

Clinical Report 2 (Kampo Medicine)

Clinical Experiences and Practices of hainosankyuto for Suppurative Diseases

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Abstract

Aim: Hainosankyuto is called as an “antibiotics of traditional Japanese medicine”, but in current status on development of western antibiotics, its effect is limited. In this report, clinical experiences and practices of hainosankyuto for suppurative diseases in our hospital were reviewed.

Methods: Thirty three patients including sixteen men and seventeen women were treated by hainosankyuto between July 2012 and August 2014. These cases were retrospectively researched in views of clinical backgrounds, western medical diagnosis, treatment period, concomitant drugs and clinical outcomes.

Results: Most of diseases are cellulitis of extremity, colonic diverticulitis, and herpes zoster-induced skin erosion. Mean treatment period was about 30 days. About 90% patients were also treated with antibiotics, anti-viral drug or anti-fungal drug. In clinical outcomes, about 90% were healing or nimble, but remaining about 10% were immutable or worsening.

Conclusion: As a target for “penetrating with the outside-world, that is superficial and open”, hainosankyuto may be more effective, but not useful to cases of poor general conditions and intractable situations. Several kinds of suppurative diseases

that hainosankyuto may be beneficial were recognized.

Key words: hainosankyuto, suppurative diseases, antibiotics

Introduction

Hainosankyuto is mixed traditional Japanese medicine that Todo Yoshimasu devised in Edo period on Japanese history. According to source book, that is, “Kinkiyoryaku”(1), hainosan (mixture of Kijitsu, Kikyo and Shakuyaku) using at mature stage of inflammation and hainoto (mixture of Kanzo, Kikyo, Shokyo and Taiso) using at early or post-drainage end stage of inflammation, were mixed for treating suppurative diseases during all over the stage of inflammation.

In views of current status on development of western antibiotics, its effect is limited and poorer than that of western antibiotics. Its drug adaptation of the attached documents in Japan are painful lesions such suppurative diseases as carbuncle, furuncle, facial furuncle and other furunculosis with their reddish and swollen conditions from early stage to post-drainage end stage.

In this present report, clinical experiences and practices of hainosankyuto for suppurative diseases in our hospital were reviewed.

Patients and Methods

Thirty three patients including 16 men and 17 women (mean age 75 y.o., 41~93 y.o.) were treated by hainosankyuto (Tsumura & Co., Tokyo, 7.5g/day, or Kotaro & Co., Tokyo, 7.5g/day) in our hospital between July 2012 and August 2014.

These cases were retrospectively researched in views of clinical backgrounds, western medical diagnosis, treatment period, preceding or concomitant drugs and clinical outcomes by three-

step evaluation (healing, nimble and immutable or worsening).

Results

Most diseases of western medical diagnosis are cellulitis of extremity, colonic diverticulitis, herpes zoster-induced skin erosion (Fig. 1). Mean treatment period was about 30 days (median 14 days, range 3~180 days).

Fig. 1 : Hainosankyuto and its origin

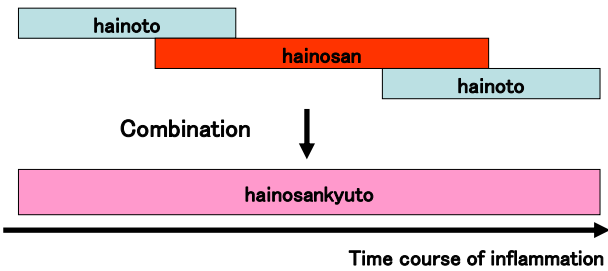
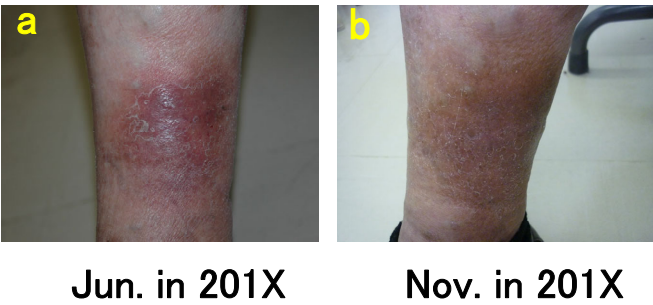


Fig. 1: Hainosankyuto and its origin

12.1% of patients were only treated by hainosankyuto. 87.9% of patients precedingly or simultaneously treated with antibiotics, anti-viral drug or anti-fungal drug. Honestly, 66.6% of patients simultaneously treated with antibiotics, anti-viral drug or anti-fungal drug.

