BRIEF NOTE

**Effect of Thyrotropin Releasing Hormone Instillation
on Keratitis in Dairy Cattle**

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Clinical keratitis has relatively often been encountered in dairy cows. Many cases, however, have already had severe symptoms when presented to the initial examination. In the present study, the instillation of an aqueous solution of thyrotropin releasing hormone (TRH) was tested for effect on traumatic and infectious keratitis in dairy cows. Niwa [4] suggested that polypeptides might have a beneficial effect on repairing experimental corneal wounds in the rabbit. Abe and Ono [1] reported a successful clarification of the lens opacity in canine senile cataract by the instillation of TRH tartarate containing 0.01% of TRH for more than four months. Kawamura [3] treated infectious bovine keratoconjunctivitis (IBKC) simultaneously by washing the eyes with 3% boric acid solution and by instillation of penicillin-streptomycin or by application of oxytetracycline ointment. As a result, the symptoms were improved after about one month. Leukoderma was found, however, as a sequela in some or whole part of the surface of the cornea in cows with moderate symptoms. It was complete leukoderma of high severity with ulcer formation in the central part of the cornea. In the present

series, there were two cases of traumatic keratitis, which were used for a preliminary test and for a long-term observation, respectively (Example 1). In addition, nine severe cases of IBKC were used. Of them, six cases were treated by instillation with TRH and three cases served as unmedicated controls. The diagnosis of IBKC was made exclusively by the criteria of Hughs et al. [2] based on clinical findings. In the clinical cases, ulcer or grayish white swelling and opacity were present in the central part of the cornea. Results better than expected were obtained by a twice-a-day instillation of TRH tartarate [TRH(T)] aqueous solution containing 0.01% TRH. The opacity of the cornea was improved to such degree that only slight nebula remained. No side-effects appeared in any case which recovered.

1. Traumatic keratitis
(Preliminary test)

A Holstein cow 7 years old had the cornea of the right eye injured 3 months after whipped with a rope.

Present symptoms: The right cornea had a site of frosted-glass opacity about 15 mm in diameter projected from the center to-

Table 1. Clinical cases of infectious bovine keratoconjunctivitis

Case No.	Age (years ; months)	Date of initial examination	Affected eye	Clinical sign of cornea	Duration in day of instillation	Result
1	2 : 6	July 3, 1979	Left	Ring-shaped nebula in central part swelling in surrounding area	33	Cured, minute nebula
2	2 : 8	July, 30, "	"	Small ring-shaped nebula in central part, iris generally visible	10	Cured, no nebula
3	4 : 10	Aug. 7, "	"	Grayish white swelling in central part, opacity, ulcer and pannus in surrounding area	54	Cured, minute nebula
4	5 : 11	Aug. 31, "	"	Ring-shaped nebula in central part, opacity and swelling in surrounding area	30	Cured, minute nebula
5	1 : 1	Sept. 23, "	Right	Ring-shaped nebula in central part, iris partially visible	16	Cured, minute nebula
6	1 : 2	Oct. 18, "	Left	Grayish white swelling in central part, pannus in surrounding area	10	Cured, moderate nebula
7	0 : 2	Sept. 23, "	"	Ulcer and grayish white swelling in central part, pannus in surrounding area	Untr-eated	Cured, moderate nebula
8	0 : 2	Sept. 25, "	"	The same as above	"	Loss of eyesight, prolapse, pano-phthalmitis
9	0 : 2	Oct. 14, "	Right	The same as above	"	The same as above

Lacrimation, photophobia, hyperemia of the conjunctiva and swelling of the cornea were seen in all the cases. All the animals, but one (No. 9), were female. Nos. 1 and 2 were introduced from a rearing pasture.

ward 9 o'clock. The corneal wound had already been healed. There remained moderate photophobia, but no lacrimation was noticed. The pupillary reflex was normal. The iris could be visualized in the front part of the eye, through the turbid part of the cornea.

Course of treatment: The instillation of 0.01% aqueous solution of TRH was performed twice a day for six days. Since the corneal opacity was alleviated during that period, the treatment was continued further for eight days.

As a result, the cornea became transparent and the iris could be wholly visualized. Then it was considered that complete recovery had taken place.

Example 1. Female Holstein calf 3 months old. The patient was brought to the clinic due to injury of the right cornea which was stabbed by a wire attached to the feed tub about 4 days before.

Present symptoms: Corneal opacity, marked lacrimation and puslike discharge

were present in the right eye. Grayish white swelling was seen in the injured central part of the cornea, and marginal hyperemia in the peripheral part of the cornea. The iris was not visualized (Fig. 1).

Course of treatment: The instillation of 0.01% aqueous solution of TRH alone was started immediately and continued for 55 days. The findings of the lesion of the cornea over a period from the 5th to the 76th day of treatment are shown in Figs. 2 to 6.

2. Infectious bovine keratoconjunctivitis

IBKC in the present cases was considered to have been caused by contact with pregnant cows introduced from IBKC-contaminated pastures. The diagnosis of the disease was made clinically on the basis of localized unilateral corneal opacity and swelling followed by pannus invasion and ulcer formation, as shown in Fig. 7 (Case 3) and in Fig. 11 (control). As indicated in Table 1, instillation with 0.01% aqueous solution of TRH was performed twice a day in six

cases, and the other three cases served as untreated controls. In the treated cases, almost complete recovery was noticed without residual keratoleukoma. Prominent leukoderma was persistent in the control cases (Fig. 12). The following typical severe case took a course of recovery as indicated.

