Local Antiinflammatory Effect of L-Carnosine (β alanyl 1-histidine) associated with Pains of Post Dental Extraction

By

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Summary

L-carnosine (β alanyl 1-histidine), used in the form of a dental cone in the amount of 5mg per root, proved successful in relieving pains associated with dental extraction, as endorsed by the inhibition of edemata and postoperative pain complaints.

This antiinflammatory effect of 1-carnosine is believed to be found in the promotion of defense mechanism inherent in the vital tissues. The effective dosage of the present clinical study corresponds to 1/35 of what is usually contained in the vital tissue.

1. Introduction

Carnosine is chemically β alanyl 1-histidine which was discovered by Gleuwitsch in 1900 from a meat infusion. This substance usually exists in the skeletal system of mammals anywhere from 0.1 to 0.2%. On the ground that carnosine is predominantly found in the skeletal system, it has been studied in connection with the contraction of various muscles but, to date, there is no definite theory to establish its physiological significance.

In 1970, NAGAI and his associates discovered an antiinflammatory effect of carnosine as confirmed by its inhibition of edematous formation [1, 4]. At the same time, it was also discovered that carnosine possesses a promotive effect of inflammatory granulations.

It has been made clear by other investigators that the anti edematous effect of carnosine disappears in animals which are adrenalectomized, while it will be again restored when cortisone is conjointly administered. A combination of carnosine and cortisone enhances the promotion of new granulations to a further degree than the former used singly.

An effective dosage of carnosine for the promotion of granulations is established at $2.0\mu\text{g}/100\text{g}$ rat iv. and this nearly corresponds to 1/35 of what is usually contained in the gastrocnemius of rats. These facts certainly throw light on new implications of carnosine from a physiological point of view. Histamine, serotonin and various

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SRS chemicals are known to act as chemical mediators in the inflammatory mechanism. A supposition has been proposed that some specific chemical mediator would exist in the latter phase of an inflammation, i.e., repair of the inflamed tissues to the normal state. And carnosine may, it is hoped, prove itself as a chemical mediator which is specifically involved in the restoration of inflammatory tissues, though a definite confirmation needs yet to come.

Moreover, carnosine inhibits the Arthus's phenomenon and thus prevents the possibility of local anaphylaxy. It is generally maintained that, in all these reactions, bradykinine is present and, in this connection, carnosine in the amount of 100mg/Kg prevents an increase in the blood vessel permeability of rats induced by 0.31 to 5 μ g of bradykinine [2, 3].

An inflammatory pain is said to be brought about by the presence of some localized pain-producing substance and of these pain-producing substances, bradykinine is now receiving much attention.

In the belief that the inflamed tissue repair effect of carnosine, which is further enhanced by its anti-bradykinine action, would check an inflammation associated with an extraction of tooth or teeth to a minimum degree and reduce the postoperative pain, the authors studied the effect of dental cones prepared of carnosine and carried out a series of clinical tests to be reported here.

2. Clinical Testing

2.1 Subjects used for the study were selected from the patients treated in the Dental Clinic of Kawaguchi-Saiseikai Hospital, Imperial Foundation, the total sample being 76.

The medication of carnosine was on a double blind basis.

2.2 Dental cones were prepared of synthetic carnosine, one cone containing 5mg. This amount of 5mg was designed to work on one dental root; therefore, a tooth having more than one root was given so many cones corresponding to the number of roots encountered.

The composition of a carnosine dental cone was as follows:

Carnosine	5.0mg
Lactic sugar	29.5mg
Mg-St	0.2mg
Ns-300	0.3mg

To insure the accuracy of data, no surgical medication including analgic agents and antibiotics was employed throughout the testing period.

2.3 Assessment of results

For assessing various test results, the following 4-point score was used.

- 1) Of 3 items of pain, redness and swelling brought about by an inflammation, they were assessed in terms of (—) for the three items, (—) for two items, and (—) for 1 item only.
- 2) As regards the pain item, it was assessed whether (—) or (+).

3) As regards the redness item, it was assessed whether (–) or (+).

4) As regards the swelling item, it was assessed whether (–) or (+).

All the subjects were placed under observation for 5 days from the operation and the presence or absence of postoperative pains were directly inquired of them the day following the operation. X statistical method was adopted for the calculation of significant differences of the data obtained.

