


Rapid Health Evaluation of Analgesia with Long-Acting Local Anesthesia After Hip and Knee Arthroplasty

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Purpose: To evaluate the local anesthetic drugs commonly used after hip arthroplasty and knee arthroplasty, and to provide a reference for clinical drug use and drug selection in medical institutions.

Methods: Based on the “Quick Guide for Drug Evaluation and Selection in Chinese Medical Institutions (Second Edition)”, the included drugs were evaluated from five dimensions of pharmaceutical properties, effectiveness, safety, economy, and other attributes using a 100-point scoring method.

Results: The quantitative scoring results were ranked from high to low as Dishili-Ropivacaine injection (75 points), Naropin-Ropivacaine injection (68.97 points), liposomal bupivacaine (65.06 points), bupivacaine injection (61.05 points), and levobupivacaine injection (60.35 points).

Conclusion: The Dishili-Ropivacaine injection of the collectible variety is a strongly recommended variety, which is recommended to be introduced or retained in the drug catalog of medical institutions, and the Naropin-Ropivacaine injection and liposomal bupivacaine can be adjusted according to the actual situation and clinical needs of medical institutions.

Keywords: local anesthetic drugs, local anesthetics, drug selection, rapid health evaluation, postoperative analgesic

Introduction

Hip arthroplasty and knee arthroplasty are both surgeries that treat serious joint diseases and can effectively relieve pain and restore joint function. Pain management after joint replacement is very important for the recovery of patients. Currently, multimodal analgesia, which combines different analgesics and collaborates with each other to reduce pain and adverse reactions, is considered as the ideal program for postoperative pain. Multimodal analgesia has also been widely used in the clinical practice of postoperative analgesia in patients with hip arthroplasty and knee arthroplasty.¹ Local anesthesia drugs (hereinafter referred to as local anesthetics) ropivacaine injection, bupivacaine injection, and levobupivacaine injection are commonly used drugs for multi-mode analgesia.^{2,3} In recent years, liposomal bupivacaine, a new drug that prolongs the action duration of local anesthetics by changing the dosage form, has also become a new choice for local anesthetics in multi-mode analgesia.^{1,3} However, it is not clear whether there are differences in pharmaceutical properties, effectiveness, and safety among different local anesthetics. A unified standard drug evaluation and selection system is needed to scientifically evaluate the clinical value of local anesthetics.

Rapid Health Evaluation is an emerging methodology that allows for the rapid integration of existing evidence and is characterized by its rapidity, comprehensiveness, science, objectivity, and impartiality. Decision makers can use rapid health evaluation to objectively select and evaluate medicines entering and leaving healthcare facilities according to the actual needs of healthcare facilities.

The Quick Guide for Drug Evaluation and Selection in Chinese Medical Institutions (Second Edition)⁴ (hereinafter referred to as the “Selection Guide”) has revised and refined the evaluation indicators on the basis of the first edition, so

that the quantitative score can better conform to national policies and hospital operability. Based on the “Selection Guide”, this paper will evaluate the included local anesthetics from five dimensions of pharmaceutical characteristics, effectiveness, safety, economy, and other attributes, to provide references for drug selection and clinical medication program decision-making in medical institutions.

Materials and Methods

Scoring Method

According to the “Selection Guidelines”, the clinical comprehensive score of commonly used local anesthesia drugs after the joint replacement was conducted from five quantitative indicators of pharmaceutical properties, effectiveness, safety, economy, and other attributes.

The evaluation information was obtained from authoritative databases such as manual, CNKI, Wanfang, Chinese Medical Journal full-text Database, PubMed, National Essential Drugs Catalogue, national medical insurance information database, websites of drug regulatory departments in various countries, Guangzhou Drug Procurement Platform, and other official websites. Personalized adjustment was made according to the characteristics of evaluation drugs, and a 100-point scoring system was adopted.

The score was independently evaluated by two pharmacists. When the evaluation results of two pharmacists were significantly different (> 3 points), experts in related fields (the third person) were invited to discuss and determine. The final evaluation of 70~100 points, 60~70 points, and < 60 points three levels (① There are three recommendations for the introduction of new varieties. More than 70 points is a strong recommendation; 60 ~ 70 points, depending on whether there are alternative treatment drugs in the clinic, it is recommended to be weakly recommended or not recommended; Recommendations below 60 points are not recommended.②When it comes to drug dispensing, there are three recommended recommendations. Below 60 points, it is recommended to transfer; 60 ~ 70 points, depending on whether there are alternative therapeutic drugs in the clinic, it is recommended to temporarily retain or transfer; More than 70 points, it is recommended to retain), to provide a basis for the introduction or transfer of new varieties in medical institutions.

