

EVALUATION OF THE CLINICAL AND RADIOGRAPHIC
SUCCESS OF DIFFERENT ANTIBIOTIC COMBINATIONS
IN LESION STERILIZATION AND TISSUE REPAIR
THERAPY FOR INFECTED PRIMARY MOLAR TEETH

Rüveyda Nur Culfa^{1✉}, Pınar Demir²

Received on March 11, 2025

Presented by D. Damianov, Member of BAS, on April 29, 2025

Abstract

This study aimed to assess the clinical and radiographic success of lesion sterilization and tissue repair (LSTR) therapy with different antibiotic combinations, focusing on evaluating whether the alternative combination of clindamycin instead of minocycline is as effective as the standard 3Mix-MP formulation. The study included 50 mandibular primary molars from 43 children (aged 4–10) with irreversible pulpitis or necrosis. Follow-ups were conducted at 1, 3, 6, 9, and 12 months to assess clinical and radiographic outcomes. No significant differences were found between the clinical, radiographic, and overall success rates of 3Mix-MP and Alternative 3Mix-MP at 12 months ($p = 1.000$, $p = 0.612$, $p = 1.000$). A significant decrease in success rates for the 3Mix-MP group was observed over time ($p = 0.029$, $p = 0.003$, $p = 0.019$). Primary second molars were more successful than primary first molars at 12 months ($p = 0.011$). Clinical success (90%) was greater than radiographic success (74%) throughout the follow-up period. Comparable success was observed with both 3Mix-MP and Alternative 3Mix-MP mixture, where clindamycin replaced minocycline, suggesting that it is a viable alternative. These findings support LSTR therapy as a reliable method for non-instrumental endodontic treatment, with alternative antibiotic combinations offering a safe and effective option.

Key words: clindamycin, primary teeth, antibiotics, pulpitis, pulp necrosis

Introduction. Primary endodontic infections are often associated with clinical symptoms such as pain, periapical lesions, tenderness to percussion, swelling, and sinus tract formation [1]. The American Academy of Pediatric Dentistry (AAPD) stated that treatment options for these conditions include extraction, root canal therapy (pulpectomy), or lesion sterilization and tissue repair (LSTR) [2].

The technique offers several advantages, including simplicity and overall effectiveness, as it is faster and less invasive than traditional methods [3]. In primary dentition, LSTR has demonstrated a high rate of clinical success, making it a viable substitute for pulpectomy [4,5].

Clinical evaluations are important for dentists to understand the success of alternative materials they can use.

Materials and methods. Ethical considerations. Approval for this study was received from the Clinical Research Ethics Committee of Inonu University in Malatya, Türkiye (Protocol: 2022/74), and the study was conducted in accordance with the World Medical Association's Declaration of Helsinki [7]. Verbal and written information was provided to the parents, and informed consent was obtained.

Study design and patient selection. This study was a randomized controlled clinical trial that followed the recommendations of the Consolidated Standards of Reporting Trials (CONSORT). At least 21 teeth per group were determined, with an effect size of 0.90, a confidence level of 0.95 and a statistical power of 0.80 [8]. LSTR treatment was applied to 29 teeth in each group to ensure the required sample size. Fifty-eight mandibular primary molar teeth from 51 systemically healthy patients aged 4–10 years were included. However, due to the Kahramanmaraş earthquake on February 6, 2023, 8 children with 8 primary molars were unable to attend follow-up visits and were excluded from the study. Teeth meeting the inclusion criteria were randomized without consideration of their diagnosis or tooth group. Randomization was performed via an online resource (<https://www.randomizer.org>).

The inclusion criteria for the study consisted of the following: spontaneous pain, pain on percussion, the presence of abnormal or pathological mobility, the presence of a sinus tract or dentoalveolar abscess, widening of the periodontal ligament, periradicular radiolucency, and evidence of external and/or internal resorption.

On the other hand, the exclusion criteria included patients who required infective endocarditis prophylaxis, those who had used antibiotics in the two weeks prior to treatment, or individuals allergic to the medications used in the study. Additional exclusion criteria were teeth with pulp floor perforation, advanced internal and/or external root resorption, root canal obliteration, excessive bone loss in the furcation area involving the permanent tooth follicle, and teeth with severe coronal destruction deemed nonrestorable.

