

## Original Article

# Application of mineral trioxide aggregate pulpotomy in the treatment of early pulpitis of primary molars

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**Abstract:** Objective: To evaluate the effectiveness of mineral trioxide aggregate (MTA) on pulpotomy in primary molars. Methods: Two hundred and sixty-three cases (310 teeth) of children with early pulpitis of primary molars admitted between February 2019 to February 2022 were enrolled, and their clinical data were retrospectively analyzed. Of them, 130 cases with 155 teeth treated with root canal treatment were set as the control group (CG) and 133 cases with 155 teeth receiving MTA pulpotomy were set as the observation group (OG). Clinical data such as efficacy evaluation, inflammatory factor levels, postoperative adverse reactions, and quality of life (QoL) were compared. Results: After surgery, the overall response rate in the OG was statistically higher than that in the CG, while the levels of inflammatory factors in the OG were significantly lower than those in the CG (all  $P < 0.05$ ). Moreover, the total incidence of complications was significantly lower in OG at 3, 6, and 12 months after surgery ( $P = 0.018$ ,  $P = 0.007$ ,  $P = 0.015$ , respectively). The QoL of the two groups differed insignificantly before surgery; however, after the treatment, the QoL in OG was significantly higher than those in the CG at 3, 6, and 12 months after surgery ( $P = 0.037$ ,  $P = 0.012$ ,  $P = 0.028$ , respectively). Moreover, the teeth location and treatment method were independent factors of efficacy ( $P = 0.047$ ,  $P = 0.001$ , respectively). Conclusions: MTA pulpotomy outperformed root canal treatment for superior efficacy in children with early pulpitis of primary molars, with a positive effect on improving QoL, and patient prognosis.

**Keywords:** Mineral trioxide aggregate, MTA, pulpotomy, pulpitis, primary molars

## Introduction

Pulpitis refers to an inflammatory disease that occurs in dental pulp tissue, and it is one of the most common diseases of the oral cavity [1]. The occurrence of pulpitis is often related to dental caries. When bacteria attack teeth, patients usually develop dental caries, which is a precursor to irreversible pulpitis. The dental pulp is inside the pulp cavity of the tooth and contains tissues such as nerves and blood vessels. When dental caries or bacteria and their metabolites from periodontal tissue invade the pulp tissue, it is highly susceptible to infection and can lead to pulpitis [2]. With more diversified and refined food choices for children, the incidence of child pulpitis is rising, ranging from 20% to 60% [3]. Acute and severe pain are the most typical initial symptoms of pulpitis [4]. Specifically, early severe pulpitis can cause a loss of precision of primary molars, which can

reduce chewing efficiency, as well as lead to migration of adjacent teeth and a lack of space, resulting in tooth deformities and abnormal eruption [5]. Therefore, the most important treatment goal for pediatric pulpitis is to ensure the integrity of primary teeth as much as possible before the eruption of permanent teeth [6].

In the context of current oral treatment technology, root canal treatment is still recognized as the most effective scheme for early primary teeth pulpitis [7]. However, the failure rate of traditional root canal treatment is nearly 30% [8], and there are many postoperative adverse reactions and related complications. In serious cases, these include voice disorders, mature permanent teeth dysplasia, inability to chew, and other adverse consequences [9]. A pulpectomy is a treatment method that removes pulp tissue from the crown and preserves healthy pulp tissue at the root. It is mainly used for pulp

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exposure and pulpitis in primary teeth. However, the combination of pulpotomy and traditional pulp capping materials cannot effectively isolate oral pathogenic microorganisms, and most patients may experience endodontic infections within 3 months after surgery, leading to surgical failure. In severe cases, bacteria entering the bloodstream can be life-threatening [10].

