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Construction of an Evidence-Based Bundled Nursing Protocol for GnRHa Injections in Children with Precocious Puberty

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Abstract: Objective: To construct an evidence-based bundled nursing protocol for gonadotropin-releasing hormone agonist (GnRHa) injections in children with precocious puberty, so as to provide a basis for standardized clinical nursing practice. Methods: Clinical questions were formulated under the PIPOST-D framework. Literature on pain management, induration prevention and injection techniques for GnRHa administration was systematically retrieved from domestic and international databases and guideline websites. An evidence-based nursing team performed quality appraisal and evidence extraction for the included studies. A bundled nursing protocol was developed after evidence assessment using the FAME criteria. Eligible children and nurses from the pediatric outpatient and inpatient departments of our hospital were enrolled for baseline audit, and barriers to clinical practice were analyzed. Results: A total of 15 high-quality studies were included, from which 17 pieces of best evidence were extracted. Two pieces of evidence were excluded after FAME assessment. The final bundled nursing protocol comprised 15 core measures in four dimensions: pre-injection cold compress and medication rewarming, Z-track technique combined with the air-bubble technique during injection, post-injection hot compress, and cognitive-behavioral pain interventions. Thirteen audit indicators, together with corresponding assessment methods covering operational specifications and pain interventions, were established through baseline audit. Conclusion: The evidence-based bundled nursing protocol for GnRHa injection developed in this study is scientifically valid and clinically applicable. It helps standardize clinical procedures, reduce injection-related complications and improve children's medical experience, thereby laying a foundation for subsequent clinical translation and quality improvement.

Keywords: evidence-based nursing, precocious puberty, gonadotropin-releasing hormone agonist, bundled nursing, injection-related complications.

INTRODUCTION

Precocious puberty is an abnormal disorder of growth and development in children, generally defined as the appearance of secondary sexual characteristics in girls before 7.5 years of age and in boys before 9 years of age. Central precocious puberty (CPP) results from premature activation of the hypothalamic-pituitary-gonadal axis, with an incidence of 1/10000 to 1/5000, and the incidence is markedly higher in girls than in boys[1,2]. In recent years, the incidence of CPP has been increasing and the age of onset has shifted earlier[3]. CPP not only impairs adult height potential but also predisposes children to complex psychobehavioral problems such as low self-esteem, anxiety, depression and social dysfunction[4-6]. Currently, subcutaneous or intramuscular injection of gonadotropin-releasing hormone agonists (GnRHa, e.g., leuprorelin acetate and triptorelin) is the first-line treatment for CPP[7].

However, most GnRHa preparations are high-concentration microsphere suspensions with high viscosity[8,9], and original pre-filled syringes are usually equipped with large-gauge needles (e.g., 25G / No. 10 needle) to ensure smooth injection. This objective limitation of a "large-gauge needle plus high-viscosity suspension", together with the long-term monthly treatment cycle, readily induces severe needle phobia in children. In addition, the wide needle tract and slow drug absorption predispose patients to drug reflux, which may cause severe injection-site pain, erythema, induration and even subcutaneous lipoatrophy[10,11]. At present, clinical nurses lack unified evidence-based standards for key procedures such as cold compress application, Z-track injection and post-withdrawal compression, resulting in inconsistent nursing quality. Therefore, this study aimed to develop a standardized and feasible bundled nursing protocol for GnRHa injection in children with precocious puberty using evidence-based methods, in order to address clinical challenges and improve nursing quality and treatment adherence.

SUBJECTS AND METHODS

Formulation of Clinical Questions

Clinical questions were developed according to the PIPOST-D framework[12]. P (Population): children with precocious puberty receiving subcutaneous or intramuscular GnRHa therapy; I (Intervention): an evidence-based bundled nursing protocol including pre-injection cold compress, Z-track technique combined with the air-bubble technique, slow and uniform injection, standardized compression and post-injection hot compress; P (Professionals): pediatric clinical nurses; O (Outcomes): injection pain score (FLACC scale), incidence of induration, satisfaction and implementation rate of standardized procedures; S (Settings): the inpatient and outpatient departments of the children's hospital; T (Time): guidelines, systematic reviews and randomized controlled trials (RCTs) published within the past 10 years; D (Design): development of the evidence-based protocol and its clinical translation.

