

Review Article

Efficacy of vitapex on chronic periapical periodontitis of deciduous teeth in children and risk factors affecting the efficacy

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Abstract: To explore the efficacy of Vitapex on chronic periapical periodontitis of deciduous teeth in children and the risk factors affecting the efficacy. A total 188 children with chronic periapical periodontitis of their deciduous teeth were admitted to our hospital and enrolled, of which 82 patients were treated with zinc oxide-eugenol paste as a control group, and the rest were treated with Vitapex paste as an intervention group. The clinical indexes (time for restoration of dental function and treatment time), efficacy, and adverse reactions during treatment of the two groups were evaluated. The verbal rating scale (VRS) was employed to evaluate the pain degree of the children, enzyme-linked immuno-sorbent assay (ELISA) was used to determine the levels of serum inflammatory factors in the children, including interleukin-6 (IL-6), interleukin-1 β (IL-1 β), and tumor necrosis factor- α (TNF- α), and logistic regression was used to analyze risk factors affecting treatment efficacy in the children. After treatment, the intervention group experienced shorter time for restoration of normal dental function and shorter treatment time than the control group, as well as showing a higher total effective rate than the control group. In addition, after treatment, the incidence rate of adverse reactions of the intervention group was significantly lower than that of the control group, and the VRS score of the intervention group was lower than that of the control group. The levels of inflammatory factors (IL-6, IL-1 β and TNF- α) in the intervention group were also lower than those in the control group. The multivariate logistic regression analysis revealed that tooth brushing, premature delivery, treatment methods, time for restoration of dental function, treatment time, VRS score, and IL-6, IL-1 β , and TNF- α were all risk factors affecting treatment efficacy in the children. Vitapex is effective in alleviating pain degree, shortening the time for restoration of normal dental function, and lowering the levels of inflammatory factors in the treatment of chronic periapical periodontitis of deciduous teeth.

Keywords: Vitapex paste, zinc oxide-eugenol paste, chronic periapical periodontitis of deciduous teeth, efficacy, risk factors

Introduction

Periodontal disease is a complex disease with many properties [1]. It is reported that children and adolescents may suffer from various kinds of periodontitis [2]. Mainly caused by bacterial infection, periodontitis can lead to inflammatory responses, and even loss of teeth [3-7]. Chronic periapical periodontitis is one of the main causes of premature loss of deciduous teeth, and it is related to infection of dental pulp in children [8]. One study has concluded that bone loss is likely to occur around the primary molars in children between 5 and 8 years old, causing aggressive periodontitis accompanied by premature loss of deciduous teeth, and the

study proposed early diagnosis and treatment for it [9]. However, clinical treatment of chronic periapical periodontitis is complex due to a difficulty of instrument application and complex root tips.

Dental pulp of deciduous teeth is usually treated by root canal and filling with iodoform paste, calcium hydroxide, and zinc oxide-eugenol. However, one clinical study has pointed out that zinc oxide-eugenol has slow tooth absorption and simulates root tip tissues, resulting in cementum and bone necrosis [10]. Vitapex paste can diffuse out or be absorbed by periodontal macrophages of children within 1 to 2 weeks after being filled in at the tooth root and

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around the cusp, and it is weakly antibacterial [11]. Some studies have concluded that vitapex paste is an ideal material for root canal fillings that can be absorbed extremely quickly in clinical practice [12]. For example, a study by Tang Y et al. [13] has shown that vitapex paste is effective for root canal fillings in treating chronic periapical periodontitis, and contributes to low recurrence of the periodontitis.

At present, there are few studies on the efficacy of vitapex paste and zinc oxide-eugenol paste on chronic periapical periodontitis of deciduous teeth and the related influencing factors, so we decided to compare the efficacy of each of them on chronic periapical periodontitis of deciduous teeth, which is of great significance for the selection of treatment strategies for children with this disease.

