapy against medical recommendation. The most important reasons for this are gastrointestinal (GI) side effects like nausea and vomiting in the first few days and constipation in the course of ongoing treatment; GI tolerability is one of the leading causes of treatment discontinuation for patients who take prescription pain medications [12].

Our study has revealed that compared to commonly employed narcotics, tapentadol appear to produce a lower incidence of nausea, vomiting, and constipation when compared to what would be considered high (oxycodone). Tapentadol IR may offer an advance over standard controlled-release opioid preparations in that it offered improved gastrointestinal tolerability and CNS, less nausea and vomiting, and less constipation. These findings validate and extend the tolerability findings of the two earlier studies that established comparable efficacy of these tapentadol and oxycodone doses [13, 14].

Thus, tapentadol IR is an effective treatment option for the management of moderate to severe acute pain. However, further studies evaluating its clinical utility in relation to that of tramadol and opioids other than oxycodone are warranted. Because tapentadol IR offers the prospect of reduced opioid-related gastrointestinal adverse events while maintaining adequate analgesia, it is a potentially valuable addition to the analgesic armamentarium [15].

Our data is too small to draw any conclusions on the tolerability of exposure to tapentadol IR and oxycodone IR in patients with low back pain or pain from osteoarthritis of the knee or hip, but majority of the authors agree that tapentadol IR may offer an advance over standard controlled-release opioid preparations in that it offered improved gastrointestinal tolerability and CNS [16, 17].

Conclusion

Tapentadol IR has been shown to offer comparable analgesia to that provided by oxycodone IR, with lower incidences of gastrointestinal adverse effects and CNS symptoms and lower rates of discontinuation due to adverse effects.

Conflict of interest: None declared

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