Mineral trioxide aggregate (MTA) is a new material first reported by Lee et al. in 1993 for the treatment of pulpitis [11]. It has been widely used in various clinical fields such as direct pulp capping, repair of pulp perforation, apical induction shaping, apical inverted filling, and pulp revascularization [12]. As a nanoceramic material, MTA has good biocompatibility, long-lasting sealing properties, and the ability to induce tissue regeneration. When used in the treatment of pulpitis, it can promote the function of calcified bridges. For those with mild symptoms of pulpitis, MTA can also reduce the occurrence of leakage [13]. The application of MTA in the treatment of pulpotomy has been proven to effectively reduce the incidence of dental pulp infections [14]. However, in China, MTA pulpotomy is still in the research stage. Currently, various short-term studies have been conducted with few included cases. The number of cases is mostly around 30-100, and the number of affected teeth does not exceed 120. The results obtained may not fully reflect the actual clinical situation [15]. Therefore, in order to further validate the application value of MTA pulpotomy in early pulpitis of primary molars compared to traditional radical surgery, this study included more cases and conducted a large sample study to demonstrate the application advantages of MTA pulpotomy in this medical environment, contributing to the clinical promotion of MTA pulpotomy in optimizing early pulpitis of primary molars.

### Materials and methods

#### *Study design and patients*

In this retrospective study, through the electronic medical record system, a total of 310 affected teeth from 263 children with early pulpitis of primary molars who received treatment from February 2019 to February 2022 in the People's Hospital Affiliated to Shandong First Medical University were included. This retrospective analysis was approved by the ethics

committee of People's Hospital Affiliated with Shandong First Medical University. Informed consent was obtained from all the children and their family members.

Inclusion criteria: (1) Children (aged 3-12 years old) clinically diagnosed with early pulpitis and received MTA pulpotomy or root canal treatment without MTA; (2) The case records of the eligible patients must be complete, and the patients must have received corresponding treatments and received outcomes evaluation after surgery; (3) In the records, children with no other abnormal manifestations in X-ray and related examinations; (4) The clinical examination results showed no loose or painful teeth and no redness, swelling, or fistula in the gums; (5) The deep caries cavity of the affected tooth is close to the pulp, and the pulp is exposed or very close to the pulp after the caries is removed; (6) The child may experience bright red and bleeding from the exposed area of the dental pulp during the surgery, but it can be controlled within 10 minutes.

Exclusion criteria: (1) Children with no pulp exposure or pulp exposure size <1 mm and diameter >5 mm; (2) Children with necrotic pulp tissue that judged by the absence of bleeding or the presence of pale necrotic pulp tissue; (3) Children who cannot receive full treatment; (4) Children with other oral diseases; (5) Children unwilling to participate in the study.

#### *Treatment details*

Children in the OG received MTA pulpotomy. During the surgery, the doctor assisted the child in obtaining a reasonable position for local anesthesia, installed a rubber barrier, thoroughly removed decayed tissue, and performed a thorough cleaning. Then, a ball drill was used to uncover the top of the pulp cavity to fully expose it. The inflamed pulp tissues were cleaned, and the formation and bleeding of the crown pulp were observed. 0.9% sodium chloride injection was used to wash the pulp fragments, and dentin debris, and stop bleeding on the wound surface. After filling the root canal with Vitax (Neo Dental Chemical Products Co., Ltd., Tokyo, Japan), we covered the pulp section with 1-3 mm of prepared MTA (Dentsply Tulsa Dental Specialty, Inc., Johnson City, TN), and then a small cotton ball dipped in sterile distilled water was covered above the MTA.

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After 3 minutes, we removed the cotton ball, took a glass ionomer cement (Tokuyama Dental Corp., Japan) pad, and filled it with 3M resin (3M ESPE Dental Products). After completion, we adjusted the jaw polishing treatment.

Children in the CG received root canal treatment. After local anesthesia, a rubber barrier was installed, the top of the pulp chamber was opened, and the necrotic pulp was removed. After removal, root canal preparation work was carried out. Based on conventional root canal preparation, the root canal was rinsed, and the interior of the root canal was filled with vitapex until there was a paste overflow at the root canal mouth. Finally, the root canal was cushioned and filled.

### *Data collection*

Preoperative data of eligible patients were collected, including general information and disease-related data of the patient before surgery. General information includes the children's gender, age at the time of treatment (months), tooth position (maxillary or mandibular primary molars), and diseased tooth position (first or second primary molars). Disease related information includes the patient's dental records, documents related to early pulpitis surgery for primary molars, and medical history in electronic and paper files. X-ray and related examination data were reviewed to comprehensively evaluate the dental pulp and periodontal condition of the patient.

