

Case Report

Addition of Modified Jadad Method to Evaluate the Rationality of Over-explanatory Drug Use: Taking Naloxone as an Example

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Abstract: Objective to evaluate the rationality of naloxone injection superdrug specification by evidence-based medicine and adding modified Jadad scale, and to establish the evaluation standard of rational drug use. Methods 540 medical records of naloxone used in 2019 were extracted, and the use of naloxone was analyzed. At the same time, the evidence-based medical evidence used in naloxone superscript was collected and the literature was graded by improved Jadad scale. ≥ 4 points were used as high quality literature. Combined with evidence-based medicine and improved Jadad scale, 540 medical records with naloxone were reviewed. Results In evidence-based medical evidence collection, the guidelines for clinical treatment of craniocerebral trauma clearly put forward that naloxone injection in craniocerebral injury has a clear indication, but also given a clear dosage and course of treatment. By using the modified Jadad scale to screen and score the literature after 2013, it is determined that the coma caused by cerebral infarction is also a reasonable indication of overstatement. Combined with evidence-based medicine and improved Jadad scale method, 87.3% of the indications for the use of naloxone injection in our hospital were within the range of rational use, and the evaluation standard of rational use of naloxone was established. Conclusion: It is a new attempt to provide evidence-based basis for over-explanatory drug use through evidence-based medicine and improved Jadad scale method.

Keywords: Evidence-based Medicine, Modified Jadad Scale Method, Naloxone Injection, Superscript, Rational Application

1. Introduction

As one of the non-specific antagonists of opioid receptors, naloxone was first synthesized by Feshman in 1960 and used in the rescue of opioid and other anesthetic analgesics poisoning in 1971. The clear indications of the drug instructions are for the use of opioid compound anesthesia after surgery, antagonizing respiratory depression caused by such drugs to awaken patients, for opioid overdose, complete or partial reversal of opioid induced respiratory depression, rescue of acute ethanol poisoning and for the diagnosis of acute opioid overdose. According to the Prescription Administration [1] and the Standard of Management of Hospital Prescription Evaluation (Trial Implementation)" [2] The monthly evaluation of outpatient prescriptions and inpatient orders has become the routine work of hospitals, but

it is found that the indications and usage of naloxone are higher than the drug instructions. In 2015, our country issued the Consensus on Super-Outtal Drug Use, which has the function of industry standard in the absence of laws, regulations and administrative regulations, but its clinical application value is limited because it does not evaluate the specific drug use of super-Outtal Drug [3] and the 2015 edition of Evidence-based Evaluation of the Use of Drug Overtapping Instructions [4] Nor was evidence-based evaluation of the use of naloxone superscript. Evidence-based medicine can provide a reliable basis for clinical treatment practice by collecting all clinical research results corresponding to each clinical specialty and branch of specialty worldwide, conducting statistical analysis and systematic evaluation, and continuously collecting new results to update these evaluations. Its research methods include

rigorous evaluation, systematic review and Meta analysis, evidence-based clinical practice guidelines and evidence-based clinical pathways, which are usually the basis for evaluating the use of over-the-counter drugs, but some evidence is reliable and can be used, such as controlled, but not randomized, It can also be used as a reasonable super instruction. For this reason, the purpose of this paper is to explore the use of evidence-based medical evidence and the addition of improved Jadad scale method to establish the rational drug use evaluation standard of naloxone superdrug specification. This evaluation standard can provide a reference for the evaluation of drug use in the evaluation of doctor's orders, and can standardize the hospital over instructions drug management.

2. Information and Methodology

2.1. Clinical Application of Naloxone

The present situation of clinical drug use of naloxone through the hospital information system based on the special doctor's order evaluation template, collected from January to December 2019 all involved in the use of naloxone medical records a total of 540, clinical diagnosis, drug use, adverse reactions and other information were summarized and analyzed.

2.2. Retrieval and Collection of Drug Evidence Drug Use in Over-Oriented Instructions

2.2.1. Domestic and Foreign Authoritative Medicine Monograph Collection and Application

The over-the-counter drug use in authoritative medical monographs at home and abroad is reviewed with the key words of Luo Luoxone, such as "Surgery ", " Chinese Medical Pharmacists' Clinical Drug Guide ", " Martindale Drug Code" and so on, and the over-the-counter drugs collected in neurosurgery are collected.