2.4 Classification of the teeth extracted

The teeth extracted of the subjects were arranged in the following three categories.

- a. Simple extractions   25 (Carnosine group)
                                                            25 (Placebo group)
- b. Bone scaling   9 (Carnosine group)
                                                            1 (Placebo group)
- c. Root fraction   9 (Carnosine group)
                                                            1 (Placebo group)

When the subjects were further classified in terms of the manifestation of an acute inflammation, it was absent in 64 (carnosine 38; placebo 26) and was present in 12 (carnosine 5; placebo 7).

Table 1. Distribution of carnosine and placebo groups

Subjects by age groups	Carnosine group (24–84 yrs.) 45.4±15.9			Placebo group (25–84 yrs.) 45.1±17.1		
	M	F	Total	M	F	Total
20–29	3	4	7	5	5	10
30–39	5	4	9	2	4	6
40–49	6	2	8	3	5	8
50–59	3	4	7	4	2	6
60–69	2	0	2	2	2	4
70–	4	1	5	2	2	4
Total	23	15	38	18	20	38

3. Clinical Findings

For the convenience of presenting data obtained from the above clinical tests, they are summarized in a tabular form below (Table 2).

Table 2. Comprehensive tabulation of various clinical test results

A. Antiinflammatory effects (pain, redness, swelling)

		3 items (–)	2 items (–)	1 item (–)	3 items (+)	2 items (+)	1 item (+)	Total
1 day	C	21*	5	9	2	2	2	38
	P	10	7	10	2	10	1	38
3 days	C	24*	0	10	0	1	2	35
	P	6	0	15	0	1	1	24

B-1 Cases of postoperative pain (—)

	Immediately after	1	2	3	4	5
C	23*	24	7	23	4	1
P	10	24	9	22	8	2

B-2 Cases of preoperative pain (+)

	Immediately after	1	2	3	4	5
C	9	3	0	0	0	0
P	21*	3	0	0	0	0

Note: Statistical effect was attested to with placebo.

C-1 Cases of redness (—)

	1	2	3	4	5
C	22*	5	24	2	1
P	11	5	6	4	0

C-2 Cases of redness (+)

	1	2	3	4	5
C	5	2	2	0	0
P	13*	2	1	0	0

D-1 Cases of swelling (—)

	1	2	3	4	5
C	26*	7	24	2	1
P	19	7	6	4	1

D-2 Cases of swelling (+)

	1	2	3	4	5
C	4	2	2	0	0
P	11*	2	2	0	0

Note: * indicates a statistical effect at $\lambda 0.5$

4. Discussion

As is shown by Table 2, an application of carnosine in the form of dental cones (5mg per cone) proved quite effective in inhibiting extractive inflammatory effects, as manifested in the postoperative pain, swelling and redness.

As the amount of carnosine which works to interfere with bradykinine established by NAGAI et al. is 100–300mg/Kg, that contained in one dental cone corresponds to 500mg%–1000mg% in concentration on the basis that the volume of 5mg to 10mg

carnosine is postulated at 1ml. Therefore, one dental cone is considered as being sufficiently potent and, as in the present clinical test, the antiinflammatory action of carnosine is also helped by its anti-bradykinine effect.

A local pain which occurs as a result of an inflammation is regarded as being caused by a pain producing substance (P.P.S.) physiologically. For this reason, a local anti-pain agent such as carnosine has effects that i) it promotes the decomposition of P.P.S. in the localized area, ii) it interferes with the production of P.P.S., iii) it promotes an elimination of P.P.S. through the blood stream, and iv) it disrupts the chemical reaction between a chemical mediator working in favor of repairing the inflamed tissues and P.P.S. It is assumed that all these effects combine themselves in bringing the inflamed tissues back to normalcy and, consequently, alleviation of pains associated with them.

This antiinflammatory action of carnosine can be schematically represented, as in Fig. 1 below. This kind of horizontal effect, as it were, is not seen on the part of various antiinflammatory drugs hitherto in use.

5. Conclusions

1. An application of carnosine in the form of dental cone (5mg per cone) proved highly successful in eliminating pains associated with the extraction of teeth.
2. This action of carnosine is to be sought in inhibiting the production of a pain producing substance (P.P.S.).

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