### *Outcome measures*

Main outcome measures: (1) Clinical efficacy: pain, swelling and fistula in the affected teeth, discomfort during percussion, and pathological loosening were observed in two groups. Effective: the symptoms have improved significantly or completely subsided, or the symptoms have been alleviated; Ineffective: the symptoms have not improved significantly or worsened. (2) Response rate was also observed via X-ray. Effective: no pathological root resorption, no lesion at the root tip, and the permanent tooth germ hard bone plate was intact; Ineffective: X-ray showed shadow or pathological absorption at the root tip.

Secondary outcome measures: (1) Postoperative adverse reactions including tooth tapping pain, periodontal redness and swelling,

and periodontal infection were observed; (2) The level of quality of life (QoL): child-oral impacts on daily performances (Child-OIDP) was used to evaluate the QoL of our children. Child-OIDP includes 8 scoring dimensions (diet, speech, oral hygiene, sleep, smile, learning, emotions, and social interaction), each with a score of 9 points, with a total score of 72 points. The score is positively correlated with the quality of life level of the child [16].

All indicators were followed up at 3, 6, and 12 months after surgery. The patients' QoL was also evaluated one week before surgery. It should be noted that our data on inflammatory factor levels were derived from another study that has not yet been published, and due to the need for their study, the children who underwent the treatment in question were tested for serum inflammatory factors both preoperatively and postoperatively. Children were not given antibiotics prior to treatment. The evaluation was conducted by three certified pediatric dentists who received clinical and radiological training and calibration for follow-up. When the evaluation results varied between reviewers, we accepted the opinion with majority support.

### *Statistical methods*

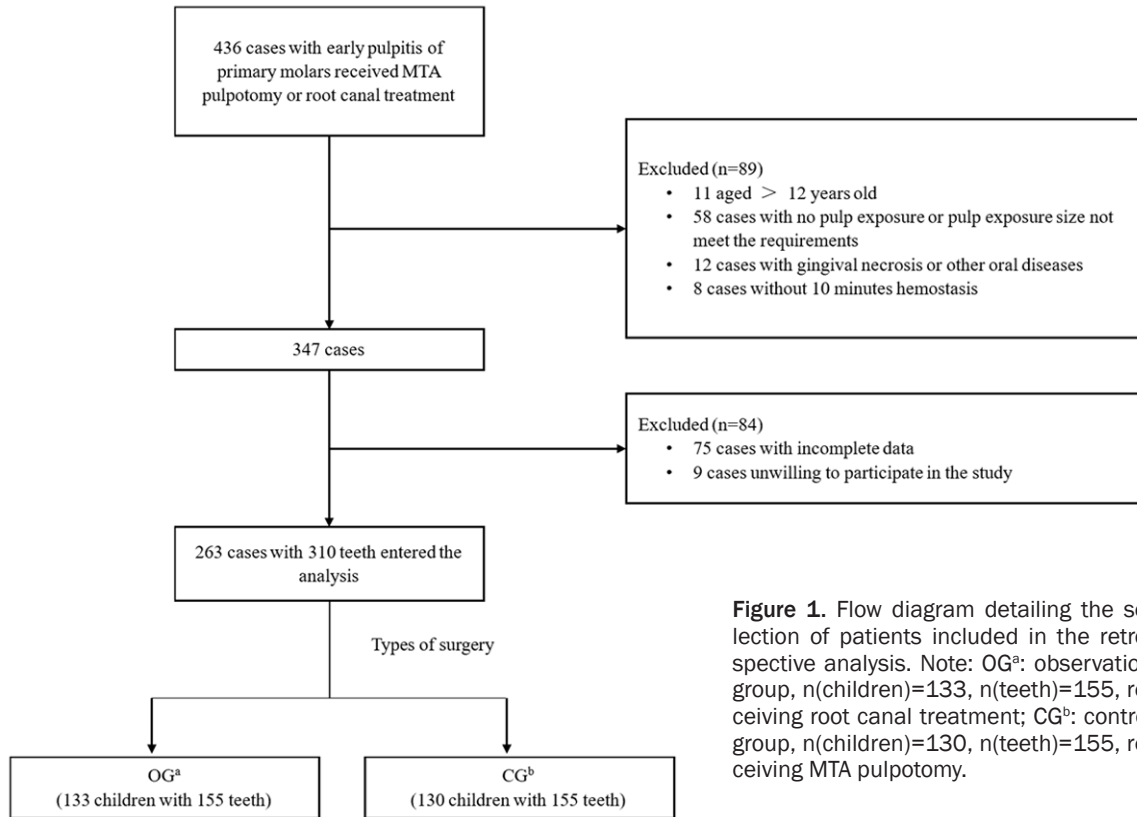
IBM SPSS Statistics 26.0 and GraphPad 9.5.0 were used for statistical analyses. Measured data were expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm sd$ ). Independent t test was carried out for comparison between groups. Comparison of data before and after treatment within the group was performed using paired-sample t test. Counted data were expressed by number (percentage) [n (%)] and compared by the chi-square test. ANOVA followed by post hoc Bonferroni test was adopted to compare the difference between repeated measurements like QoL. Univariate and multivariate logistic regression models were used to evaluate the relevant factors affecting efficacy. Risk ratio (HR) is the ratio of hazard rates corresponding to the risk of failure. Statistical significance was set at  $P < 0.05$ .