In clinical outcomes, 84.4% of patients were healing or nimble, but remaining 15.2% were immutable or worsening because of translocation physician, operation or basic illness-related death (Fig. 2).

Fig. 2 : Right pretibial cellulitis



- Fig. 2: Case 1 Clinical course of pretibial cellulitis
- a. On the anterior side of right lower leg, reddishness and swelling with partially skin peeling were observed.
 - b. Reddishness and swelling were almost disappeared leaving the pigmentation

Remarkable adverse effects were not detected. They belonged to either “Kyo-sho” meaning subjects who have weak constitutions and low vital energy or “Jitsu-sho” meaning subjects who have strong constitutions and high vital energy. “Sho” means universal proof in Oriental medical sense.

Table 3 demonstrated all 33 cases in detail. In addition, more meaningful three cases were presented for clinical significance as following.

Table 3	Age	Sex	Western medical diagnosis	Treatment periods	Clinical outcome	Prescribed drug	Concomitant drug	SI
1	63	Male	Cellulitis of extremity	10	Cure	-	Cefazolin Sodium Hydrochloride Hydrate	JH
2	41	Male	Cellulitis of extremity	7	Cure	-	Levofloxacin Hydrate	JH
3	71	Female	Subcutaneous abscess	8	Immutable	-	Cefazolin Sodium	JH
4	47	Male	Cellulitis of extremity	7	Cure	-	Levofloxacin Hydrate	JH
5	66	Female	Pharyngitis	49	Cure	Piperasillin Sodium	Ceftriaxone Sodium Hydrate	KI
6	93	Female	Cellulitis of extremity	30	Cure	Levofloxacin Hydrate	-	KI
7	74	Male	Cellulitis of extremity	7	Cure	-	Cefazolin Sodium Hydrochloride Hydrate	JH
8	67	Female	Infectious paronychia cyst	12	Cure	-	Levofloxacin Hydrate	SH
9	63	Male	Pressure ulcer	180	Worsening	Cefazolin Sodium	Vancomycin Hydrochloride	KI
10	62	Male	Cellulitis of extremity	55	Worsening	Cefazolin Sodium Hydrochloride Hydrate	Cefazolin Sodium Hydrochloride Hydrate	KI
11	62	Male	Cellulitis of extremity	7	Cure	-	Cefazolin Sodium Hydrochloride Hydrate	KI
12	77	Female	Herpes zoster induced skin erosion	11	Cure	Valacyclovir Hydrochloride	-	JH
13	62	Female	Cellulitis of extremity	3	Cure	-	Fucidic Acid Sodium	JH
14	79	Male	Peritonsillar abscess	14	Cure	-	Cefazolin Sodium Hydrochloride Hydrate	KI
15	60	Male	Herpes zoster induced skin erosion	4	Cure	Valacyclovir Hydrochloride	-	KI
16	66	Female	Cellulitis of extremity	14	Cure	-	Ceftriaxone Sodium Hydrate	KI
17	72	Female	Cellulitis of extremity	140	Nilable	-	-	SH
18	62	Male	Cellulitis of extremity	7	Cure	Levofloxacin Hydrate	-	KI
19	61	Female	Pressure ulcer	180	Cure	Pseudoephedrine Hydrochloride	Vancomycin Hydrochloride	KI
20	77	Female	Liver Abscess	14	Cure	Mercaptopurine Hydrate	Mercaptopurine Hydrate	SH
21	62	Male	Cellulitis of extremity	21	Cure	Levofloxacin Hydrate	-	JH
22	76	Male	Cellulitis of extremity	28	Immutable	Cefazolin Sodium Hydrochloride Hydrate	Miconazole Hydrochloride	JH
23	66	Female	Skin erosion after laser treatment	3	Immutable	-	-	KI
24	61	Male	Cellulitis of extremity	14	Cure	-	Levofloxacin Hydrate	JH
25	62	Female	Herpes zoster induced skin erosion	27	Cure	Valacyclovir Hydrochloride	Cefazolin Sodium Hydrochloride Hydrate	KI
26	66	Female	Alveolar pyorrhea	63	Nilable	-	-	SH
27	60	Female	Cellulitis of extremity	21	Nilable	Levofloxacin Hydrate	Cefazolin Sodium Hydrochloride Hydrate	JH
28	66	Female	Pressure ulcer	7	Immutable	-	-	KI
29	63	Male	Cellulitis of extremity	7	Cure	Levofloxacin Hydrate	Cefazolin Sodium Hydrochloride Hydrate	JH
30	60	Male	Cellulitis of extremity	7	Cure	-	Levofloxacin Hydrate	JH
31	62	Female	Cervical flow and Urinary infection	28	Cure	-	Fluconazole	KI
32	66	Female	Herpes zoster induced skin erosion	14	Cure	Levofloxacin Hydrate	-	KI
33	60	Male	Infectious spondylitis	14	Nilable	-	Cefazolin Sodium Hydrochloride Hydrate	SH