Evaluated Drugs

The drugs evaluated in this study are commonly used local anesthetics after hip and knee arthroplasty, and the basic information is shown in Table 1.

Results

Pharmaceutical Properties

Pharmacological Effects

All the drugs included in the evaluation are amide local anesthetics, which can block the generation and conduction of nerve impulse by increasing the threshold of nerve electrical excitation, slowing down the transmission of nerve impulse,

Table 1 Local Anesthetic Drugs Included in the Evaluation

Drug Generic Name	Specifications	Manufacturer	Prices (CNY)*
Liposomal bupivacaine	20mL:266mg(1 bottle/box)	Jiangsu Hengrui Medicine Co.	382
Levobupivacaine injection	10mL:50mg(5 pcs/box)	Jiangsu Osaikang Pharmaceutical Co.	29
Bupivacaine injection	5mL:37.5mg(1 pcs/box)	Anhui Changjiang Pharmaceutical Co.	29.87
Ropivacaine injection (Dishili)	10mL:0.1g(5 pcs/box)	Guangdong Jiabo Pharmaceutical Co.	19.04
Ropivacaine injection (Naropin)	10mL:100mg(1 pcs/box)	AstraZeneca AB	33.32

Note: *Drug price information from Guangzhou Pharmaceutical Group Procurement Platform (as of September 15, 2024).

and reducing the rate of action potential increase to exert the dual effects of anesthesia and analgesia.⁵ Local anesthetics had a definite curative effect and a clear mechanism of action, so the scores were all 4 points.

In vivo Process

The score of the bupivacaine injection was 3 points due to incomplete pharmacokinetic parameters in the instructions, and the remaining pharmacokinetic parameters were complete, and the score of the in vivo process was 5 points.

Frequency of Administration

Liposomal bupivacaine and levobupivacaine injection can be administered once for analgesia after joint replacement with appropriate frequency due to their relatively long half-life, and the score is 2 points. Bupivacaine injection and ropivacaine injection had a short half-life and needed continuous administration, so the score was 1.

Storage Conditions

Liposomal bupivacaine was kept in closed condition at 2–8°C, and the score was 2 points. Levobupivacaine injection and bupivacaine injection should be kept under dark light and sealed, and the scores of storage conditions for both drugs were 3 points.

In summary, in the evaluation of pharmaceutical characteristics, liposomal bupivacaine scored 21.5 points, levobupivacaine injection scored 22.5 points, bupivacaine injection scored 19.5 points, and ropivacaine injection scored 22.5 points. The results of specific scoring rules are shown in [Table 2](#).

Table 2 Scores of Pharmaceutical Properties

Pharmacological Properties (28 Points)	Details (indicator Information and Data Sources)	Liposomal Bupivacaine	Levobupivacaine Injection	Bupivacaine Injection	Ropivacaine Injection - Naropin	Ropivacaine Injection - Dishili
Pharmacological effect (5 points)	5 Clinical efficacy obvious, action mechanism is clear, mechanism or target is innovative	4	4	4	4	4
	4 Clinical efficacy obvious, mechanism is clear					
	2 Clinical efficacy general, mechanism is unclear					
In vivo processes (5 points)	1 Clinical efficacy poor, mechanism is unclear	5	5	3	5	5
	5 In vivo process clear, pharmacokinetic parameters complete					
	3 In vivo process clear, pharmacokinetic parameters not complete					
	1 In vivo process not clear, pharmacokinetic					

(Continued)

Table 2 (Continued).