Materials and methods

General materials

A total of 188 children with chronic periapical periodontitis of deciduous teeth were admitted to Jinzhou 968 Hospital and enrolled; of which 82 patients were treated with zinc oxide-eugenol paste as a control group, and the rest were treated with vitapex paste as an intervention group. The control group consisted of 45 males and 37 females, aged between 2 and 6 years old, with an average age of (5.43 ± 1.41) years. The intervention group consisted of 51 males and 55 females, aged between 2 and 7 years old, with an average age of (5.04 ± 1.40) years. This study was approved by the Ethics Committee of Jinzhou 968 Hospital, and all participants and their family members signed informed consent forms after understanding the study. The inclusion criteria of the children were as follows: Children diagnosed with chronic periapical periodontitis of their deciduous teeth [14], children who had not received pulp therapy and had not taken antibiotics within 2 weeks, and children with complete clinical data. The exclusion criteria were as follows: Children who dropped out from the experiment, or who had taken drugs that may affect indexes of this study, children with other comorbid oral diseases or infectious diseases, and children lost to follow up.

Efficacy assessment

Treatment of a child with the following outcomes was determined as curative: The child

did not have any subjective symptoms after treatment, and he/she showed no recurrence of symptoms and experienced good chewing function recovery during six month follow-up. Treatment of a child with the following outcomes was determined as effective: The child did not have any subjective symptoms after treatment, and he/she showed no recurrence of symptoms and experienced good chewing function recovery during a six month follow-up, but he/she felt a slight pain in percussion. Treatment of a child with the following outcomes was determined as ineffective: The child had subjective symptoms after treatment, and he/she showed recurrence of symptoms in the affected teeth during a six month follow-up. Moreover, he/she felt a strong pain in percussion. The total effective rate = (The number of patients with curative efficacy + the number of patients with effective efficacy)/the total number of patients $\times 100\%$.

Treatment methods

Before treatment, the overall situation of the periodontal tissues in the children in the both groups was evaluated and analyzed using X ray to understand the periodontal lesions in the children, and correspondingly root canal fillings was carried out. Opening of the pulp chamber was required in the children under anesthesia, in order to uncover the root of the pulp chamber to remove necrotic pulp and histocytes, and the sinus passage was flushed with normal saline. Afterwards, the root canal was repeatedly rinsed and disinfected with 3% hydrogen peroxide and 0.9% sodium chloride. After the water was sucked out and dried with cotton balls, any children with pus exudation were given open drainage in the root canal for 1-2 days, and then the open site was sealed with zinc oxide temporarily according to the situation of each child. Preparations were made for root canal fillings according to the situation of the children in the return visit. Children in the intervention group were given root canal fillings with vitapex paste at a filling dosage determined according to the condition of the children as follows: The tip of an injection syringe with vitapex paste (Morita & Company, Japan, YYJ-075-VITAPEX2) was inserted gently to 4/5 of the root canal. Subsequently, the vitapex paste was gently injected to the root canal, and then the syringe was slowly lifted to fill the inside of the root canal with paste. Afterwards, gutta-percha points were added in the root canal after the excess paste was

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Table 1. Comparison between the two groups in general data [n (%), mean \pm SD]

Factor	n	The control group (n=82)	The intervention group (n=106)	χ^2/t	P-value
Sex				0.847	0.358
Male	96	45 (54.88)	51 (48.11)		
Female	92	37 (45.12)	55 (51.89)		
Average age (Y)	188	5.43 \pm 1.41	5.04 \pm 1.40	1.888	0.061
Course of disease (Month)	188	7.01 \pm 0.31	7.07 \pm 0.33	1.269	0.206
Disease site				1.901	0.168
Primary molar	118	56 (68.29)	62 (58.49)		
Deciduous front teeth	70	26 (31.71)	44 (41.51)		
Halitosis				0.007	0.940
No	98	43 (52.44)	55 (51.89)		
Yes	90	39 (47.56)	51 (48.11)		
Mode of delivery				0.653	0.419
Caesarean	90	42 (51.22)	48 (45.28)		
Eutocia	98	40 (48.78)	58 (54.72)		
Mother's childbearing age				1.951	0.163
<30 years old	90	44 (53.66)	46 (43.40)		
\geq 30 years old	98	38 (46.34)	60 (56.60)		
Father's childbearing age				1.074	0.300
<30 years old	86	34 (41.46)	52 (49.06)		
\geq 30 years old	102	48 (58.54)	54 (50.94)		
Tooth brushing (day)				1.933	0.380
No tooth brushing	65	24 (29.27)	41 (38.68)		
Once	72	33 (40.24)	39 (36.79)		
Twice	51	25 (30.49)	26 (24.53)		
Premature birth				1.341	0.247
Yes	108	51 (62.20)	57 (53.77)		
No	80	31 (37.80)	49 (46.23)		