Literature Search Strategy

Following the "6S" model of evidence-based healthcare, literature searches were performed in UpToDate, BMJ Best Practice, JBI, Cochrane Library, PubMed, Embase, CNKI, Wanfang Data and the Chinese Biomedical Literature Database (CBM). The search period was from January 2016 to January 2026. Chinese search terms included precocious puberty, gonadotropin-releasing hormone agonist, leuprorelin, cold compress, subcutaneous injection, Z-track technique, air-bubble technique, pain management, induration and nursing care; the corresponding English terms were precocious puberty, GnRHa, leuprorelin, cold compress, subcutaneous injection, Z-track method, air-bubble technique, pain management, induration and nursing care.

Inclusion and Exclusion Criteria

Inclusion criteria: (1) participants were children with precocious puberty receiving GnRHa treatment; (2) literature types included guidelines, evidence summaries, expert consensus statements, systematic reviews or RCTs; (3) the content addressed injection techniques, pain management or complication prevention; (4) articles were published in Chinese or

English. Exclusion criteria: (1) guideline interpretations, narrative reviews, grey literature and conference minutes; (2) publications with incomplete information; (3) studies that failed quality appraisal.

Literature Quality Appraisal

Two nurses trained in evidence-based practice conducted independent quality appraisal. The AGREE II instrument[13] was used for guidelines, JBI criteria for expert consensus were applied to expert consensus statements, and JBI Evidence-Based Healthcare Center criteria[14] were used for RCTs and systematic reviews. Disagreements were resolved by a third expert.

Evidence Synthesis and FAME Assessment

Evidence was extracted and synthesized from the included literature. The FAME principle (Feasibility, Appropriateness, Meaningfulness and Effectiveness) was adopted to evaluate the clinical applicability of the evidence. Evidence that was inappropriate or unfeasible in the local context of our hospital was excluded, and the final bundled nursing protocol was formulated accordingly[15-18].

Baseline Audit and Barrier Analysis

Children receiving GnRHa injections and nurses performing the injections in the pediatric outpatient and inpatient departments of our hospital between May and September 2026 were enrolled. Child inclusion criteria: aged 6 to 14 years, diagnosed with CPP and requiring regular injections, with informed consent. Nurse inclusion criteria: registered nurses with at least 3 months of independent injection experience. Thirteen audit indicators were assessed through record review, on-site observation, questionnaires and telephone follow-up, and brainstorming was used to identify the major barriers to clinical practice.

RESULTS

Literature Search and Screening Results

A total of 1850 articles were initially retrieved, of which 1230 remained after duplicate removal. After screening of titles and abstracts, 186 articles were retained, and 15 high-quality articles were finally included after full-text assessment. The included literature comprised 6 clinical guidelines[19-24], 2 expert consensus statements[25,26], 3 systematic reviews[27-29] and 4 RCTs[30-33].

Summary of Best Evidence

A total of 17 pieces of best evidence were extracted from the 15 included articles, covering four dimensions: pre-procedure, intra-procedure, post-injection and pain intervention. The evidence levels were mainly Level 1 and Level 5; 12 items were rated as strong recommendations and 5 as weak recommendations.

Pre-procedure preparation: ① Apply an ice pack or cold compress at 5–10 °C to the injection site for 2 minutes before injection to constrict blood vessels and reduce skin sensitivity [28] (Grade Ⅰ, Strong Recommendation A); ② Refrigerated medications should be warmed to room temperature (20–25 °C) prior to injection to alleviate pain and induration induced by cold stimulation (Grade Ⅰ, Strong Recommendation A); ③ Assess skin integrity and blood circulation before cold compress [26]. Cold compress is contraindicated for patients with Raynaud's disease or cold allergy (Grade Ⅲ, Recommendation B).