Pharmacological Properties (28 Points)	Details (indicator Information and Data Sources)	Liposomal Bupivacaine	Levobupivacaine Injection	Bupivacaine Injection	Ropivacaine Injection - Naropin	Ropivacaine Injection - Dishili
Pharmacy and the use of drugs (12 points)	2 Main ingredients and excipients (all clear 2, one item clear 1)	2	2	2	2	2
	2 Specification and Packaging (all applicable to clinical application/dose adjustment 2, one appropriate 1)	2	2	2	2	2
	2 Dosage form (oral/inhalation/topical preparations (2), subcutaneous/intramuscular injections (1.5), intravenous drip/injection (1))	1.5	1.5	1.5	1.5	1.5
	2 Dose of administered (fixed dosage (2), dosage adjustment required during use (1.5), dosage based on body mass or body surface area (1))	1	1	1	1	1
	2 Administration frequency (≤ 1 times.d-1 2; 2 times.d-1 1.5; ≥ 3 times.d-1 1)	2	2	1	1	1
	2 Convenient use (self-administered without assistance (2), self-administered without assistance, with help or training (1.5), administered by medical personnel (1))	1	1	1	1	1
	Storage conditions (4 points)	3 Room temperature storage 2 Storage in the shade 1 Refrigerated/frozen storage 1 No need for shading/sheltering	1 1	3	3	3
Expiration dates (2 points)	2 ≥ 60 months					
	1.5 ≥ 36 months, < 60 months					
	1 ≥ 24 months, < 36 months	1	1	1	1	1
	0.5 ≥ 12 months, < 24 months 0.5 < 12 months					
The results of the pharmacological properties		21.5	22.5	19.5	22.5	22.5

Efficacy Indications

Commonly used local anesthetics have dual effects of anesthesia and analgesia, large doses can produce surgical anesthesia, and small doses can produce sensory block (analgesia). The included evaluation of drug efficacy is accurate, evidence-based evidence is sufficient,⁶⁻¹⁹ and the indication score is 5 points.

Guideline Recommendation

At present, the Expert Consensus on Perioperative Pain Management for Accelerated Orthopedic Rehabilitation 2022 recommends that ropivacaine be the main formula for peri-incision infiltration analgesia “cocktail”, and ropivacaine and bupivacaine are commonly used for peripheral nerve block, and liposomal bupivacaine, which can prolong post-block analgesia time, is also recommended.²⁰ Local anesthetics commonly recommended for postoperative analgesia include bupivacaine, levobupivacaine, ropivacaine, etc., in the Guidelines for Postoperative Pain Management of Clinical Pharmacists.² The drugs included in the evaluation were recommended by expert consensus, among which levobupivacaine injection was recommended to be published by the Pharmaceutical society, with 5 points and the remaining drugs with 6 points.

Clinical Efficacy

Self-assessment is the gold standard for pain intensity assessment and should be used as the preferred assessment method. The visual analogue scale (VAS), which is the most sensitive, reliable, and acceptable, is used as the main endpoint of efficacy, and the amount of postoperative opioids is taken as the secondary endpoint of efficacy to evaluate clinical efficacy.³ Combined with the literature related to local anesthetics after joint replacement, such as real-world studies, randomized controlled trials, meta-analysis and other literatures, and the evidence pyramid grading method, the end points of local anesthetics were assigned, respectively. Due to the lack of head-to-head comparative studies on five local anesthetics, indirect results from the latest systematic review and meta-analysis showed that there was no difference between the primary and secondary clinical efficacy of liposomal bupivacaine and bupivacaine and ropivacaine injections. The main efficacy indexes of liposomal bupivacaine, bupivacaine, and ropivacaine injections were all scored 6 points, and the secondary efficacy indexes were all scored 4 points. In the randomized controlled study, the primary and secondary efficacy of liposomal bupivacaine was superior to levobupivacaine injection, and the primary efficacy index of levobupivacaine was 5.5 points, and the secondary efficacy index was 3.5 points. The evidence-based evidence of clinical efficacy is shown in Table 3.

In summary, in the effectiveness evaluation, liposomal bupivacaine scored 21 points, levobupivacaine injection scored 19 points, bupivacaine injection scored 21 points, and ropivacaine injection scored 21 points. The results of specific scoring rules are shown in Table 4.