Table 2. Clinical symptoms of the two groups (mean \pm SD)

Group	The number of children	Time for restoration of dental function (days)	Treatment time (days)
The control group	82	26.49 \pm 3.96	14.42 \pm 3.99
The intervention group	106	17.61 \pm 2.05	8.84 \pm 2.03
T	-	19.910	12.470
P-value	-	<0.001	<0.001

cleaned. Children in the control group were given root canal filling with zinc oxide-eugenol paste (Shanghai Dental Material Co., Ltd., item number: H20023630049; the ratio of powder to liquid was 1.6 g:0.5 ml) at a filling dosage determined according to the condition of the children. The zinc oxide-eugenol paste was injected into the root canal with an enlarge needle, and the gutta-percha points were added in the root canal after the excess paste was cleaned.

5 were analyzed using the continuity correction chi square test. Measurement data were expressed as the mean \pm standard error of mean (mean \pm SEM), and compared between groups using the independent-samples T test, and compared within groups using the paired t test. The data were visualized as figures using GraphPad Prism 6 (GraphPad Software, San Diego, United States). Logistics multivariate regression analysis was carried out using SPSS 22.0 (Beijing EASYBIO Technology Co.,

Outcome measures

The adverse reactions after treatment, time for restoration of normal dental function, and treatment time in the two groups were recorded.

The pain degree of the children during treatment was evaluated using the verbal rating scale (VRS) with a total of 10 points. A higher score indicates more severe pain.

The expression of interleukin-6 (IL-6), interleukin-1 β (IL-1 β), and tumor necrosis factor- α (TNF- α) of the two groups of patients was determined using corresponding enzyme-linked immunosorbent assay (ELISA) kits (Shanghai Hengfei Biotechnology Co., Ltd., China, K101536P, 130-093-563, and 130-110-100) according to the kit instructions.

Statistical analysis

In this study, enumeration data were expressed as the number of cases/percentage (n/%), and compared between groups using the chi-square test. Data with theoretical frequency in chi-square test less than

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Table 3. Clinical efficacy on children in the two groups [n (%)]

Group	n	Recuperative	Effect	Ineffective	The total correction efficiency (%)
The control group	82	29 (35.37)	35 (42.68)	18 (21.95)	64 (78.05)
The intervention group	106	61 (57.55)	37 (34.91)	8 (7.55)	98 (92.45)
χ^2 value	-	-	-	-	8.049
P-value	-	-	-	-	0.005

Table 4. Adverse reactions in the two groups [n (%)]

Item	The control group (n=82)	The intervention group (n=106)	χ^2 value	P-value
Pyorrhea	3 (3.66)	0 (0.00)	3.941	0.047
Facial swelling	4 (4.88)	2 (1.89)	1.339	0.247
Pain during mastication	3 (3.66)	1 (0.94)	1.637	0.201
Total	10 (12.20)	3 (2.83)	6.299	0.012

bearing age, tooth brushing, or premature birth (all $P < 0.05$) (**Table 1**).

Clinical symptoms of the two groups

The intervention group experienced much shorter time for restoration of normal dental

function and treatment time than the control group (both $P < 0.05$) (**Table 2**).

Clinical efficacy of children in the two groups

The total effective rate in the intervention group was significantly higher than that in the control group after treatment (92.45% vs. 78.05%, $P < 0.05$) (**Table 3**).

Adverse reactions in the two groups

Both groups suffered adverse reactions during treatment, and the rate of adverse reactions in the control group was significantly higher than that in the intervention (12.20% vs. 2.83%, $P < 0.05$) (**Table 4**).

VRS score of the two groups

Before treatment, there was no significant difference in VRS score between the two groups ($P > 0.05$). While after treatment, both groups had a lower VRS score, and the intervention group had a significantly lower VRS score than the control group ($P < 0.05$) (**Figure 1**).

Inflammatory factors in the two groups

Before treatment, the two groups were not significantly different in the levels of serum IL-6, IL-1 β , and TNF- α (all $P > 0.05$). While after treatment, both groups showed lower levels of serum IL-6, IL-1 β , and TNF- α , and the levels of them in the intervention group were significantly lower than those in the control group (all $P < 0.05$) (**Figure 2**).