Example 2. A Holstein cow 5 years old (Case 3 of Table 1).

It was brought to the clinic because of severe lacrimation and photophobia.

Present symptoms: The left eye was affected with conjunctival hyperemia, corneal edema, severe lacrimation and photophobia. Ring-shaped leukoderma was observed in the central part of the cornea and the iris could be visualized.

Course of treatment: The instillation with the aqueous solution of TRH was performed twice a day. On the third day of treatment, severe grayish white swelling was produced rapidly all over the cornea.

On the 4th day of treatment conspicuous lacrimation and photophobia, conjunctival edema, ciliary hyperemia, and prominent pannus in the periphery of the cornea, grayish white swelling in the central part of the cornea, and opacity around the swollen part were present. The iris was not visualized (Fig. 7).

On the 10th day such symptoms as lacrimation, photophobia and conjunctival hyperemia disappeared. No conjunctival edema was present any longer (Fig. 8). Ciliary hyperemia was scarcely noticed. The ulcer showed signs of recovery. The pannus was significantly absorbed.

On the 19th day the peripheral part of the cornea became clear, but the opacity in the central part and the pannus still remained (Fig. 9). The corneal symptoms were gradually improved thereafter.

On the 68th day complete recovery was

found, except a small pin-point nebula remaining in the central part of the cornea (Fig. 10).

Essentially the same course of recovery as mentioned above was taken by the remaining five cases of IBKC treated with TRH(T). It included the cessation of lacrimation and photophobia in 11 to 33 days, the gradual clarification of the cornea, and the disappearance of the ulcer and nebula. These findings indicated a normalization of the pathological changes of the cornea caused by IBKC. Moreover, the corneal transparency was significantly restored without such residual corneal leukoderma as seen in the control cases (Fig. 12). The internal anterior chamber and the eyeground were almost clear. The eyeground could be visualized. Panophthalmitis was absent.

An attempt was made in one treated and two control animals to isolate *Moraxella bovis*, which is regarded as the causative agent of IBKC, but in vain. This result seems to indicate the effect of TRH instillation on IBKC.

It will be necessary, however, to test the form, dosage, frequency and duration of application of TRH(T) and examine the effect of a combination of TRH(T) and an antimicrobial agent.

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References

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要 約

乳牛の角膜炎に対する Thyrotropin Releasing Hormone の点眼効果 (短報): 加藤寿次 (常南酪農業協同組合診療所), 小野浩臣 (武田薬品工業株式会社畜産事業部)——1979年5月より10月に至る, 乳牛の創傷性角膜炎2例及び伝染性角膜結膜炎6例に対して, 合成甲状腺刺激ホルモン放出ホルモン酒石酸塩水溶液 (TRH 0.01%) の1日2回 11~55日間連続点眼を試みた. 1) 両症による角膜炎に対する TRH の透明化効果が臨床的に認められた. 2) とくに, 従来の治療法によっても, 中等度以上の伝染性角膜結膜炎の後遺症状と考えられる角膜の白斑が, TRH によって殆んど完全に除かれ, 角膜の透明度が増加したことは注目に値する. 3) 伝染性角膜結膜炎の進行期の流涙, 羞明, 結膜炎, 角膜中央部の潰瘍化などの症状の進行は抑制できなかった. 初期において原因菌に対する抗菌剤の併用が必要かも知れない. 4) TRH 酒石酸塩の長期点眼治療は, 牛体に何ら副作用を示さなかった. 5) 治療中止6カ月後再発はみられなかった.

Explanation of Figures

Fig. 1. Example 1. Right traumatic keratitis. Female Holstein calf 3 months old. Initial symptoms: corneal opacity and lacrimation after stabbing by wire.

Fig. 2. Example 1. The 11th day of instillation with TRH (T) solution. Clinical symptoms reduced. Nebula diminished in the peripheral part of the cornea. Traumatic pannus developed.

Fig. 3. Example 1. The 18th day of treatment. Wound protruded in the central part and nebula in the peripheral part of the cornea. New growth of blood vessels is seen.

Fig. 4. Example 1. The 25th day of treatment. Leveling of wound in the central part of the cornea. Transparency increased in the cornea. The iris can be visualized.

Figs. 5 and 6. Example 1. The 77th day of treatment. Cornea and eyeground a normalized.

Fig. 7. Example 2. Infectious bovine keratoconjunctivitis. Holstein cow 5 years old. The 5th day of instillation with TRH. Lacrimation, photophobia and conjunctival swelling are

seen. Cornea shows round ulcer protruded in the central part, and nebula and hyperemia in the peripheral part.

Fig. 8. Example 2. The 10th day of treatment. Contraction of ulcer and alleviation of bleeding are seen in the cornea.

Fig. 9. Example 2. The 19th day of treatment. Ulcer has a smooth surface. Nebula in the central part and vascular and formation are obvious in the cornea.

Fig. 10. Example 2. The 15th day after discontinuation of the treatment (or the 70th day of treatment). Cornea is almost normal.

Fig. 11. Control case of IBKC. Female Holstein calf 2 months old. The 10th day after initial examination. Ulcer with a lip-shaped projection is seen in the central part of the cornea. Around it nebula and hyperemia are present in the peripheral part of the cornea. Profuse lacrimation and ocular discharge are noticed.

Fig. 12. Control case. The 30th day after initial examination. Nebula in the central part of the cornea and pannus formation are obvious.