Table 3 Analgesic Effect of Local Anesthetics After Joint Replacement

References First Author and Year of Publication	Type of Study	Intervention Group vs Control Group	Clinical Efficacy Conclusion
Nasir Hussain 2021 ⁶	Systematic Review and Meta-Analysis	Liposomal bupivacaine vs bupivacaine	Periarticular infiltration of liposomal bupivacaine did not improve VAS pain scores 24–48 hours after total knee arthroplasty, and liposomal bupivacaine did not reduce opioid consumption, improve safety, or improve functional prognosis.
Lue Liu 2020 ⁷	Systematic Review and Meta-Analysis	Liposomal bupivacaine vs bupivacaine/ropivacaine	Liposomal bupivacaine had similar analgesic efficacy in patients with postoperative pain after arthroplasty compared with continuous local anesthetic nerve block with bupivacaine/ropivacaine (no statistical differences in VAS pain scores, opioid consumption on postoperative days 0–2).
Hao Sun 2018 ⁸	Systematic Review and Meta-Analysis	Liposomal bupivacaine vs bupivacaine/ropivacaine	There were no statistically significant differences in opioid use, antiemetic dosage, naloxone dosage, mean anesthetic medication use, range of motion, or length of hospital stay in the liposomal bupivacaine group compared with the conventional PAI group (periarticular injection of bupivacaine/ropivacaine) in total knee arthroplasty with a significant reduction in VAS scores at 6 and 12 hours.
Kun Wang 2017 ⁹	Systematic Review and Meta-Analysis	Liposomal bupivacaine vs bupivacaine/ropivacaine	Bupivacaine liposomal and interosseous groove nerve blocks for postoperative pain control after arthroplasty did not show significant differences in terms of VAS scores, or opioid consumption compared to bupivacaine and ropivacaine.
Xi Wang 2017 ¹⁰	Systematic Review and Meta-Analysis	Liposomal bupivacaine vs bupivacaine	Liposomal bupivacaine significantly reduced VAS pain scores 48 hours after surgery and reduced morphine use on the first day after total knee arthroplasty.

(Continued)

Table 3 (Continued).

References First Author and Year of Publication	Type of Study	Intervention Group vs Control Group	Clinical Efficacy Conclusion
Ting-Ting Ma 2017 ¹¹	Systematic Review and Meta-Analysis	Liposomal bupivacaine vs bupivacaine	Liposomal bupivacaine was more effective than bupivacaine injection in VAS (P=0.018) and length of hospitalization (P=0.000) at 24 hours after hip arthroplasty. There were no significant differences in VAS at 48 and 72 hours and total morphine consumption at 24 hours (P>0.05).
Nanyang 2024 ¹²	RCT	Liposomal bupivacaine vs levobupivacaine	Used for peripheral nerve block of the hip joint capsule, the resting and motor VAS scores of the observation group were lower than those of the control group in the 12–72h postoperative period (P<0.05), liposomal bupivacaine reduced the dosage of opioids and other analgesic medications of the patients, and had a slight effect on the movement of the lower limbs without prolonging the length of hospitalization.
Krupp, Ryan 2023 ¹³	RCT	Liposomal bupivacaine vs ropivacaine	The liposomal bupivacaine group had significantly less pain at 24h and 48h after arthroplasty (p<0.001), significantly lower 48h MME (morphine milligram equivalents) (p=0.001), significantly smaller reduction in quality of recovery scores at 48h postoperatively (p<0.001), and significantly lower maximum pain scores (p=0.048).
Thomas W. Hamilton 2022 ¹⁴	RCT	Liposomal bupivacaine + bupivacaine vs bupivacaine	Used for pain with periarticular anesthetics in patients undergoing knee arthroplasty, there was no significant difference in VAS scores, or opioid consumption.
Safa B 2021 ¹⁵	RCT	0.5% ropivacaine vs 1% ropivacaine vs bupivacaine	There was no significant difference between 0.5% bupivacaine, 1% ropivacaine, and 0.5% ropivacaine in the mean duration of analgesic block after arthroplasty (p=0.51). Also time to first opioid use, duration of motor block, and cumulative opioid consumption were similar between groups.
Zuleyha Kazak Bengisun 2010 ¹⁶	RCT	Bupivacaine/ levobupivacaine vs saline	The VAS scores and area under the curve values for total tramadol consumption were significantly lower in the bupivacaine and levobupivacaine groups than in the control group at 48 hours after total knee arthroplasty (p-values were, respectively, p=0.032, p=0.029, and p<0.05). For the first time, the effectiveness of intra-articular administration of bupivacaine and levobupivacaine was compared with the control group in postoperative pain management.
Marcel A de Leeuw 2008 ¹⁷	RCT	Levobupivacaine vs bupivacaine vs ropivacaine	At 4 hours postoperatively after total hip arthroplasty, VAS scores were significantly lower in the ropivacaine group than in the levobupivacaine group, with a p-value of 0.037. There were no significant differences between the three groups in terms of VAS scores at the other different time points (8, 12, 24, and 48 hours) or in terms of opioid consumption. The analgesic efficacy of levobupivacaine, ropivacaine and bupivacaine in combined lumbar interspace-sciatic nerve block for postoperative analgesia after total hip arthroplasty was similar.
Florian Heid 2008 ¹⁸	RCT	Levobupivacaine vs ropivacaine	There were no significant differences in pain scores, incidence of motor blockade, or opioid requirements at 72 hours between the two groups of patients undergoing total knee arthroplasty.
Andrea Casati 2003 ¹⁷	RCT	Levobupivacaine vs bupivacaine vs ropivacaine	There were no differences between the three groups on VAS scores and on opioid consumption (P=0.55) within 12 hours after total hip arthroplasty.
Chang-Hwa Mary Chen 2020 ¹⁹	Retrospective cohort study	Liposomal bupivacaine vs ropivacaine	Endotracheal tube block for total knee arthroplasty showed no statistically significant difference in the highest pain scores between the two groups, and the bupivacaine liposomal group had significantly lower opioid use at 8 hours postoperatively, as well as a shorter hospital stay.