Intra-procedure standardization: ④ Adopt the Z-track injection technique: pull the skin to form a Z-shape before needle insertion, withdraw the needle slowly after drug injection and release the skin to prevent drug reflux [27] (Grade Ⅰ, Strong Recommendation A); ⑤ Retain 0.2–0.3 mL of air after aspirating the drug solution, and inject the air together with the medication to seal the needle tract via positive pressure (Grade Ⅱ, Strong Recommendation A); ⑥ Apply vertical compression with a cotton swab for 3–5 minutes after needle withdrawal; rubbing is prohibited (Grade Ⅰ, Strong Recommendation A); ⑦ Establish an injection site rotation record card for alternate left and right-site injection (Grade Ⅲ, Recommendation B); ⑧ Select the needle insertion angle according to subcutaneous fat thickness: 90° for intramuscular injection and 45° for subcutaneous injection (Grade Ⅱ, Recommendation B); ⑨ For high-viscosity medications, the Z-track technique must be combined with the air-bubble technique (Grade Ⅰ, Strong Recommendation A); ⑩ Aspirate to confirm no blood return before intramuscular injection (Grade Ⅰ, Strong Recommendation A).

Post-injection management: ⑪ Apply a warm towel of 40–45 °C to the indurated area 24 hours after injection to promote blood circulation and drug absorption [15] (Grade Ⅱ, Recommendation A).

Pain intervention: ⑫ Guide children aged 6–12 years to perform deep breathing or guided imagery to modulate the autonomic nervous system and reduce anxiety (Grade Ⅰ, Strong Recommendation A); ⑬ Allow children to watch animations or play games on electronic devices during injection for distraction (Grade Ⅰ, Strong Recommendation A) [34]; ⑭ Encourage children to engage in interactive activities such as counting or describing toys (Grade Ⅲ, Recommendation B); ⑮ Encourage appropriate limb movement after injection to facilitate drug dispersion [35] (Grade Ⅲ, Recommendation B).

Results of FAME Assessment

All 17 pieces of evidence underwent FAME assessment, and 15 passed the evaluation, with Feasibility, Appropriateness, Meaningfulness and Effectiveness all rated as "Yes". Two pieces of evidence were excluded: (1) "cartoon-shaped cold packs should be prioritized" was considered unfeasible because such supplies were unavailable in our hospital; and (2) "inject the medication slowly and uniformly (≥10 seconds)" was judged inappropriate because uniform injection is difficult to achieve when high-viscosity suspensions are delivered through large-gauge needles. Ultimately, 15 pieces of evidence for clinical translation were retained.

Results of Baseline Audit and Barrier Analysis

A total of 85 children and 10 nurses were enrolled in the baseline audit, with an effective data recovery rate of 100%. Thirteen audit indicators were established, including the implementation rates of pre-injection cold compress, rewarming of refrigerated medication, Z-track injection, standardized injection of high-viscosity drugs and cognitive-behavioral pain intervention.

Three core barriers were identified. (1) Staff skill-related barriers: the Z-track technique combined with the air-bubble technique involves complicated procedures, making it difficult for nurses to modify established operating habits, and some nurses lacked in-depth understanding of the underlying evidence-based principles. (2) Patient psychological barriers: children developed anticipatory anxiety triggered by previous painful experiences, and parents held misconceptions regarding the timing and temperature control of cold and hot compresses at home. (3) Supply and monitoring barriers: conventional ice packs are rigid and inadequately child-friendly, and no systematic follow-up of induration and pain after discharge was in place.