Table 3 List of all 33 cases

Case 1 (No.17): 72-year-old woman (Fig. 2)

She was medicated for rheumatoid arthritis. On June in 201X, she was diagnosed as cellulitis of right lower extremity (right pretibial cellulitis) and was taken therapy by Dermatologist. Although only ointment made her not enough to be recovery, hainosankyuto (Tsumura & Co., Tokyo, 7.5g/day) was started. 140 days later, reddish and swollen lesions were recovered with leaving only the pigmentation.

Oriental medical findings: “Chukan-sho” (meaning subjects between “Kyo-sho” and “Jitsu-sho”, previously described). Pulse finding was slightly precipitation. Tongue finding was pink. Abdominal finding was moderate.

Case 2 (No.19): 81 year-old woman (Fig. 3)

She was medicated for Hypertension. Years ago, she was pointed out collagen disease, but had taken no therapy. On January in 201Y, she was admitted to our hospital because of bone fracture of left femur. On admission, pressure ulcer on her left heel was detected. Next month, operation was done. One week later, good clinical course made her remaining stitches take off, but serum C-reactive protein (CRP) did not normalized. After then, culture of pressure ulcer portion revealed Methicillin resistant *Staphylococcus aureus* (MRSA). Blood culture at high fever state also revealed MRSA sepsis. A sensitive antibiotic, vancomycin, was used for therapy. At the same periods, hainosankyuto (Tsumura & Co., 7.5g/day) was started. 90 days later, her pressure ulcer was almost healing, and 180 days later, was almost cured.

Oriental medical findings: “Kyo-sho”. Pulse finding was precipitation. Tongue finding was crimson. Abdominal finding was mild.

Fig. 3: Case 2 Clinical course of left heel pressure ulcer
c. Skin ulcer with purulent change.
d and e. Skin ulcer were shrinkened with approaching epithelialization.
f. Epithelialization and almost scarring.

Case 3 (No.9): 84-year-old man (Fig. 4)

He was medicated for Hypertension, diabetes and chronic renal failure. On October in 201Z, he was taken operation for bone fracture of left femur. Next month, he was transferred to our hospital for rehabilitation. At the same time, sacral pressure ulcer was detected. On February in next year, cutaneous flap was constructed. But, MRSA-induced flap necrosis (wound infection) occurred unfortunately. Then, other therapies of continuous pus aspiration and plastic sheet therapy (so-called, Japanese original technique, Wrap therapy), were started. But, blood culture at high fever state revealed MRSA induced bacteremia. A sensitive antibiotic, vancomycin, was used for therapy. At the same periods, hainosankyuto (Kotaro & Co., Tokyo, 7.5g/day) was started. 180 days later, his sacral pressure ulcer was closed and almost cured.

Oriental medical findings: “Jitsu-sho”. Pulse finding was slightly floating. Tongue finding was pink. Abdominal finding was moderate.

Fig. 3: Left heel pressure ulcer



Fig. 4: Sacral pressure ulcer



Fig. 4: Case 3 Clinical course of sacral pressure ulcer

- g. Pressure ulcer on right buttock.
- h. After skin flap procedure.
- i. Opened state after flap infection
- j. Skin wound was shrinkened and progressing to epithelialization.
- k. Skin wound was completely closed and scarring.