2.2.2. Database Retrieval

The key words of database retrieval are "naloxone or

chlolen" and "brain ", Search of China Knowledge Network Database, Wanfang Database, PubMed 、 and Cochrane Library, All databases were retrieved from 2014 to August 2020, Evaluation of literature quality through improved Jadad scales, According to the improved Jadad scale, Prevent evaluation bias, Scoring criteria include random sequence generation, randomization hiding, blind method and withdrawal and withdrawal, 1-3 documents considered low quality, 4-7 classified as high-quality literature, The modified Jadad scale score ≥ 4 as screening criteria [5].

2.3. Adverse Reactions

The adverse reactions were retrieved from the information system doctor's order and literature. The key words were "naloxone ", " adverse reaction ", " side effect ", " cause" and "cause ". All databases were searched from 2014 to August 2020.

3. Fruit

3.1. Clinical Application of Naloxone

Clinical status of naloxone used in 540 inpatients from January to December 2019, Most of them are in neurosurgery and intensive medicine, the proportion was 40.6% and 36.7% respectively. Indications, Only the Department of Digestive Medicine, The rest of the departments exceeded the indications of the drug instructions, Most of them are coma patients with craniocerebral injury or consciousness disorder. In terms of usage, every department is different, the doses range from 2 mg to 20 mg, Concentration up to 0.32 mg/ml, Far beyond the concentration recommended in the drug specification (mg/ml 0.004), The frequency of administration is also more than 3 times a day. The route of administration, only intensive medicine, respiratory and critical medicine, geriatrics and endocrinology are continuously pumped, other departments were intravenous drip. And the course of treatment, the longest is neurosurgery, For 40 days, Average 13 days.

Table 1. Summary of inpatients' use of naloxone from January to December 2019.

| Departments | Number of cases/examples (%) | Clinical diagnosis or presentation | Usage | Route of administration | Average course of treatment (days) |
|--|------------------------------|--|---|-------------------------|------------------------------------|
| Neurosurgery | 219 (40.6) | Brain injury, concussion | 4mg q8h+0.9% sodium chloride injection 100 ml | Intravenous drip | 13 |
| Department of Intensive Medicine | 198 (36.7) | Brain injury coma | 12-20 mg+0.9% sodium chloride injection 120 ml qd | Pump in | 2.4 |
| Department of Neurology | 54 (10) | Disorder of consciousness or cerebral infarction | 2-4 mg+5% glucose injection 250 ml | Intravenous drip | 3.5 |
| Department of Oncology | 28 (5.2) | Sleepiness | Two mg+5% glucose injection 250 ml | Intravenous drip | Temporary dose |
| Department of Respiratory and Critical Care Medicine | 13 (2.4) | Pulmonary encephalopathy coma | mg -16 mg+0.9% sodium chloride injection 50 ml qd | Pump in | 4.5 |
| Geriatric Respiratory Section | 11 (2) | Pulmonary encephalopathy coma | 8mg+0.9% sodium chloride injection 48 ml q12h | Pump in | 2.9 |

| Departments | Number of cases/examples (%) | Clinical diagnosis or presentation | Usage | Route of administration | Average course of treatment (days) |
|---------------------------------------|------------------------------|------------------------------------|--|-------------------------|------------------------------------|
| Endocrinology | 9 (1.7) | Metabolic encephalopathy | 4 mg+0.9% sodium chloride injection 48 ml q12h | Pump in | 3.1 |
| Department of Rehabilitation Medicine | 5 (0.9) | Cerebral hemorrhage lethargy | 4mg q8h+0.9% sodium chloride injection 100 ml | Intravenous drip | 6 |
| Department of Digestive Medicine | 3 (0.5) | Alcoholism | mg+5% glucose injection 500 ml | Intravenous drip | Temporary dose |

Note: according to the modified Jadad scale method, indications: neurosurgery, intensive medicine and neurology are reasonable instructions; usage: only digestive medicine is reasonable, the other departments are unreasonable instructions.