DISCUSSION

Clinical Significance of the Bundled Nursing Protocol

GnRHa treatment is a long-term therapeutic process for children with CPP, and injection-related complications and pain not only compromise treatment efficacy but also exert profound effects on children's psychological health. The protocol developed in this study is not merely a combination of isolated techniques but a systematic intervention strategy based on best evidence. It integrates cold compress for analgesia, the Z-track technique for preventing drug reflux, the air-bubble technique for sealing the needle tract, and cognitive-behavioral interventions[20-22], thereby blocking the pathways leading to pain and induration from physical, mechanical and psychological perspectives. Compared with conventional experience-based nursing, this protocol has explicit evidence-based foundations and standardized operating procedures. It effectively fills the clinical gap in standardized practice for injections of high-viscosity medications through large-gauge needles and helps ensure patient safety.

Evidence Base and Mechanisms of Core Techniques

All core techniques in this protocol are supported by solid evidence. Pre-injection cold compress and medication rewarming: studies have shown that local cold compress induces vasoconstriction and reduces the sensitivity of peripheral nerve endings, thereby alleviating puncture pain[28]; rewarming of the medication avoids tissue spasm and induration caused by direct irritation from cold injectate. Z-track technique combined with the air-bubble technique[23]: for high-viscosity microsphere suspensions, conventional perpendicular injection readily causes drug leakage along the needle tract because of elastic recoil of the tissue. The Z-track method displaces subcutaneous tissue to create an offset tract, which is sealed by tissue repositioning after needle withdrawal, while the air-bubble technique uses positive air pressure to deliver residual drug in the needle dead space completely into the tissue. The combination of the two techniques can substantially reduce the incidence of induration. Cognitive-behavioral intervention: pain perception in school-age children is

strongly modulated by emotion and attention. Deep breathing, guided imagery and interactive electronic activities can effectively activate the descending pain inhibitory pathway and break the vicious cycle of fear-pain-resistance[34,35].

Implementation Barriers and Countermeasures

Despite adequate evidence, clinical translation remains challenging. To address difficulties in nurses' skill transfer, stepwise training with high-fidelity manikins and specialized workshops are recommended, and evidence-based operation videos should be produced to deepen nurses' understanding of the rationale and avoid mechanical implementation. For children with anticipatory anxiety, the "3-2-1 injection cue method" combined with tablet-based interactive activities can transform passive tolerance into active participation; in addition, a Home Care Diary can be distributed to provide hands-on empowerment education for parents and correct misconceptions about cold and hot compresses. Regarding the limited availability of child-friendly supplies, cooling patches can be used as an alternative when cartoon-shaped cold packs are unavailable, so as to improve children's acceptance. To address the lack of follow-up data, a closed-loop follow-up system based on WeChat mini-programs or telephone calls should be established to dynamically monitor induration and pain at home and achieve seamless continuity between hospital and home care.

Study Limitations

This study has several limitations. First, the baseline audit enrolled 85 children and 10 nurses, which met the basic requirements for indicator development; however, it was a single-center study with a relatively homogeneous sample. Although the audit indicators and assessment methods were established, quantitative comparative data before and after intervention were not obtained, and larger samples are needed for verification in future clinical practice. Second, owing to the available supplies in our hospital, evidence such as the use of cartoon-shaped cold packs was excluded[21], which may affect the cold compress experience of some children. Third, the recommendation of slow injection was excluded because of the characteristics of the equipment and medication; the optimal injection speed for high-viscosity drugs administered through large-gauge needles warrants further investigation.

CONCLUSION

Following rigorous evidence-based nursing methodology, this study systematically retrieved and appraised relevant domestic and international literature and developed a bundled nursing protocol comprising 15 core measures for GnRHa injection in children with precocious puberty. Covering the entire workflow of pre-injection preparation, standardized procedures, post-injection management and psychological pain intervention, the protocol is scientific, applicable and operable. Thirteen quality audit indicators were identified through baseline audit, and the major barriers to clinical translation were analyzed in depth. In the future, in-hospital training, operation manuals and PDCA quality improvement programs will be used to promote implementation of the protocol, with the

aim of reducing injection pain and complication rates and improving the quality of specialized pediatric endocrine nursing and children's medical experience.

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