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Pharmacokinetic comparison of two doxycycline-gels for topical subgingival application

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Introduction

Controlled release delivery systems enable the clinician to extend the half-life period of locally administered antibiotics in gingival crevicular fluid (GCF) significantly.

Objectives

The aim of this split-mouth-study was to compare the pharmacokinetic profile of two different doxycycline-gels (DOXY and ATRI) for topical subgingival application. Pharmacokinetics of both doxycycline-gels were analyzed in GCF and saliva.

Material and Methods

Patients:

- 10 patients during supportive therapy
- initial diagnosis: severe chronic periodontitis
- 10 pairs of contralateral infrabony defects
- Pocket probing depth (PPD) mimimum 5 mm and BOP or PPD mimimum 6 mm

Methods:

- random assignment either to the application of DOXY or ATRI.
- Clinical examinations at baseline:
  Plaque index [PlI]
  Pocket probing depth [PPD]
  vertical attachment level [RAL-V],
  gingival index [GI]) showed no significant differences between sites treated with DOXY and ATRI (Table 1).

Patient No./	Tooth a=ATRI d=DOXY	PD [mm]	CAL-V [mm]	GI	PII	amount of applied doxy-cycline-gel [g]
1	a:14	6	8.5	2	2	0.0612
	d:25	6	7.5	2	0	0.0726
2	a:15	7.5	11.5	0	0	0.1996
	d:24	7	9	2	0	0.0334
3	a:14	6	7.5	2	0	0.2836
	d:25	5	6.5	2	0	0.0115
4	a:22	5	8.5	2	2	0.0161
	d:13	5	6.5	2	0	0.0464
5	a:24	7.5	8.5	2	0	0.0846
	d:14	7	12	2	0	0.0099
6	a:14	8	11	0	2	0.0494
	d:23	7	7.5	2	2	0.0113
7	a:15	6	7	2	3	0.0337
	d:21	9	13	2	1	0.0105

8	a:14	8	7.5	2	1	0.0876
	d:24	6	6	2	2	0.0101
9	a:14	7.5	8	2	0	0.0386
	d:25	8	7.5	2	0	0.0432
10	a:13	6	5	2	0	0.0206
	d:21	5	4	2	0	0.022
	a: 6.75		8.30	1.60	1.00	0.088
arithmetic mean	d:6.50		7.95	2.00	0.50	0.027
std. dev.	a:1.06		1.87	0.84	1.16	0.087
	d:1.35		2.73	0.00	0.85	0.021

Table 1: Clinical parameters and applied amount of doxycycline

- In each patient, the site for the first application of the antibiotic gel was randomly chosen from the two contralateral teeth.14 days after the topical application of the first antibiotic gel, the application of the second gel in the contralateral defect took place.
- Samples of sulcus fluid and saliva were drawn baseline, 2, 5 and 24 hours after application, 2, 3, 4, 7, 9 and 11 days after application.
- HPLC-Analysis (Table 2).

column:	symmetryshield RP 8; 5µm 3.0 x 150 mm (Waters)
injected volume:	100 µl
mobile phase:	water-acetronitrile-70 % $HClO_4$ (699;298;5;2.5 V/V) Na_2EDTA (0.6 mmol/l) and oxalate (5 mmol/l)
flowrate:	0.7 ml/min
wavelength:	260 nm
pump:	L-6200 A intelligent (Merck Hitachi)

Table 2: HPLC-Analysis

Results

crevicular fluid specimens (Fig. 1):

- sites treated with ATRI exhibited a faster decrease of median doxycycline concentration (972, 298, 257, and 160 µg/ml measured 2, 5, 24, and 48 hrs. after application) than sites treated with DOXY (1219, 934, 734, and 146 µg/ml).

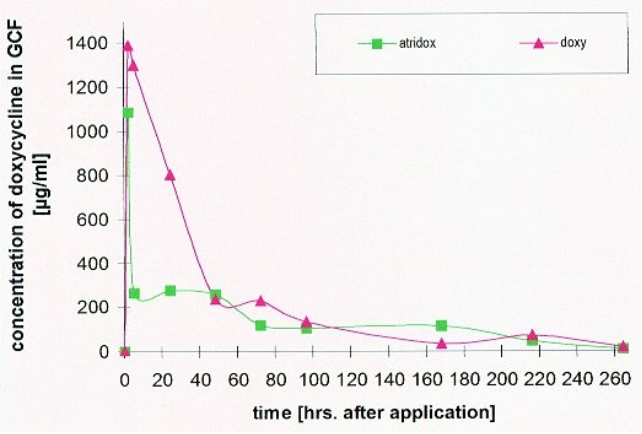

Fig. 1: Time-dependent changes of doxycycline in GCF after application of ATRI- and DOXY-gel

saliva specimens (Fig. 2):

- time-dependent changes of median doxycycline concentration were almost identical for both doxycycline-gels and declined from a maximum 2 hours after application (ATRI: 2984 ng/ml; DOXY: 2951 ng/ml) to zero values 3 days after application.