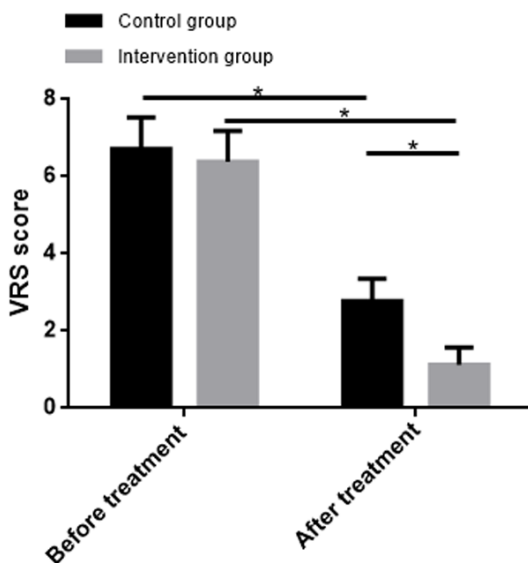


Figure 1. VRS score of the two groups. After treatment, the intervention group had a decreased VRS score, lower than that of the control group. Note: * indicates $P < 0.05$.

Ltd., China) to analyze risk factors affecting treatment efficacy on chronic periapical periodontitis of deciduous teeth. $P < 0.05$ indicates a significant significance.

Results

General materials

There was no significant difference between the two groups in sex, average age, disease course, disease site, halitosis, mode of delivery, mother's childbearing age, father's child-

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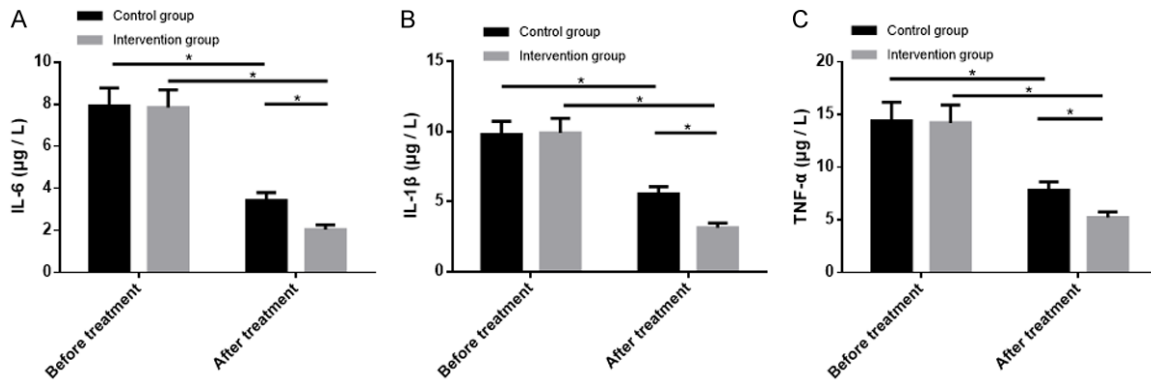


Figure 2. Inflammatory factors in the two groups. A. After treatment, the intervention group showed significantly lower level of serum IL-6, lower than that in the control group. B. After treatment, the intervention group showed significantly lower level of serum IL-1 β , lower than that in the control group. C. After treatment, the intervention group showed significantly lower level of serum TNF- α , lower than that in the control group. Note: * indicates $P < 0.05$.

Risk factors affecting the efficacy of chronic periapical periodontitis in deciduous teeth

The comparison between children with effective efficacy and children with ineffective efficacy in terms of clinical parameters and relevant indicators revealed that in this study, there were 162 patients with effective efficacy and 26 patients with ineffective efficacy. There was no significant difference between the effective efficacy group and the ineffective efficacy group in sex, average age, course of disease, disease site, halitosis, mode of delivery, mother's childbearing age, and father's childbearing age (all $P > 0.05$). There was however a significant difference between them in tooth brushing, premature delivery, treatment method, time for restoration of normal dental function, treatment time, VRS score, and IL-6, IL-1 β , and TNF- α (all $P < 0.05$). The factors with significant differences were analyzed using multivariate logistic regression, and it was found that tooth brushing ($P = 0.028$), premature delivery ($P = 0.026$), treatment method ($P = 0.008$), time for restoration of dental function ($P = 0.022$), treatment time ($P = 0.031$), VRS score ($P = 0.012$), and IL-6 ($P = 0.013$), IL-1 β ($P = 0.011$), and TNF- α ($P = 0.014$) were independent risk factors affecting treatment efficacy on the children. As shown in **Tables 5-7**.