## **Results**

### *Patients and tooth characteristics*

The initial search revealed 436 cases with early pulpitis of primary molars received MTA pulpotomy or root canal treatment from February

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**Figure 1.** Flow diagram detailing the selection of patients included in the retrospective analysis. Note: OG<sup>a</sup>: observation group, n(children)=133, n(teeth)=155, receiving root canal treatment; CG<sup>b</sup>: control group, n(children)=130, n(teeth)=155, receiving MTA pulpotomy.

**Table 1.** Baseline variables of patients and primary molars between the two groups [n (%),  $\bar{x} \pm sd$ ]

Variable	OG <sup>a</sup>	CG <sup>b</sup>	$\chi^2/t$	P
Age (months)	65.80 ± 9.68	65.32 ± 9.43	0.529	0.434
Gender			0.917	0.877
Male	70 (52.63)	69 (53.10)		
Female	63 (47.37)	61 (46.92)		
Teeth Location			2.209	0.938
Maxillary	46 (34.59)	45 (34.61)		
Mandibular	87 (65.41)	85 (65.16)		
Lesion			1.966	0.671
First	48 (36.10)	42 (32.31)		
Second	85 (63.91)	88 (67.69)		
Apical Foramen			1.877	0.653
Close	61 (45.86)	62 (47.69)		
Not	72 (54.14)	68 (52.31)		

Note: OG<sup>a</sup>: observation group, n(children)=133, n(teeth)=155; CG<sup>b</sup>: control group, n(children)=130, n(teeth)=155.

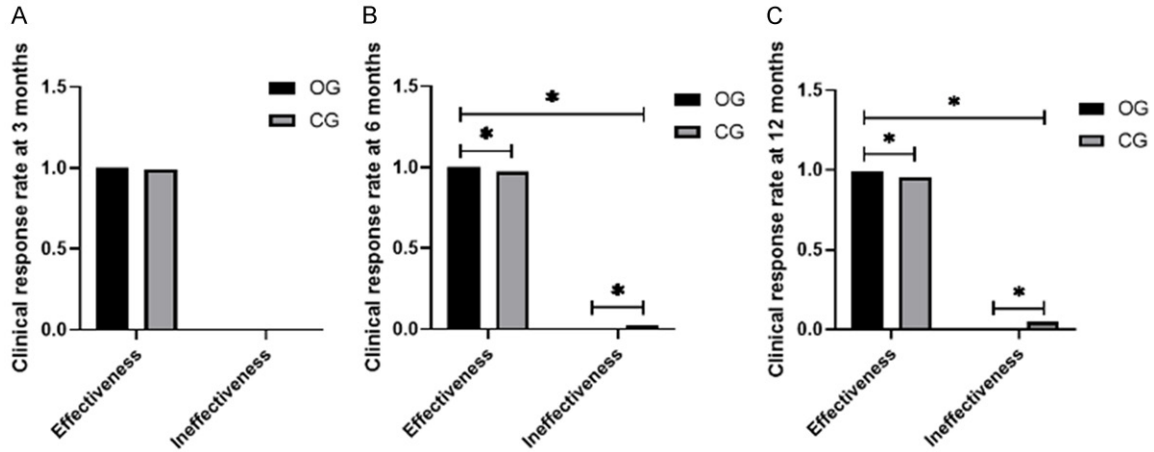
cases with incomplete data and 9 cases unwilling to participate in the study, finally 263 patients were eligible for the study, including 310 teeth. Details are shown in **Figure 1**. The cases were divided into two groups based on the types of surgery: a control group (CG) including 130 children with 155 teeth receiving root canal treatment, and an observation group (OG) including 133 children with 155 teeth receiving MTA pulpotomy. The average age of children in OG was  $65.80 \pm 9.68$  months, while that in CG was  $65.32 \pm 9.43$  months. There were no significant differences in average age, gender, tooth position, and region between the OG and CG groups (all  $P > 0.05$ , **Table 1**).