Discussion

Hainosankyuto is mixed traditional Japanese medicine. According to source book, “Kinkiyoryaku” (1), hainosan and hainoto were mixed. It has a lot of quality indicating “qing heat-detoxification”, “expectoration-drainage”, “pain-kill” and “stomach calm”. Its clinical target is wide for treating suppurative diseases during all over the stage of inflammation. Namely, hainoto was used for absorption at early condition under not so highly uplifting from skin surface. On the other hand, hainosan was used for drainage at stonely swollen condition under uplifting hemispherically. It was originated from “Kinkiyoryaku”(1), and was effective for suppurative diseases such as carbuncle and furuncle. “Kinkiyoryaku”(1) also showed only “Ho” meaning drug orientation, but not “Sho”. In source book of Todo Yoshimasu, “Ruijyuhō”(2), it has virtuosity in senses of combining “Kikyo” having drainage effect with “Kijitsu” having exclusive effect of inflammatory mass.

In community medicine including our hospital, a lot of suppurative diseases are found if clinicians are consciously careful for them. As hainosankyuto is well-known to be effective against sinusitis, otitis media, mastitis, carbuncle and furuncle, a target for “penetrating with the outside-world, that is, superficial and open” may be more effective during all over the stage of inflammation. But it was not useful to the cases of poor general conditions and intractable ones implicating “kyo-sho”.

In our clinical experiences and practices, not only to many diseases based on classic Bible, but also to colonic diverticulitis, herpes zoster-induced skin erosion, pressure ulcer (namely bed sore),

periodontal abscess, alveolar pyorrhea, candida flow, urinary infection, infectious pancreatic cyst and liver abscess, adapted diseases were trying to become wider. Subsequently, clinical outcome were good. Although most of them simultaneously took antibiotics or anti-viral drug, pure effect of hainosankyuto did not be evaluated.

By the way, though the meaningful 3 cases (Case 1, 2 and 3) had unfortunately inconvenient past history and basic illness such as collagen diseases, diabetes and chronic renal failure, significance of its long-term use is deeply valuable.

There are many clinical reports as to usefulness of hainosankyuto. In area of pediatric surgery, perianal abscess is well-known to its effectiveness on decreasing operation(3,4). In area of dermatology, there are a few effective reports to palmoplantar pustulosis(6,7,8,9). In area of ophthalmology, there is an effective report to hordeum, which is sole paper with randomized controlled trial that Japanese Eastern Medical Society certified as “Kampo Evidence report 2013”. In area of gynecology, there is an effective report to pyometra(11). In reference to this report, it was used for candida flow and urinary infection and resulted in good clinical course.

In basic research about periodontal diseases, anti-inflammatory reaction of hainosankyuto was researched in vitro model, indicating that it increased amount of interleukin-6 and interleukin-8 by stimulating lipopolysaccharide(12). In reference to this paper, it was used for two cases trying to therapy for periodontal abscess and alveolar pyorrhea. In mouse model(13), while Group A-beta streptococcus was infected to mice, promoting interferon- γ and interleukin-12 by enhanced macrophage phagocytosis. This remarkable approach except using antibiotics may be promising. It is well-known that Streptococci are inducible to bacterial cellulitis, so cellulitis of extremity was entered in our clinical experiences with promising strategy in purpose.

In addition, viral infection such as mumps virus(14), common wart(14), hand-foot and mouth disease(15), subacute thyroiditis(16) and others were sporadically reported indicating hainosankyuto may have a role on interferon induction.

According to Nojima's report(17) about analysis of 68 cases of sacral pressure ulcer, the treatment period was average 6.2 months. As the cases of them received an additional therapy after surgery, as the treatment period was longer. Compared bacteria positive group in culture of pressure ulcer with bacteria negative group, the latter had better clinical course. In Case 3 suffered from sacral pressure ulcer, four months later since admission, cutaneous flap was performed. After then, more 4 months later, MRSA-infected flap necrosis was detected. Under such condition, hainosankyuto after surgery considered that intractable sacral pressure ulcer was almost cured as significance of combined therapy.

Ishino's reference(18) highlighted differential diagnosis from another medication on usage of hainosankyuto as following. Senkinaitakusan is suitable to the delicate and easily tired person ("kyo-sho") with pulurent chronic diseases. Jyumihaidokuto is suitable to the nervous person with epigastric discomfort for changing constitutions. Hakushusan is mainly fit to be transiently used at early chronic phase, but not acute phase. Keibohaidokusan is preferable to the local reddishness and swelling together with headache repeatedly. Keigairengyoto is suitable to the person whose skin is swarthy with distension of rectus abdominis muscle to make better constitution in middle-aged periods.