Safety

Adverse Reactions

Levobupivacaine and bupivacaine injection instructions did not provide the incidence of ADR adverse reactions, and the ADR score was 0. The most common adverse reactions of local anesthetics were mild to moderate adverse reactions such as nausea and vomiting. According to the incidence data of adverse reactions of corresponding drug instructions, liposomal bupivacaine scored 2 points and ropivacaine injection scored 2 points. Among the severe adverse reactions, anaphylactic shock was the most serious allergic reaction, and the incidence of ADR recorded by ropivacaine injection was rare (<0.1%), scoring 4 points. The incidence of ADR recorded by bupivacaine liposomal drug-induced hypersensitivity reaction was relatively rare (<2%), scoring 2 points;

Table 4 Results of Efficacy Scores

Index System and Weight Coefficient (27 Points)	Details (indicator Information and Data Sources)	Liposomal Bupivacaine	Levobupivacaine Injection	Bupivacaine Injection	Ropivacaine Injection - Naropin	Ropivacaine Injection - Dishili
Indications (5 points)	5 clinically necessary, preferred 3 Clinical needs, second choice 1 More medicines to choose from	5	5	5	5	5
Guide recommendation (12 points)	12 Diagnosis and treatment norms/clinical pathways, consensus issued by national health administrative agencies/management measures, etc., guideline level I recommendation (A-level evidence 12, B-level evidence 11, C-level evidence and others 10) 9 Guidelines level II and below recommendations (A-level evidence 9, B-level evidence 8, C-level evidence and others 7) 6 Expert consensus recommendation (consensus 6 issued by the society based on systematic reviews, consensus 5 issued by the society, and others 4) 3 Systematic review/Meta-analysis (large sample, high-quality systematic review/Meta-analysis 3, small sample, low quality systematic review/meta-analysis 2, systematic review/meta-analysis of non-RCT study 1)	6	5	6	6	6
Clinical efficacy (10 points)	6 Score by primary efficacy endpoint 4 Score by secondary efficacy endpoint	6	5.5	6	6	6
Effectiveness score		21	19	21	21	21

Special Population

No safety studies have been conducted on children under 12 years of age for all participating drugs, so the available score for children is 0.5. Ropivacaine injection is FDA pregnancy drug grade B with a score of 1, Bupivacaine injection is FDA pregnancy drug grade C with a score of 0.8, and there is no data to support the remaining drugs with a score of 0.5. The lactation grade of ropivacaine and bupivacaine injection was L2 with a score of 1, while the remaining drugs had no data to support them and a score of 0.5. Levobupivacaine injection was contraindicated in patients with severe hepatic and renal insufficiency, and the score was 2 points.