2019 to February 2022. Eleven cases were excluded due to age limit. After excluding 58 cases with no pulp exposure or pulp exposure size not meeting the requirements, 12 cases with gingival necrosis or other oral diseases, 8 cases without 10 minutes hemostasis, 75

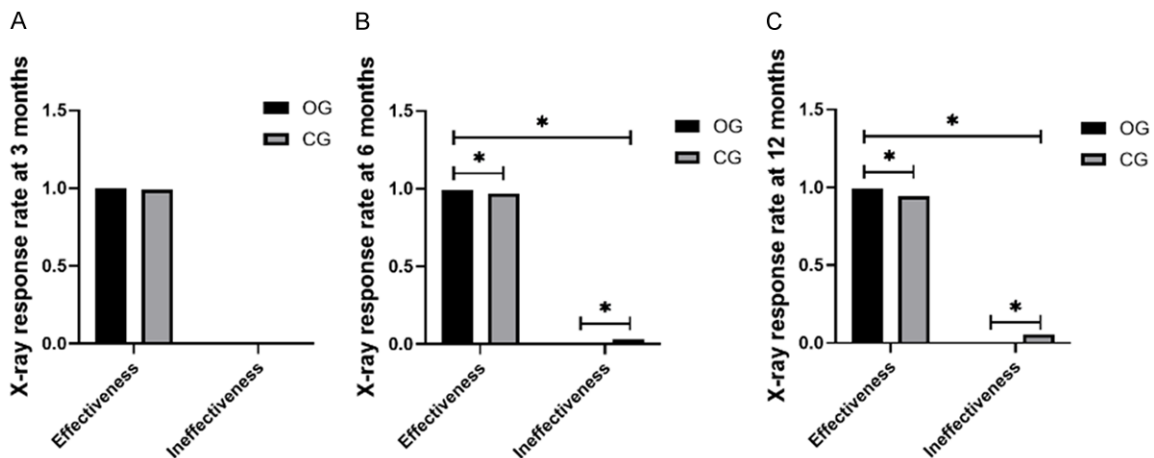
## Clinical efficacy between two groups

The clinical response rates between two groups at 3, 6, and 12 months after surgery are shown in **Figure 2**. At 12 months after surgery, one patient in the OG withdrew from the study due

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**Figure 2.** Comparison of clinical response rates between the two groups at 3, 6, and 12 months. A: Comparison of clinical response rates between groups at 3 months; B: Comparison of clinical response rates at 6 months; C: Comparison of clinical response rates at 12 months. OG: observation group, n(children)=133, n(teeth)=155; CG: control group, n(children)=130, n(teeth)=155. Note: \*P<0.05.



**Figure 3.** Comparison of response rates (X-ray display) between the two groups at 3, 6, and 12 months after surgery. A: Comparison of response rates at 3 months; B: Comparison of response rates at 6 months; C: Comparison of response rates at 12 months. OG: observation group, n(children)=133, n(teeth)=155; CG: control group, n(children)=130, n(teeth)=155. Note: \*P<0.05.

to personal reasons, while two patients in the CG withdrew. At 3 months after surgery, the overall response rates of the OG and the CG were 100.0% and 99.23%, respectively, with no statistical difference ( $\chi^2=1.833$ ,  $P=0.126$ ). At 6 and 12 months after surgery, the clinical overall response rate in the OG were 100.0% and 99.24%, respectively, significantly higher than 97.69% and 95.31% in the CG ( $\chi^2=4.124$ ,  $P=0.042$ ;  $\chi^2=6.946$ ,  $P=0.022$ , respectively).