3.2. Evidence-based Medical Outcomes

3.2.1. Fingerpost

Domestic and foreign authoritative medical monographs on the use of naloxone injection over instructions to consult domestic and foreign neurosurgery monographs, guidelines or consensus, found "craniocerebral trauma clinical treatment guidelines" (4th edition) [6] Update time is relatively new, reprinted in 2015, compared with the previous version, more attention to system evaluation. Therefore, in the Guide to Clinical Treatment of Brain Trauma, 4th Edition summarized the relevant literature of naloxone in the treatment of acute medium and severe craniocerebral injury before 2013. Through the method of systematic evaluation, the efficacy index was analyzed to objectively evaluate the effectiveness and safety of naloxone in the early application of medium and severe craniocerebral injury. The deadline for searching the literature is December 2013. The final guidelines draw clear conclusions: early use of opioid receptor antagonists (naloxone) in patients with craniocerebral trauma can

significantly reduce intracranial pressure, reduce brain edema, shorten coma time, reduce mortality and disability rate; indications: acute medium and severe craniocerebral trauma patients, severe craniocerebral trauma long-term coma patients, traumatic shock, severe trauma respiratory dysfunction patients, other causes of coma, such as narcotic drugs, drugs, ethanol. The recommended dosage is: early intravenous drip 0.3 mg/kg, diluted to 500 with normal saline or balance solution ml continuous infusion of infusion pump 24 h, after 3 days, changed to 4.8 mg/d, after 7 d of withdrawal.

3.2.2. Database Retrieval Results

Database retrieval was 225 articles, all of which were Chinese literature. The improved Jadad scale score ≥ 4 points were used as the screening criteria, and 5 articles were selected as the reference basis for the use of the superscript, as shown in Table 2. The indications of naloxone injection in our hospital were intracranial injury and cerebral infarction (87.3%) in the indications listed in the high quality literature.

Table 2. High-quality literature on the use of naloxone injection.

| Incorporation of studies | Clinical Research | Usage and course of treatment | Evaluation of the improved Jadad scale methodology | | | | Jadad scale score (score) |
|--------------------------|------------------------------|---|--|---------------|---------------|---------------------------|---------------------------|
| | | | Production of random sequences | Random hiding | Blind methods | Withdrawal and withdrawal | |
| Huang Quanqing 2018 [7] | Cerebral infarction | 2~4 mg/ times, 1/d, intravenous drip for 20 days | 2 | 1 | 1 | 0 | 4 |
| Gao Lichen 2017 [8] | Cerebral infarction | 2 mg+0.9% sodium chloride 500 ml ivgtt qd, 1 weeks | 2 | 2 | 0 | 0 | 4 |
| Xu Chao 2016 [9] | Severe craniocerebral injury | 0.4 mg/kg/d pumped for 14 days | 2 | 2 | 0 | 0 | 4 |
| Li Xin 2016 [10] | Cerebral infarction | Two mg +0.9% sodium chloride injection 250 ml ivgtt qd, for 2 weeks | 2 | 2 | 0 | 0 | 4 |
| Qian Jun 2014 [11] | Cerebral infarction dementia | 0.8 mg+0.9% sodium chloride injection for 200 ml ivgtt qd/, 10 days | 2 | 2 | 0 | 0 | 4 |

3.3. Adverse Reactions

No adverse reactions caused by naloxone injection were found in 540 medical records, and no adverse reaction reports were received by the pharmacy department. And literature retrieval, Literature search results were published by June 2010 [12] Literature analysis of 27 adverse reactions of naloxone, Referring to 74 per cent of those over 30 years of

age who had adverse reactions, 92.6 per cent were administered intravenously and intravenously, The main adverse reactions were cardiovascular reactions, such as arrhythmia, hypertension, Two deaths from cardiac arrest and one from myocardial infarction, Because the maximum dose of 3.2 mg and rapid drip. There were only two documents since June 2010 [13, 14]. The adverse reactions caused by naloxone were facial edema and pulmonary edema.

3.4. Evaluation Standard for Rational Use of Naloxone Injection

The clear indications in the drug instructions are that after opioid compound anesthesia, antagonism of respiratory depression caused by such drugs causes patients to wake up, is used for opioid overdose, completely or partially reverses opioid-induced respiratory depression, rescues acute ethanol poisoning and is used for the diagnosis of acute opioid overdose. and retrieved through evidence-based medical evidenceGuidelines for Clinical Treatment of craniocerebral trauma, issued by academic institutions, are confirmed by systematic evaluation, Meta analysis and multi-center large sample randomized controlled trials. The evidence level is in the expert consensus on the use of drugs in the superscript. The evidence is highly reliable and can be recommended for the use of superscript drugs, andA modified Jadad scale method establishes the following evaluation criteria: indications: availableAcute medium and severe craniocerebral trauma patients, severe craniocerebral trauma patients with long-term coma, cerebral infarction caused by coma and other causes of coma, such as narcotic drugs, drugs, ethanol and so on. The recommended dosage is: early intravenous drip 0.3 mg/kg, diluted to 500 with normal saline or balance solution ml continuous infusion with infusion pump 24 h, after 3 days, changed to 4 mg/d, long-term use not more than 14 days.