Drug Interaction

The metabolism of local anesthetics is affected by enzymes, especially cytochrome P450 enzyme system, which changes the plasma concentration and toxicity of drugs. Drugs that interact with the CYP450 enzyme system may affect the metabolism of local anesthetic drugs, and the interaction score is 2.

Other

Local anesthetics have irreversible adverse effects, and there may be irreversible nervous system reactions (including persistent anesthesia, paraesthesia, weakness, and paralysis) after soft tissue infiltration and analgesia with liposomal bupivacaine. Levobupivacaine injection may cause permanent muscle weakness or sensory impairment. The cardiotoxicity of bupivacaine injection should be noted in particular because resuscitation is difficult once the heart has stopped beating. Ropivacaine injection may cause persistent increase in methemoglobin levels, and serious adverse reactions including convulsion, coma, arrhythmia, and death, with a score of 0. The results of the ropivacaine injection mouse lymphoma cell test were weakly positive, and the carcinogenic effect was 0. There were fatal adverse events due to improper use of local anesthesia drugs, and the special drug warning was rated 1 point.

In summary, in the safety evaluation, liposomal bupivacaine scored 15.5 points, levobupivacaine injection scored 9.5 points, bupivacaine injection scored 12.3 points, and ropivacaine injection scored 17.5 points. The results of specific scoring rules are shown in [Table 5](#).

Economy

The economic evaluation examined the difference of average daily treatment cost between five local anesthetics and drugs with the same generic name and the main indication alternative drugs. The daily treatment cost was calculated according to the price, usage, and dosage of anesthetics in different places. Among them, liposomal bupivacaine was developed in China and produced by a single manufacturer, so the same generic name scored 3 points, and Dishili-Ropivacaine injection had the highest economic score under the same usage and dosage because of the nature of collectivized drugs and cheap price.

In summary, in the economic evaluation, liposomal bupivacaine was 3.36 points, levobupivacaine injection was 4.85 points, bupivacaine injection was 2.75 points, Naropin-Ropivacaine injection was 0.97 points, Dishili-Ropivacaine injection was 8.5 points. The results of specific scoring rules are shown in [Table 6](#).

Table 5 Safety Score Results

Safety (25 Points)			Liposomal Bupivacaine	Levobupivacaine Injection	Bupivacaine Injection	Ropivacaine Injection - Naropin	Ropivacaine Injection - Dishili
Adverse reactions (multiple choices) (8 points)	Moderate adverse reactions (3 points)	3 incidence rate < 1% 2 incidence rate 1% to <10% 1 incidence rate > 10% 0 ADR occurrence data not provided	2	0	0	2	2
	Severe adverse reactions (5 points)	5 incidence rate < 0.01% 4 incidence rate 0.01% to <0.1% 3 incidence rate 0.1% to <1% 2 incidence rate 1% to <10% 1 incidence rate > 10% 0 ADR occurrence data not provided	2	0	0	4	4

(Continued)

Table 5 (Continued).

Safety (25 Points)		Liposomal Bupivacaine	Levobupivacaine Injection	Bupivacaine Injection	Ropivacaine Injection - Naropin	Ropivacaine Injection - Dishili
Special groups (multiple choices) (11 points)	<p>2 available for children (2 points for all, 1.9 points for 3 months and older, 1.8 points for 6 months and older, 1.7 points for 9 months and older, 1.6 points for 1 year and older, 1.5 points for 2 years and older, 1.4 points for 3 years and older, 1.3 points for 4 years and older, 1.2 points for 5 years and older, 1.1 points for 6 years and older, 1.0 points for 7 years and older, 0.9 points for 9 years and older, 0.7 points for 10 years and older, 0.6 points for 11 years and older, 0.5 points for 12 years and older). (0.9 points for ages 9+, 0.8 points for ages 9+, 0.7 points for ages 10+, 0.6 points for ages 11+, and 0.5 points for ages 12+).</p> <p>1 Available for the elderly (available 1, use with caution 0.5)</p> <p>1 Available to pregnant women (available in the first trimester 1, available in the second trimester 0.8, and available in the third trimester 0.5)</p> <p>1 Available for lactating women (available 1, use with caution 0.5)</p> <p>3 Abnormal renal function is available (severe available 3, moderate available 2, mild available 1)</p> <p>3 Abnormal liver function available (severe available 3, moderate available 2, mild available 1)</p>	0.5	0.5	0.5	0.5	0.5
Adverse reactions caused by drug interactions (3 points)	<p>3 No dosage adjustment required</p> <p>2 Need to adjust dosage</p> <p>1 Prohibited to use at the same time</p>	2	2	2	2	2
Others (multiple choices) (3 points)	<p>1 Adverse reactions are reversible</p> <p>1 No teratogenic, carcinogenic</p> <p>1 No specific medication warnings</p>	1	1	1	1	1
Safety score		15.5	9.5	12.3	17.5	17.5