### Response rates (X-ray display) between two groups

Response rates in the two groups at 3, 6, and 12 months after surgery are shown in **Figure 3**.

At 3 months after surgery, the overall response rate indicated by X-ray of the OG and the CG were 100.0% and 99.23%, respectively, with no statistical difference ( $\chi^2=1.833$ ,  $P=0.126$ ). At 6 and 12 months after surgery, the clinical overall response rate indicated by X-ray in the OG were 99.25% and 99.24%, respectively, significantly higher than 96.92% and 94.53% in the CG ( $\chi^2=5.425$ ,  $P=0.017$ ;  $\chi^2=7.446$ ,  $P=0.006$ , respectively).

### Adverse reactions between two groups

By comparing the incidence of complications (tooth tapping pain, periodontal redness and swelling, and periodontal infection) between

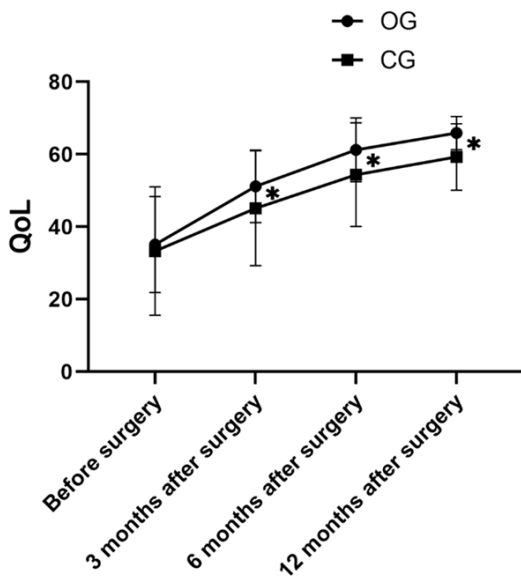


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**Table 2.** Comparison of adverse reactions between two groups at 3, 6, and 12 months

Time (months)	Group	Toothache [n (%)]	Periodontal redness and swelling [n (%)]	Periodontal infection [n (%)]	Total Incidence [n (%)]	X <sup>2</sup>	P
3	OG <sup>a</sup> (n=133)	7 (5.26)	6 (4.51)	4 (3.01)	17 (12.78)	5.527	0.018
	CG <sup>b</sup> (n=130)	12 (9.23)	12 (9.23)	6 (4.62)	30 (23.08)		
6	OG <sup>a</sup> (n=133)	4 (3.01)	2 (1.50)	2 (1.50)	8 (6.02)	6.732	0.007
	CG <sup>b</sup> (n=130)	10 (7.69)	8 (6.15)	5 (3.85)	23 (17.69)		
12	OG <sup>a</sup> (n=133)	1 (0.76)	0	0	1 (0.76)	4.377	0.015
	CG <sup>b</sup> (n=13028)	8 (6.25)	4 (3.13)	2 (1.56)	14 (10.94)		

Note: OG<sup>a</sup>: observation group, n(children)=133, n(teeth)=155; CG<sup>b</sup>: control group, n(children)=130, n(teeth)=155.



**Figure 4.** Comparison of QoL between two groups before surgery and at 3, 6, and 12 months. OG: observation group, n(children)=133, n(teeth)=155; CG: control group, n(children)=130, n(teeth)=155. Note: \*P<0.05. QoL: Quality of Life.

two groups, it was found that the total incidence of adverse reactions in OG was significantly lower at 3, 6, and 12 months than that in CG (P=0.018, P=0.007, P=0.015, respectively) (Table 2).