Preparation of antibiotic pastes. Metronidazole (Flagyl 500 mg tablets, Sanofi-Aventis, Türkiye), ciprofloxacin (Cipro, 750 mg tablets, Biofarma, Türkiye), minocycline (Minoz, 100 mg, Ranbaxy, India) and clindamycin (Klindan, 150 mg capsules, BİLİM, Türkiye) were pulverized after the coating was peeled off. The drugs were renewed after one month and mixed just before use. All powders were mixed in a 1:1:1 ratio, and equal amounts of propylene glycol and macrogol (Sigma-Aldrich®, USA) were mixed in a separate glass as carriers. Then, 3Mix-MP (metronidazole, ciprofloxacin, and minocycline combined with macrogol and propylene glycol) or Alternative 3Mix-MP mixtures (clindamycin, metronidazole, and ciprofloxacin combined with macrogol and propylene glycol) were formed, as seven parts of the powder and one part of the liquid were mixed on a glass surface [9].

Clinical procedures. All the clinical procedures were carried out by one clinician with two years of clinical experience in pediatric dentistry under rubber dam isolation and local anaesthesia via mandibular nerve block, (Maxicaine Fort Ampoule, VEM, Türkiye). After the removal of carious tissues, an endodontic cavity was prepared, and infected coronal pulp tissue was removed up to the canal orifices via a sterile round steel bur. A sterile round steel bur was then used to prepare a medication cavity 2 mm deep and 1 mm wide. The root canals were not instrumented, and only the access cavity was irrigated with a 2.5% NaOCl solution. In cases where haemostasis could not be achieved, a sterile cotton pellet soaked in 5% NaOCl was placed in the pulp chamber and left for 1 minute. Once haemostasis was achieved, the endodontic cavity was dried using a sterile, dry cotton pellet. Pastes were then applied to the medication cavity and covered with a glass ionomer cement (Nova Glass II F, Imicryl, Türkiye) and a stainless steel crown (Kids Crown, Shinhung, Seoul, Korea) at the same visit.

Clinical and radiographic evaluations were performed at 1, 3, 6, 9, and 12 months. During follow-up, the teeth were assessed on the basis of the following clinical criteria: pain, dentoalveolar abscess and/or fistula, and tooth loss. The radiographic criterion was periapical radiolucency. If at least one of the clinical findings was present, the treatment was considered unsuccessful. However, even if teeth fail radiographically, they are not classified as clinical or overall failure if no clinical signs are present. Both radiographic and clinical observations were carried out by two precalibrated and blinded dentists (RNC and PD). The Kappa test showed excellent agreement between observers for both clinical success (Kappa = 1.000) and radiographic success (Kappa = 0.947), with both results being highly significant ($p < 0.001$).

Statistical analyses. The data were analyzed via IBM SPSS V.23. Fisher's exact test and Yates' correction were used to examine relationships between categorical variables. The Kaplan–Meier test was applied to compare survival times according to the materials used. Cochran's Q test was used to compare success rates over time within materials. The Kappa test was used to assess interob-

server agreement. Categorical data are presented as frequencies (percentages). A significance level of $p < 0.050$ was considered statistically significant.

Results. At the outset, LSTR treatment was applied to 50 teeth from 43 children (18 girls, 25 boys) aged 4–10 years (mean age: 6.16 ± 1.67). A total of 15 mandibular primary first molars and 35 mandibular primary second molars were treated in this study. Twenty-eight teeth were treated with 3Mix-MP, and 22 teeth were treated with Alternative 3Mix-MP.

All the clinical symptoms were completely resolved, and the radiographic symptoms remained the same at the first month of assessment, so they were not included in the statistical evaluations. Clinical diagnosis before treatment showed a 50:50 irreversible pulpitis-necrosis ratio in 3Mix-MP cases versus 31.8:68.2 for the alternative formulation ($p > 0.05$).

A total of 7 teeth of 50 primary molars were extracted due to failure. At the 9th month, one instance of early tooth exfoliation was observed in Alternative 3Mix-MP group. At 12 months, one instance of on-time tooth exfoliation was recorded in Alternative 3Mix-MP group, whereas in the 3Mix-MP group, two cases of early and two cases of on-time tooth exfoliation were observed. Regarding physiological exfoliation, cases with early tooth loss were still considered successful when the timing aligned with eruption patterns of the successor tooth (Fig. 1).