Discussion

Periodontitis is a microbial infection in the oral cavity, manifested by gingival inflammation, which can be classified into two forms, aggressive periodontitis and chronic periodonti-

tis, according to the severity. Chronic periodontitis affects 50% of population in the world [15, 16]. Chronic apical periodontitis is associated with hyperextended radial bacterial biofilm on cementum [17], which is the main cause of premature loss of deciduous teeth, and may also cause permanent tooth dysplasia in children [18]. One study has concluded that because of the frequent dental pulp replacement in deciduous teeth of children, treatment procedures in the dental department need to be developed and improved [19].

In the past, many scholars have contributed to relevant research on the efficacy and treatment mechanism of vitapex paste and zinc oxide-eugenol paste on teeth. For example, Nurko C et al. [20] used vitapex paste for patients undergoing pulp amputation, and found no significant adverse reactions, but found excellent imaging results in radiation examination. Pilonic KJ et al. [21] have concluded that vitapex paste is a more suitable dental pulp material than zinc oxide-eugenol paste in deciduous teeth resection. In this study, we compared the efficacy of vitapex paste and zinc oxide-eugenol paste, finding that the intervention group experienced much shorter time for restoration of dental function and treatment time than the control group, and also showed significantly higher total effective rates than the control group. This suggested that vitapex paste could shorten the course of treatment and provide excellent efficacy. In this study, children suffered from adverse reactions such as pyorrhea, facial swelling, and pain during mastication, but the adverse reactions were all con-

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Table 5. Univariate analysis of factors affecting treatment efficacy on children with chronic periapical periodontitis of deciduous teeth [n (%), mean \pm SD]

Factor	n	The effective group (n=162)	The ineffective group (n=26)	χ^2/t	P-value
Sex				0.291	0.560
Male	96	84 (87.50)	12 (12.50)		
Female	92	78 (84.78)	14 (15.22)		
Average age (Y)	188	5.41 \pm 1.42	5.14 \pm 1.41	0.901	0.369
Course of disease (Month)	188	7.11 \pm 0.32	7.05 \pm 0.31	0.891	0.374
Disease site				0.332	0.564
Primary molar	118	103 (87.29)	15 (12.71)		
Deciduous front teeth	70	59 (84.29)	11 (15.71)		
Halitosis				0.055	0.815
No	98	85 (86.73)	13 (13.27)		
Yes	90	77 (85.56)	13 (14.44)		
Fetal age (week)				2.125	0.145
<37	90	81 (90.00)	9 (10.00)		
\geq 37	98	81 (82.65)	17 (17.35)		
Mother's childbearing age				1.071	0.301
<30 years old	90	80 (88.89)	10 (11.11)		
\geq 30 years old	98	82 (83.67)	16 (16.33)		
Father's childbearing age				0.002	0.964
<30 years old	86	74 (86.05)	12 (13.95)		
\geq 30 years old	102	88 (86.27)	14 (13.73)		
Tooth brushing (day)				9.704	0.008
No tooth brushing	65	49 (75.38)	16 (24.62)		
Once	72	66 (91.67)	6 (8.33)		
Twice	51	47 (92.16)	4 (7.84)		
Premature birth				4.682	0.031
Yes	108	88 (81.48)	20 (18.52)		
No	80	74 (92.50)	6 (7.50)		
Treatment method				8.049	0.005
Vitapex paste	106	98 (92.45)	8 (7.55)		
Zinc oxide-eugenol paste	82	64 (78.05)	18 (21.95)		
Time for restoration of dental function (days)	188	18.34 \pm 2.12	26.17 \pm 3.82	24.570	<0.001
Treatment time (days)	188	9.02 \pm 2.07	14.77 \pm 4.01	17.470	<0.001
VRS score	188	1.47 \pm 0.24	2.87 \pm 0.54	32.480	<0.001
IL-6 (μ g/L)	188	2.15 \pm 0.21	5.81 \pm 0.56	61.130	<0.001
IL-1 β (μ g/L)	188	5.26 \pm 0.50	7.41 \pm 1.02	17.050	<0.001
TNF- α (μ g/L)	188	5.13 \pm 0.45	8.13 \pm 1.59	19.790	<0.001

trollable, and the adverse reactions in the intervention group were less than those in the control group, suggesting that vitapex was safer than zinc oxide-eugenol.