Other Properties

National medical insurance, national essential drugs, national centralized procurement of drugs, original research/reference/consistency evaluation, and enterprise production status scores were all scored according to the Selection Guide, and the detailed scoring rules are shown in Table 7.

Table 6 Results of Economic Score

Economy (10 Points)		Liposomal Bupivacaine	Levobupivacaine Injection	Bupivacaine Injection	Ropivacaine Injection - Naropin	Ropivacaine Injection - Dishili
Economy (10 points)	3 Evaluation method: The drug with the lowest average daily treatment cost gets 3 points, Evaluation drug score = (minimum average daily treatment cost/ average daily drug treatment cost) × 3.	3	2.9	2.47	0.29	2.55
Alternative drugs for main indications (7 points)	7 Evaluation method: the drug with the lowest average daily treatment cost gets 7 points, Evaluation drug score = (lowest average daily treatment cost/ average daily drug treatment cost) × 7.	0.36	1.95	0.28	0.68	5.95
Economy score		3.36	4.85	2.75	0.97	8.5

Table 7 Score Results of Other Properties

Other properties (10 points)		Liposomal Bupivacaine	Levobupivacaine Injection	Bupivacaine Injection	Ropivacaine Injection - Naropin	Ropivacaine Injection - Dishili
National Health Insurance (3 points)	3 National Health Insurance Catalog Category A, and there are no payment restrictions 2.5 National Health Insurance Catalog Category A, with payment restrictions 2 National Health Insurance Catalog Category B, no payment restrictions 1.5 National Health Insurance Catalog Category B, with payment restrictions 1 Not in the National Health Insurance Catalog	1.5	2	3	2	2
National Essential Drugs (3 points)	3 National Essential Drugs, no* requirement 2 National Essential Drug, with* requirement 1 Not in the National Essential Drug List	1	1	2	2	2

(Continued)

Table 7 (Continued).

Other properties (10 points)		Liposomal Bupivacaine	Levobupivacaine Injection	Bupivacaine Injection	Ropivacaine Injection - Naropin	Ropivacaine Injection - Dishili
National Centralized Procurement of Drugs (1 points)	1 National centralized procurement of selected drugs		1			1
Original research/reference/consistency evaluation (1 points)	1 Original drug/reference drug 0.5 Generic Drugs Through Consistency Evaluation	0.5	0.5	0.5	1	0.5
Production enterprise status (1 points)	1 The top 50 pharmaceutical companies in the world by sales/ Top 100 companies in the pharmaceutical industry of the Ministry of Industry and Information Technology (1–10 of the world's top 50 pharmaceutical companies by sales 1, 11–20 0.8, 21–30 0.6, 31–40 0.4, 41–50 0.2; Ministry of Industry and Information Technology Top 100 Enterprises in Pharmaceutical Industry 1–20 1, 21–40 0.8, 41–60 0.6, 61–80 0.4, 81–100 0.2)	0.2			1	
Global usage (1 points)	1 Available in China, the United States, Europe, and Japan 0.5 Available in China and other countries	0.5			1	
Scoring for other attributes		3.7	4.5	5.5	7	5.5

Note: *Indicates that the drug should be used under the guidance of physicians with qualifications, and the drug monitoring and evaluation should be strengthened.

Discussion

Analysis of Evaluation Results and Clinical Application

The final scores of the five local anesthetics included in this evaluation ranged from 60 to 75 points, and the specific scores are shown in Table 8.