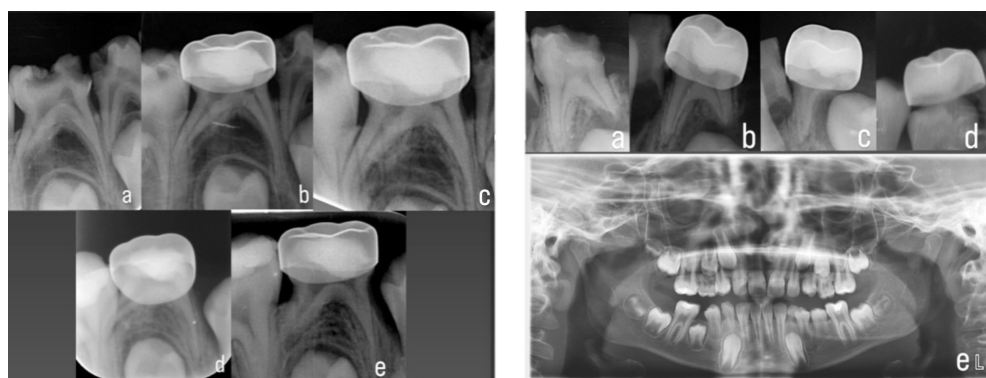


Fig. 1. Left: Radiographic follow-up of LSTR treatment with 3Mix-MP for tooth number 85. a. Pre-treatment periapical radiograph. b. 3rd-month follow-up, radiolucency in the furcation area remains stable. c. 6th-month follow-up, complete healing of the periapical radiolucency d. 9th-month follow-up, healed periapical area. e. 12th-month follow-up, healed periapical area. Right: Radiographic follow-up of LSTR treatment with Alternative 3Mix-MP for tooth number 74. a. Pre-treatment periapical radiograph. b. 3-month follow-up, reduction in radiolucency. c. 6-month follow-up, physiological resorption observed in the distal root. d. 9-month follow-up, physiological resorption, tooth extraction performed. e. Post-extraction panoramic radiograph

Discussion. The acceptability of LSTR is increasing, as recent studies have reported promising success rates. However, few studies have evaluated the success and effects of the medications used in LSTR therapy.

COLL et al. [2] recommended LSTR therapy for patients with at least 12 months of retention of healthy teeth in the oral cavity to ensure space preservation. The study revealed that 3Mix antibiotic mixtures containing tetracycline had a significantly lower success rate (56%) than did tetracycline-free antibiotic combinations (76%). Similarly, numerous studies have concluded that tetracycline-free mixtures achieve relatively high success rates [10–12]. Given the potential adverse effects of tetracycline in children, the American Academy of Pediatric Dentistry (AAPD) advised clinicians to opt for alternative antibiotic combinations without tetracycline. However, this recommendation remains conditional due to the very low quality of supporting evidence. This highlights the need for further high-quality research to strengthen the scientific basis for clinical decision-making on this subject [13]. At the 12-month follow-up, LSTR therapy demonstrated high overall success rates in this study, with the 3Mix-MP and Alternative 3Mix-MP groups achieving success rates of 85.7% and 86.4%, respectively (Table 1). No significant differences were observed in the clinical, radiographic, or overall success rates between the groups. No significant association was found between treatment outcomes and initial diagnoses (irreversible pulpitis vs. necrosis), likely because both pathology types were similarly distributed between groups (50%:50% in 3Mix-MP vs. 31.8%:68.2% in alternative 3Mix-MP). This balanced baseline distribution may partly explain why no significant correlation was observed between diagnosis and treatment outcomes.

In our study, we found that primary second molars presented significantly higher success rates than did primary first molars (Table 2). Notably, several studies have reported higher success rates for pulpectomies in primary second molars compared to first molars, supporting our findings [14,15]. The anatomical complexity of mandibular first molar mesial canals may explain their poorer prognosis, as such variations challenge consistent treatment efficacy [16]. Future studies should evaluate how tooth type affects treatment success, particularly given the anatomical variations observed.