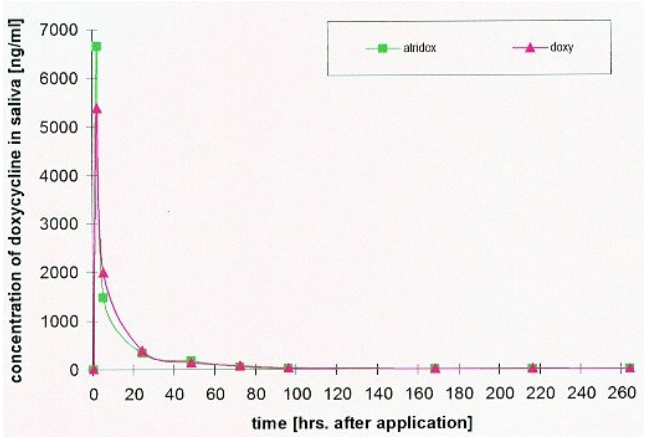

Fig. 2: Time-dependent changes of doxycycline in saliva after application of ATRI- and DOXY-gel

Discussion and Conclusions

- Both doxycycline-gels showed pharmacokinetics of controlled release delivery systems.
- The antibiotic effect seems to be limited mainly to the subgingival sites of application of the doxycycline-gels (ATRI and DOXY).
- The doxycyline-gels (ATRI and DOXY) possess the pharmacokinetic and clinical properties to deliver efficacious levels of antibiotics to the periodontal pocket and to maintain these levels for at least one week without the need of further drug retention by a periodontal dressing.

This poster was submitted by Dr. med. Dr. med. dent. Ti-Sun Kim.

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Poster Faksimile:

Pharmacokinetic comparison of two doxycycline-gels for topical subgingival application

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Goal of the study

Controlled release delivery systems enable the clinician to extend the half-life period of locally administered antibiotics in gingival crevicular fluid (GCF) significantly. The aim of this split-mouth-study was to compare the pharmacokinetic profile of two different doxycycline-gels (DOXY and ATRI) for topical subgingival application. Pharmacokinetics of both doxycycline-gels were analyzed in GCF and saliva.

Materials and Methods

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- initial diagnosis:
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- 10 pairs of contralateral infrabony defects
- PPD > 5 mm and BOP or PPD > 6 mm

Methods:

- random assignment either to the application of DOXY or ATRI
- Clinical examinations at baseline:
  - Plaque index [PII]
  - Pocket probing depth [PPD]
  - vertical attachment level [RAL-V].
  - gingival index [GI] showed no significant differences between sites treated with DOXY and ATRI (Table 1).
- In each patient, the site for the first application of the antibiotic gel was randomly chosen from the two contralateral teeth 14 days after the topical application of the first antibiotic gel, the application of the second gel in the contralateral defect took place.
- Samples of sulcus fluid and saliva were drawn baseline, 2, 5 and 24 hours after application, 2, 3, 4, 7, 9 and 11 days after application
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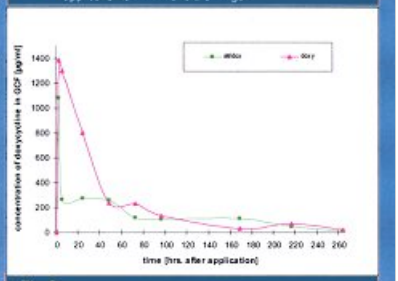

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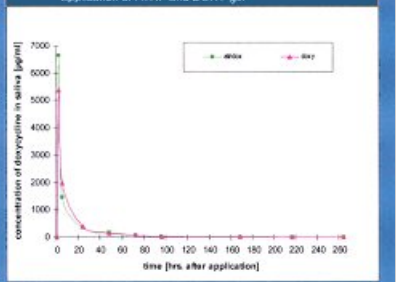

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