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Pharmacodynamic Characteristics and Influencing Factors of Tapentadol for Chronic Pain Relief Under Dose Titration

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ADMINISTRATIVE INFORMATION

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Conflicts of interest - The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 May 2024 and was last updated on 04 May 2024.

INTRODUCTION

Review question / Objective The aim of this study was to establish a pharmacodynamic model of tapentadol analgesia under dose titration conditions, to quantitatively analyze the time-effect relationship of the drug, and to identify relevant influencing factors. This model is intended to provide a pharmacodynamic reference for designing rational tapentadol dose titration schemes in clinical research.

Condition being studied Chronic pain, characterized by prolonged pain persisting beyond the typical healing period or for over three to six months, impacts approximately 20% to 30% of adults worldwide. Symptoms are varied and complex, encompassing persistent or intermittent pain—often described as shooting, burning, aching, or electrical—along with associated fatigue, sleep disturbances, reduced appetite, and mood changes such as depression and anxiety. The condition poses a considerable socio-economic challenge, affecting individual quality of life and leading to significant societal costs due to healthcare expenditures and lost productivity. For instance, in the United States, the estimated annual cost of chronic pain ranges from $560 billion to $635 billion.

METHODS

Search strategy ((((tapentadol[MeSH Terms]) OR (nucynta[MeSH Terms])) AND (((ache[MeSH Terms]) OR (suffering[MeSH Terms])) OR (pain[MeSH Terms])))) AND (clinical trial[Filter])) AND (("1900/01/01"[Date - Publication] : "2023/09/30"[Date - Publication])).

Participant or population Inclusion criteria: 1.subjects experiencing various types of chronic pain and diagnosed as functional capacity levels I-III, 2.participants aged 18 years or older; exclusion criteria: 1. subjects without a washout period before enrollment, 2. subjects with cancer pain, 3. subjects with concurrent psychiatric disorders.

Intervention Studies where tapentadol monotherapy was used as the treatment.

Comparator Not applicable.

Study designs to be included Inclusion criteria: 1. Randomized controlled clinical trials (RCTs); exclusion criteria: 1. Studies involving subjects without a washout period before enrollment; 2. Studies using a randomized withdrawal design, 3. Crossover study designs that did not report data from the first cycle.

Eligibility criteria Inclusion criteria: Studies that reported NRS scores at specific time points for chronic pain; exclusion criteria:. Studies where chronic pain was not accompanied by reported NRS baseline values.

Information sources The search was performed in the publicly accessible databases of PubMed and EMBASE.

Main outcome(s) The rate of change in Numerical Rating Scale (NRS) from baseline increased.

Quality assessment / Risk of bias analysis The risk of bias (RoB) for each included randomized controlled trial (RCT) was independently examined by two researchers utilizing the Cochrane RoB2 tool. This tool, specifically the RoB2_IRPG_beta_v9.xlsm, was employed to assess potential bias in five key areas: the randomization process, deviation from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. The RoB for each category was designated as "low" if there was a low risk of bias, "high" if there was a high risk of bias, or "unclear" if there was insufficient information or uncertainty about potential bias. In the event of discrepancies in the RoB2 assessments between the two primary researchers, a third researcher was consulted to review the assessments and make the final decision.

Strategy of data synthesis A time-effect relationship model of the percent change in Numerical Rating Scale (NRS) scores post-tapentadol intervention from baseline was constructed, along with a covariate model to identify factors significantly impacting the analgesic effects of tapentadol.

Subgroup analysis Potential influencing factors that were clinically significant but not included in the final covariate model were examined for their impact trends on tapentadol analgesia through subgroup analysis.

Sensitivity analysis Not applicable.

Country(ies) involved China.

Keywords Chronic Pain, Opioids, Tapentadol, Model-based Meta-analysis, Pharmacodynamic.

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