### QoL between two groups

The comparison of QoL between two groups at preoperative and 3, 6, 12 months after surgery are shown in Figure 4. ANOVA was performed and the results showed significant differences from different time groups in QoL (F (1, 132)=20.833, P<0.001; F (1, 132)=15.875, P=0.015; F (2, 132)=14.260, P=0.017; F (2, 132)=29.122, P<0.001, respectively). Before

surgery, there was no significant difference in the Child-OIDP scores between the two groups of children (P>0.05). At 3, 6, and 12 months after surgery, the Child-OIDP scores of the OG were statistically higher than those of the CG (P=0.037, P=0.012, P=0.028, respectively).

### Logistic regression analysis of prognosis

Patients with postoperative complications were included in the group with poor prognosis (n=40), while the remaining patients were assigned to the group with good prognosis (n=223). Univariate analysis showed that there was no significant difference in gender, age (months), lesion and apical foramen (all P>0.05); however, the age (months), gender, tooth position (upper or lower primary molars), lesion tooth position (first or second primary molars), and treatment method of the patient at the time of treatment were identified as potential risk factors. Multivariate logistic regression analysis showed that, the teeth location (maxillary or mandibular primary molars) and treatment (MTA pulpotomy or root canal treatment) were important risk factors for poor prognosis in the study population. Children with mandibular primary molars and those receiving root canal treatment had an increased risk of poor prognosis (P=0.047, P=0.001, respectively), details are shown in Table 3.

### Discussion

The results of relevant oral epidemiological surveys show that, in China, the prevalence of caries among children aged 3 and 5 years old are as high as 51% and 71% respectively [17]. Primary teeth are an important chewing organ for children, playing an important role in the

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**Table 3.** Univariate and multivariate logistic regression models for risk factors affecting prognosis of primary molar pulpectomy

Variable	Univariate HR (95% CI)	P	Multivariate HR (95% CI)	P
Age	1.01 (1.00-1.03)	0.159	1.00 (0.98-1.02)	0.719
Gender		0.749		0.614
Male	1 (Indicator)		1 (Indicator)	
Female	0.95 (0.68-1.32)		1.09 (0.77-1.54)	
Teeth Location		0.030		0.047
Maxillary	1 (Indicator)		1 (Indicator)	
Mandibular	1.52 (1.04-2.21)		1.47 (1.00-2.16)	
Lesion		0.621		0.798
First	1 (Indicator)		1 (Indicator)	
Second	1.08 (0.94-1.10)		1.01 (0.99-1.03)	
Treatment		<0.001		0.001
MTA pulpotomy	1 (Indicator)		1 (Indicator)	
Root canal treatment	2.44 (1.73-3.42)		1.85 (1.29-2.63)	
Apical Foramen		0.053		0.050
Close	1 (Indicator)		1 (Indicator)	
Not	1.69 (1.34-2.03)		1.76 (0.92-2.54)	

Note: n(children)=263, n(teeth)=310.

eruption of permanent teeth and the development of the jaw, with breast molars being the most important. Because primary molars have special histological characteristics, namely low mineralization, high pulp angle, weak acid resistance, thin tooth enamel and dentin, they are prone to caries. After ingesting food, the crevices in the crown of deciduous teeth are prone to retain plaque and food debris, which can significantly increase the incidence of caries in children's deciduous teeth [18]. According to a systematic review of 2410 studies, the prevalence of early childhood dental caries ranged from 23% to 90%, with most of them exceeding 50% [19]. After the decay of primary molars, there is a significant secondary pain sensation caused by stimulation such as sweetness and sourness, cold and heat. After the stimulation disappears, the pain also disappears. In addition, children have limited symptoms, making it very easy to progress to deep caries in a short period of time. After deep caries occur in primary molars, it can affect the child's chewing function and digestion and absorption of food [20]. In addition, caries of primary teeth can also lead to an increase in the incidence of new permanent tooth caries. Study [21] has shown that caries of the second primary molars were an important risk factor for caries of the first permanent molar. If not

treated timely, caries can progress to apical periodontitis, affecting subsequent permanent tooth germs and resulting in incomplete enamel development. If local alveolar bone damage is found, it can also affect the eruption position and sequence of inherited permanent teeth, leading to a dislocation deformity. Pulp trauma or infection can cause loss of tooth vitality, but treatment does not necessarily require the extraction of deciduous teeth. With effective treatment methods, deciduous teeth can still be preserved in the oral cavity for a long time.