An in vitro study by KARCZEWSKI et al. [17] revealed that clindamycin could serve as a suitable alternative to minocycline in 3Mix formulations. In another in vitro study, RAFATJOU et al. [6] compared 3Mix with an alternative 3Mix containing clindamycin. Their results indicated that both mixtures had similar effects, with no significant differences between them, and no limitations were identified regarding the use of clindamycin. Clindamycin rarely causes complications or drug interactions, has a long half-life, and is effective against a broad spectrum of both gram (+) and gram (–) anaerobes. Additionally, it penetrates well into most tissues and abscesses. SHANKAR et al. [18] evaluated the clinical and radiographic success of an Alternative 3Mix-MP mixture used in LSTR therapy over a 3-month period. However, the study's short duration is a limitation. The higher concentration demonstrated even greater effectiveness, with both clinical and radiographic success rates of 90.6%. However, a review of the literature revealed no in vivo

T a b l e 1

Clinical, overall and radiographic success at the follow-up appointments

			Materials used		Total	Test statist- tics	<i>p</i>
			3Mix-Mp	Alternative 3Mix-Mp			
Clinical success	3rd month	Yes	28 (100)	21 (95.5)	49 (98)	–	–
		No	0 (0)	1 (4.5)	1 (2)		
	6th month	Yes	28 (100)	21 (95.5)	49 (98)	–	–
		No	0 (0)	1 (4.5)	1 (2)		
	9th month	Yes	28 (100)	21 (95.5)	49 (98)	–	–
		No	0 (0)	1 (4.5)	1 (2)		
	12th month	Yes	25 (89.3)	20 (90.9)	45 (90)	–	1.000*
		No	3 (10.7)	2 (9.1)	5 (10)		
		Test statist- tics	9.000	3.000			
		<i>p</i> ***	0.029	0.392			
Overall success	3rd month	Yes	28 (100) ^b	21 (95.5)	49 (98)	–	–
		No	0 (0)	1 (4.5)	1 (2)		
	6th month	Yes	28 (100) ^b	21 (95.5)	49 (98)	–	–
		No	0 (0)	1 (4.5)	1 (2)		
	9th month	Yes	27 (96.4) ^{ab}	21 (95.5)	48 (96)	–	1.000*
		No	1 (3.6)	1 (4.5)	2 (4)		
	12th month	Yes	24 (85.7) ^a	19 (86.4)	43 (86)	–	1.000*
		No	4 (14.3)	3 (13.6)	7 (14)		
		Test statist- tics	9.923	6.000			
		<i>p</i> ***	0.019	0.112			
Radio- graphic success	3rd month	Yes	28 (100) ^b	21 (95.5) ^b	49 (98)	–	–
		No	0 (0)	1 (4.5)	1 (2)		
	6th month	Yes	25 (89.3) ^{ab}	20 (90.9) ^{ab}	45 (90)	–	1.000*
		No	3 (10.7)	2 (9.1)	5 (10)		
	9th month	Yes	22 (78.6) ^a	16 (72.7) ^{ab}	38 (76)	0.022	0.883**
		No	6 (21.4)	6 (27.3)	12 (24)		
	12th month	Yes	22 (78.6) ^a	15 (68.2) ^a	37 (74)	0.257	0.612**
		No	6 (21.4)	7 (31.8)	13 (26)		
		Test statist- tics	14.143	14.182			
		<i>p</i> ***	0.003	0.003			

*Yates correction; **Fisher's exact test; ***Cochran's Q test; frequency (percentage); a–b: There is no difference between times with the same letter within each material group.

T a b l e 2

Clinical and radiographic success evaluations compared with tooth number at the 12-month follow-up

		Yes	No	Total	Test statistics	p^*
Radiographic success	Teeth number					
	Primary first molars	7 (46.7)	8 (53.3)	15 (30)	–	0.011
	Primary second molars	30 (85.7)	5 (14.3)	35 (70)		
Clinical success	Teeth number					
	Primary first molars	12 (80)	3 (20)	15 (30)	–	0.152
	Primary second molars	33 (94.3)	2 (5.7)	35 (70)		

*Fisher's exact test; frequency (percentage)