Conclusion

As a target for "penetrating with the outside-world, that is, superficial and open", hainosankyuto may be more effective, but not useful to the cases of poor general conditions and intractable ones. In community medicine, some suppurative diseases that hainosankyuto may be beneficial including

long-term prescription were recognized, and wider indication of it has to be researched further.

References

1. Kinkiyoryaku, ancient classic Chinese book
2. Todo Yoshimasu, Ruijuho, ancient classic Japanese book
3. Kawahara H, Nakai H, Yoneda A, Kubota A. Management of perianal abscess with hainosankyuto in neonates and young infants. *Pediatr Int.* 53:892-6, 2011
4. Hanada M, Furuya T, Sugito K, Ohashi K, Ikeda T, Koshinaga T, Kawashima H, Inoue M, Hosoda T, Goto H. Evaluation of the efficacy of incision and drainage versus hainosankyuto treatment for perianal abscess in infants: a multicenter study. *Surg Today.* 2014 Oct 22. 2.
5. Higaki S: Shosekinohosho ni taisuru kampo-yaku no chiriyokoka (The therapeutic effect of Kampo medicine for Palmoplantar Pustulosis. written in Japanese) *The Journal of Traditional Sino-Japanese Medicine (suppl)* 12: 264-266, 1991
6. Kusaka T: Chiryo ni nanjyu shita Shosekinohosho ni hainosankyuto ga sokoshita 1 rei (A case of intractable Palmoplantar Pustulosis that hainosankyuto treatment was effective. written in Japanese) *Science of Kampo Medicine* 27: 73, 2003
7. Izumiyama T, Sato K, Kudo N, Yokoyama Y, Tosa N: Shosekinohosho ni taisuru kampo chiryo ni tsuite (The therapeutic effect of Kampo medicine for Palmoplantar Pustulosis. written in Japanese) *Science of Kampo Medicine* 26: 137, 2002
8. Atsuumi T, Rikimaru Y, Suzuki J: A case of Palmoplantar Pustulosis Successfully Treated combined Formulation Hainosankyuto and Maobushisaishinto. *Kampo Med* 59: 73-76, 2008
9. Takama N, Fujiwara T: Naibakuryushu ni taisuru hainosankyuto no yuyosei. (Efficacy of Hainosankyuto to hordelum. written in Japanese) *Japanese Review of Clinical Ophthalmology* 100: 9-11, 2006

10. Iwabuchi S: Shikyuryunosho no hainosankyuto niyoru chiken. Clinical experience of hainosankyuto to pyometra. written in Japanese) Kampo Med 45: 601–607, 1995
11. Nomura N, Matsuda M: Hainosankyuto ga choko shita munpusu no ichirei (A case of mumps viral infection effective to hainosankyuto. written in Japanese) Kampo Med 59 (suppl): 193, 2008
12. Matsuda M: Hainosankyuto no uirusu sei shikkan he no oyo: Jinjoseiyuzei, Te-ashi-kuchi byo (Application to viral infection by hainosankyuto: common wart, hand-foot and mouth disease. written in Japanese) Kampo Med 59(suppl): 193, 2008
13. Tanno Y: Uirusu kansensho ni taisuru hainosankyuto no kokoromi (Experimental attempt to viral infection of hainosankyuto. written in Japanese) Kampo Practice Journal 5: 135, 2014
14. Wang P, Masuno K, Sakai D, Okazaki J: Effect of hainosankyuto on inflammation in periodontal disease model. Pain and Kampo Medicine 24: 161-164, 2014
15. Minami M, Ichikawa M, Hata N, Hasegawa T: Protective effect of hainosankyuto, a traditional Japanese medicine, on Streptococcus pyogenes infection in murine model. PLoS ONE. 6:e22188, 2011
16. Nojima K: The surgical treatment of sacral pressure ulcers - analysis of 92 cases - Tokyo Jikeikai Medical Journal 119: 441-53, 2004
17. Ishino S: Jyuyo Shoho Kaisetsu (103) hainosankyuto, tokikenchuto (Important medication reference (103). written in Japanese) Kampo Igaku Koza 49: 54-60, 1990