This study compared the short-term and long-term efficacy of MTA pulpotomy and root canal treatment in early pulpitis of primary molars. Within 3 months after surgery, the clinical and X-ray response rates of the two groups were both over 95%, and the difference was not significant. This indicates that MTA pulpotomy and root canal treatment are safe and effective in treating pediatric pulpitis in the short term. However, at 6 and 12 months after surgery, children with MTA pulpotomy in OG had higher clinical and imaging response rates compared to children with root canal treatment in CG. At 1-year follow up, the success rate of MTA was 99.24%, significantly higher than the 94.53% of root canal treatment. The use of MTA as a pulp capping agent in pulpotomy for

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primary molars can effectively maintain the surgical effect, and the long-term efficacy was more ideal, consistent with the study of Wang et al. [22]. Also, the study of Zhang et al. [15] showed that in the root canal treatment group, the main reasons for failure were root bifurcation, root resorption, and pulp plate fracture. It was speculated that the nutrition and growth promoting effect of losing vital pulp on the root were the main reasons for the long-term increase after surgery.

In terms of safety, a comparative analysis was conducted between the two groups on the incidence of tooth tapping pain, periodontal redness, and infection. The results showed that at 3, 6, and 12 months after surgery, the total incidence of complications in the OG was significantly lower than in the CG (12.78% vs 23.08%; 6.02% vs 17.69%; 0.76% vs 10.94%), indicating that MTA pulpotomy is safer than root canal treatment in treating early pulpitis of primary molars. This is similar to the analysis of the safety of MTA pulpotomy of Dong et al. [23]. At the same time, the Child-OIDP scores of the OG were observed before surgery, and 3, 6, and 12 months after surgery. It was found that the children in the OG had higher Child-OIDP scores than CG. This suggests that MTA pulpotomy can reduce the adverse effects on the physical and mental state of the children, improve their long-term quality of life, and promote their healthy growth. Finally, multivariate logistic regression analysis found that mandatory primary molars and root canal treatment were independent risk factors for the prognosis. The success rate of MTA pulpotomy was significantly higher than that for mandibular primary molars. MTA pulpotomy is beneficial for reducing the risk of poor prognosis in children with early pulpitis of primary molars within 12 months after treatment. Some studies [24, 25] have compared the prognosis of pulpotomy for mandibular and maxillary primary molars and reported that the failure rate of pulpotomy for mandibular primary molars was higher than that for maxillary primary molars, which was consistent with our results. However, other studies [26, 27] found no significant differences between them. The difference in the success rate of pulp resection between mandibular and maxillary primary molars is not yet clear, which may be due to differences in the complexity of the root canal system. The anatomic structure of the root canal system of deciduous

molars and the number and type of auxiliary root canals varied greatly. In addition, when the permanent tooth germ and root overlap with the bone between the roots, it is usually difficult to observe the initial radiologic changes in bone density between or around the roots of the maxillary molars. However, this is not a sufficient reason for conducting three-dimensional radiographic examinations.

However, this study has some limitations. First, we only used some variables to predict the risk of dental caries and used them as the criteria for evaluating the indications of pit and fissure sealants. However, these variables have been widely recognized as risk factors for poor oral health in children [28]. In addition, this is a retrospective study, so the experimental reliability is weaker than in a randomized controlled trial (RCT). Thus, we hope to further implement a large-sample, multi-center RCT study in future research to verify the effect of MTA pulpotomy for treatment of early pulpitis of primary molars.

As far as we know, this study is the first attempt to explore the application effect under a larger sample size based on previous studies. Compared to similar studies, the innovation of this study is that we confirmed the positive impact of MTA pulpotomy in the treatment of early pulpitis of primary molars from aspects such as clinical efficacy, response rate in X-ray imaging, levels of inflammatory factors, incidence of adverse reactions, and quality of life. Then, we analyzed the factors that affect patient prognosis to make the study more comprehensive.

Therefore, MTA pulpotomy has a significant effect on improving the efficacy of early pulpotomy of primary molars patients while ensuring patient safety. It also has a positive impact on the level of inflammatory factors, occurrence of adverse reactions, and quality of life of patients.

### Disclosure of conflict of interest

None.

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