Dishili-Ropivacaine injection scored the highest, followed by Naropin-Ropivacaine injection, liposomal bupivacaine, bupivacaine injection, and levobupivacaine injection. Dishili and Naropin-Ropivacaine injection have the same scores in pharmaceutical properties, effectiveness, and safety. However, among other attributes, Dishili-Ropivacaine injection is a collectible variety, so it has a significant advantage in the economy, with the highest comprehensive score of 75 and Naropin-Ropivacaine injections of 68.97. Liposomal bupivacaine, an ultra-long-acting local anesthetic with liposome as a carrier, ranked third in 65.06 scores, showing little difference in pharmaceutical properties, effectiveness, and safety compared with ropivacaine injection. Liposomal bupivacaine, after one administration, can produce analgesic effects for

Table 8 Comprehensive Scores of Local Anesthetic Drugs

Evaluation Dimension	Liposomal Bupivacaine	Levobupivacaine Injection	Bupivacaine Injection	Ropivacaine Injection - Naropin	Ropivacaine Injection - Dishili
Pharmacological properties	21.5	22.5	19.5	22.5	22.5
Efficacy	21	19	21	21	21
Safety	15.5	9.5	12.3	17.5	17.5
Economy	3.36	4.85	2.75	0.97	8.5
Other properties	3.7	4.5	5.5	7	5.5
Total score (100 points)	65.06	60.35	61.05	68.97	75

72h, with good analgesic effect and overall safety, which can better meet the analgesic needs of patients. It is also in line with the current trend of multi-modal analgesia with less opioids, and has a good application prospect.¹

In addition, levobupivacaine injection and ropivacaine injection were the most dominant in pharmaceutical properties, followed by liposomal bupivacaine. Liposomal bupivacaine, bupivacaine injection, and ropivacaine injection were the most dominant in effectiveness scores, and Ropivacaine injection was the most dominant in safety scores, followed by liposomal bupivacaine. The highest economic score was Dishili-Ropivacaine injection, and the highest other attribute score was Naropin-Ropivacaine injection. According to different evaluation modules, the advantages and disadvantages of different local anesthetics can be clearly seen, which can be used for decision-making under different needs.

Multi-modal analgesia has become the standard analgesia protocol for hip and knee surgery, and local anesthetics are an important part of the multi-modal analgesia strategy.²⁰ The comprehensive clinical evaluation of local anesthetics based on the Selection Guidelines can effectively measure the differences in effectiveness, safety, and economy among different local anesthetics. In practical work, the score results can be referred to, combined with clinical needs, to provide a basis for clinical rational drug use, hospital catalogue adjustment, etc. The future development of health technology evaluation will also pay more attention to speediness, comprehensiveness, scientificity, objectivity, and fairness, and become an indispensable tool for hospital decision-makers in drug selection and clinical rational drug use.

Limitations of Health Technology Evaluation

Medical institutions can use health technology evaluation to quickly integrate existing evidence, objective scientific evaluation and selection of drugs entering and leaving the medical catalogue. However, this score also has some limitations: (1) The evaluation has timeliness. For example, liposomal bupivacaine will only be listed in China at the end of 2022, and the clinical use time is relatively short. With the long-term clinical use of drugs, the updating of evidence-based medicine evidence, the adjustment of drug prices, the National Essential Drugs List, and the National Medical Insurance Catalogue, the effectiveness and economy of drugs will inevitably change. (2) This evaluation is only a quick and non-comprehensive evaluation, there are many manufacturers of the same variety, and the score is affected by different drug manufacturers, so the corresponding score should be adjusted according to the specific drugs in the hospital when referring to the evaluation results. (3) Some evaluation rules need to be detailed. For example, clinical efficacy and other indicators affected by evidence-based evidence in effectiveness, the absence of head-to-head research may affect the reliability of the score, resulting in bias. To sum up, dynamic updating of local anesthetics scores is needed to provide high-quality evidence-based reference for clinical decision-making.

Conclusion

This rapid health evaluation can provide reference for medical institutions to select long-acting local anesthetics for postoperative analgesia and optimize drug list. When long-acting local anesthetics were introduced into medical institutions, the Dishili-Ropivacaine injection of collective-selected varieties was the strongly recommended drug, followed by the Naropin-Ropivacaine injection and liposomal bupivacaine. When used for drug transfer, the Dishili-

Ropivacaine injection of the collected variety is recommended to be retained in the catalog, and the remaining varieties can be retained or transferred according to clinical needs. At the same time, the methods and practices of this rapid health evaluation can also serve as a reference for hospitals in other countries to select drugs.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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