4. Discussion

There are many reasons leading to irrational use of drugs in our country. To change this situation, we need all aspects of cooperation, and through appropriate ways and methods to achieve," prescription review "has been proved to be one of the effective methods [15] In general, drug instructions and guidelines or authoritative consensus have been used as a basis for the development of evaluation criteria, but the reality of clinical over-the-counter drug use is very large, and the use of naloxone injection over-the-counter drugs has accounted for 99% of all cases of naloxone use in our hospital in 2019.5%, this is very confusing to prescription reviews, which are difficult to find out from the consensus of the guidelines, which may be that the revision of the drug instructions often lags behind the clinical practice, on the other hand, the consensus of the guidelines may not be updated in time. Prohibition or laissez-faire of all hyperdrug instructions may cause serious drug safety problems and lose the clinical significance of prescription reviews. Prescription reviews based on evidence-based medicine and improved Jadad scale is a good solution.

Evidence-based medicine (EBM) has become a new model for evaluating the efficacy of drugs because it should follow sufficient scientific basis and be regarded as an irreplaceable and reliable method for clinical practice and decision-making [16] However, some clinical case studies with controls but not validated by randomized studies can also be considered as rational over-the-counter use of drugs, while the improved Jadad scale method is used to screen high-quality literature. It

is an evaluation method to determine the rationality of over-the-counter use according to the actual effect [17]. The improved Jadad scale is the basis for the rapid evaluation of literature quality. The quality of literature is evaluated by four aspects: random sequence generation, randomization hiding, blind method, withdrawal and withdrawal. If the score ≥ 4 , it is considered to be high quality literature. According to the analysis of 540 doctor's orders, 87.3% of the indications of Naloxone injection were found in evidence-based medicine and high quality literature diseases. Therefore, acute medium and severe craniocerebral injury and coma caused by cerebral infarction were used as reasonable indications. After acute craniocerebral injury, the contents of β endorphins and dynorphins in cerebrospinal fluid increased significantly, and the degree of elevation was positively related to the severity and disturbance of consciousness. Naloxone could effectively antagonize the pathological process of secondary brain damage caused by endogenous substances such as endorphins and dynorphins [5] However, mild craniocerebral injury such as concussion was not included. This part of the patients may have a brief coma before admission, but the consciousness is clear at admission. In terms of usage, the analysis of doctor's orders in our hospital is not consistent with evidence-based medicine and the high quality literature selected, especially the preparation concentration is very high, which is partly achievedmg/ml, 0.32 High doses and rapid infusions are prone to adverse reactions in use, in which cardiovascular reactions (hypertension, arrhythmia) are more common; in a single dose, because the drug instructions state that there is an overdose test, 24 mg/70kg of drugs are treated without toxicity [18] and Hong K Kim [19] It was also mentioned that naloxone was an intrinsically safe drug, Can be used in large doses. Therefore, in establishing the evaluation criteria for rational use of naloxone injection in our hospital, Still referring to the instructions and guidelines, Requirement: 0.3 mg/kg, for early intravenous drip Dilute to 500 with saline or balance solution ml Continuous infusion with infusion pump 24 h, For three days, For mg/d. 4 And for the course of treatment, Evidence-based medicine and screening of high-quality literature with our hospital's doctor's order analysis is also poor, The guidelines for clinical treatment of craniocerebral trauma clearly suggest that after 10 days, Innaloxone is metabolized in the liver, Slower excretion, 60-70% in 72 hours, For a long time, There may be varying degrees of liver and kidney damage, And most of the patients involved in such diseases are elderly, Combined with the actual situation of our hospital, Comprehensive consideration of the course of treatment should not be more than 14 days.

5. Conclusion

To sum up, through evidence-based medical evidence and improved Jadad scale method, the use of naloxone injection in our hospital is basically reasonable in indication, the rationality of usage dosage is poor, especially the high concentration of preparation, which can increase the evaluation of usage dosage. In view of the fact that the clinical

scope and dosage of naloxone injection are both superdrug instructions, they should be reported to the hospital drug management committee and the ethics committee for approval. While preparing the patient's informed consent, we should strengthen monitoring, follow up and comment in time, and further evaluate its curative effect, adverse reaction and economy.

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