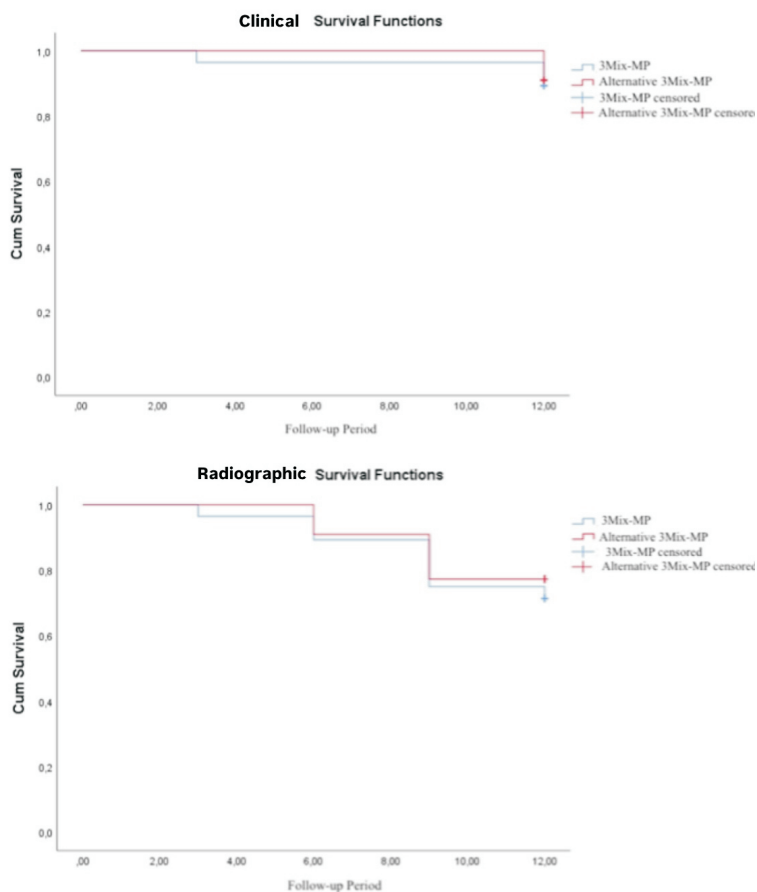


Fig. 2. Clinical and radiographic success survival graph

studies with long-term follow-up on LSTR treatment using a triple antibiotic paste with clindamycin as a substitute for minocycline. In this study, 3Mix-MP and Alternative 3Mix-MP groups demonstrated clinical and radiographic success rates of 100% and 95.5%, respectively, at the 3-month follow-up. The 12-month overall success rates of both mixtures exceeded 85% (Fig. 2).

Conclusion. Clindamycin can be a viable alternative to minocycline in LSTR therapy. Radiographic success significantly decreased over time in both groups, emphasizing the importance of long-term radiographic evaluations even when clinical symptoms resolve. Compared with second molars, mandibular primary first molars had lower success rates, indicating that the prognosis varies by tooth type and should be considered in treatment planning. Further studies with larger sample sizes and longer follow-up periods are needed to validate these findings and strengthen the evidence for the use of LSTR therapy in pediatric dentistry.

REFERENCES

- [1] NAIR P. N. (1997) Apical periodontitis: a dynamic encounter between root canal infection and host response, *Periodontol.* 2000, **13**, 121–148, <https://doi.org/10.1111/j.1600-0757.1997.tb00098.x>.
- [2] COLL J. A., V. DHAR, K. VARGAS et al. (2020) Use of non-vital pulp therapies in primary teeth, *Pediatr. Dent.*, **42**(5), 337–349.
- [3] ALI M., A. A. MORAL, S. M. ABDUL QUADER (2017) Evaluation of pain and tenderness in endodontic treatment of deciduous teeth using (LSTR) 3-Mix MP therapy, *Update Dental College Journal*, **7**(2), 9–14, <https://doi.org/10.3329/updcj.v7i2.36207>.
- [4] PRABHAKAR A. R., E. SRIDEVI, O. S. RAJU, V. SATISH (2008) Endodontic treatment of primary teeth using combination of antibacterial drugs: An in vivo study, *J. Indian Soc. Pedod. Prev. Dent.*, **26**, S5–10, <https://doi.org/10.4103/0970-4388.41746>.
- [5] TAKUSHIGE T., E. V. CRUZ, A. ASGOR MORAL, E. HOSHINO (2004) Endodontic treatment of primary teeth using a combination of antibacterial drugs, *Int. Endod. J.*, **37**, 132–138, <https://doi.org/10.1111/j.0143-2885.2004.00771.x>.
- [6] RAFATJOU R., R. YOUSEFIMASHOUF, M. FARHADIAN, S. AFZALSOLTANI (2019) Evaluation of the antimicrobial efficacy of two combinations of drugs on bacteria taken from infected primary teeth (in vitro), *Eur. Arch. Paediatr. Dent.*, **20**, 609–615, <https://doi.org/10.1007/s40368-019-00446-4>.
- [7] World Medical Association (2013) World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects, *JAMA*, **310**, 2191–2194, <https://doi.org/10.1001/jama.2013.281053>.
- [8] FAUL F., E. ERDFELDER, A. BUCHNER et al. (2009) Statistical power analyses using G* Power 3.1: Tests for correlation and regression analyses, *Behav. Res. Methods*, **41**, 1149–1160, <https://doi.org/10.3758/BRM.41.4.1149>.