As the main symptom of dental disease, pain can change people's overall function [22], and it may be caused by many factors including chemical and bacterial stimulation of periapical tissues. Clinical studies have revealed that

infection during root canal therapy for children affects the pain degree after treatment [23]. In our study, patients in the intervention group experienced much slighter pain than those in the control group after treatment, implying that vitapex was more beneficial to relieving the pain of children. Periapical periodontitis often gives rise to inflammatory responses, under which bacteria directly damage periodontal nerve tissues through exotoxins and metabo-

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Table 6. Assignment in logistic multivariate regression analysis

Factor	Variable	Assignment
Tooth brushing	X1	No =0, yes =1
Candy-eating frequency	X2	High =0, low =1
Treatment methods	X3	Treatment with vitapex paste =0, treatment with zinc oxide-eugenol paste =1
Time for restoration of dental function (days)	X4	Continuous variable
Treatment time (days)	X5	Continuous variable
VRS score	X6	Continuous variable
IL-6 (µg/L)	X7	Continuous variable
IL-1β (µg/L)	X8	Continuous variable
TNF-α (µg/L)	X9	Continuous variable

Table 7. Multivariate logistic regression analysis of factors affecting treatment efficacy on patients with periodontitis

Variable	B	S.E	Wals	P-value	OR	95% CI
Tooth brushing	1.034	0.412	5.328	0.028	2.342	1.251-6.024
Candy-eating frequency	1.297	0.644	5.332	0.026	1.162	0.532-2.423
Treatment methods	2.345	0.982	5.318	0.008	5.422	2.711-10.844
Time for restoration of dental function (days)	1.783	0.383	5.028	0.022	4.973	2.486-9.946
Treatment time (days)	1.649	0.489	5.834	0.031	3.763	1.881-7.526
VRS score	1.367	0.734	7.834	0.012	3.872	1.936-7.744
IL-6 (µg/L)	1.338	0.748	9.535	0.013	3.232	1.121-6.464
IL-1β (µg/L)	1.461	0.517	4.728	0.011	3.184	1.592-6.368
TNF-α (µg/L)	1.239	0.553	5.123	0.014	3.193	1.594-6.386

lites. Gene polymorphisms of pre-inflammatory cytokines such as IL-6, IL-1β, IFN-γ, and TNF-α are also strongly linked to patients with chronic apical periodontitis [24, 25]. We studied the effects of the two treatment methods on IL-6, IL-1β, and TNF-α in children, finding that the intervention group showed lower levels of those factors after treatment, which indicated that vitapex was strongly effective in inhibiting excessive inflammation of chronic periapical periodontitis of deciduous teeth. The inhibition of inflammatory reactions may be the mechanism of alleviating pain in children. At the end of our study, we analyzed the risk factors that affect the treatment efficacy on children in the two groups, finding that tooth brushing, candy-eating frequency, treatment method, time for restoration of dental function, treatment time, VRS score, IL-6, IL-1β, and TNF-α were all risk factors that affect the efficacy of children with chronic periapical periodontitis of their deciduous teeth. This implied that children who did not brush their teeth, ate too much candy, received zinc oxide-eugenol treatment, and had high levels of IL-6, IL-1β, and TNF-α faced a higher risk of treatment failure. One study by

Corbella S et al. [26] has concluded that premature delivery is a factor affecting the treatment efficacy on periodontitis patients, which is similar to this study.

This study selected research subjects in strict accordance with the inclusion and exclusion criteria, so the clinical baseline data of the two groups were not significantly different, which ensured the preciseness and reliability of the study. However, there is still a room for improvement in this study. For example, we can expand the research population, and supplement the study for the impact of the treatment on sleep quality, and we can also follow up the children longer than six months after treatment to analyze the recovery, so as to further improve and support the research results.

Conclusion

Vitapex is effective in alleviating pain degree, shortening the time for restoration of dental function, and lowering the levels of inflammatory factors in the treatment of chronic periapical periodontitis of deciduous teeth.

Disclosure of conflict of interest

None.

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