- [9] VIJAYARAGHAVAN R., V. M. MATHIAN, A. M. SUNDARAM et al. (2012) Triple antibiotic paste in root canal therapy, *J. Pharm. Bioallied Sci.*, **4**, S230–S233, <https://doi.org/10.4103/0975-7406.100214>.
- [10] THAKUR S., A. DEEP, P. SINGHAL et al. (2021) A randomized control trial comparing the efficacy of 3Mixtatin and Modified 3Mix-MP paste using lesion sterilization and tissue repair technique to conventional root canal treatment in primary molars of children aged 4–8 years: An in vivo study, *Dent. Res. J. (Isfahan)*, **18**, 93, <https://doi.org/10.4103/1735-3327.330874>.
- [11] PARAKH K., R. M. SHETTY (2019) Evaluation of paste containing gentamicin, amoxicillin and metronidazole in endodontic treatment of primary molars in vivo, *Chin. J. Dent. Res.*, **22**(1), 57–64, <https://doi.org/10.3290/j.cjdr.a41776>.
- [12] MOURA J., M. LIMA, N. NOGUEIRA et al. (2021) LSTR antibiotic paste versus zinc oxide and eugenol pulpectomy for the treatment of primary molars with pulp necrosis: a randomized controlled trial, *Pediatr. Dent.*, **43**(6), 435–442.
- [13] American Academy of Pediatric Dentistry (2021) Pulp therapy for primary and immature permanent teeth. *The Reference Manual of Pediatric Dentistry*. Chicago, Ill., 399–407.
- [14] VIJ R., J. A. COLL, P. SHELTON et al. (2004) Caries control and other variables associated with success of primary molar vital pulp therapy, *Pediatr. Dent.*, **26**, 214–220.
- [15] MATALON V., A. SHMAGIN, N. TICKOTSKY et al. (2021) Outcomes of calcium hydroxide with iodoform pulpectomies in primary teeth, *J. Dent. Child. (Chic)*, **88**(1), 46–51.
- [16] AL-RAMMAHI H. M., W. L. CHAI, M. S. NABHAN et al. (2023) Root and canal anatomy of mandibular first molars using micro-computed tomography: a systematic review, *BMC Oral Health*, **23**, 339, <https://doi.org/10.1186/s12903-023-03036-5>.
- [17] KARCZEWSKI A., S. A. FEITOSA, E. I. HAMER et al. (2018) Clindamycin-modified triple antibiotic nanofibers: a stain-free antimicrobial intracanal drug delivery system, *J. Endod.*, **44**(1), 155–162, <https://doi.org/10.1016/j.joen.2017.08.024>.
- [18] SHANKAR K., H. RAMKUMAR, S. DHAKSHINAMOORTHY et al. (2021) Comparison of modified triple antibiotic paste in two concentrations for lesion sterilization and tissue repair in primary molars: An in vivo interventional randomized clinical trial, *Int. J. Clin. Pediatr. Dent.*, **14**, 388–392, <https://doi.org/10.5005/jp-journals-10005-1951>.

¹*Sivas Oral and Dental Health Hospital, Sivas, Turkey*

e-mail: ruveydanurculfa@gmail.com (<https://orcid.org/0000-0001-5276-1571>)

²*Faculty of Dentistry, Nuh Naci Yazgan University, Kayseri, Turkey*

e-mail: pinardemir101@hotmail.com (<https://orcid.org/0000-0003-2030-5429>)