



Original Research Article

A comparative analysis of water immersion induced hand wrinkling in dermatological diseases

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ARTICLE INFO

Article history:

Received 02-03-2022

Accepted 05-03-2022

Available online 30-03-2022

Keywords:

Wrinkling

Psoriasis

Vitiligo

Dermatitis

ABSTRACT

Introduction: Skin wrinkling is hypothesized as an adaptive phenomenon that is generated as an evolutionary process. Water immersion-induced wrinkling is a non-invasive test graded from 0-5 that involves placing one's hands into lukewarm water for a set amount of time. Despite the increased interest in skin rejuvenation, a baseline study describing the variation in water immersion induced hand wrinkling is still missing. We aim to experimentally compare the water immersion-induced wrinkling time in various dermatological conditions in the current study.

Materials and Methods: One hundred patients from the Department of dermatology were evaluated based on their presenting Dermatoses like Psoriasis Vulgaris, Acral Vitiligo, and Hand Dermatitis were asked to place their hands in $25\pm 1^\circ\text{C}$ tap water to elicit water-induced wrinkling. Twenty-five patients were included as age-matched controls without any significant dermatoses. Following this, the time of early and complete disappearance of wrinkles was documented.

Results: Out of 100 patients, water-induced wrinkling time was seen earliest in Dermatitis > healthy controls > Psoriasis > Vitiligo. The formation of wrinkles diminished significantly as age advanced. Within the normal population, females participants took longer to develop water immersion-induced wrinkles compared to males.

Conclusion: There is a significant variation in the water immersion induced hand wrinkling pattern in patients with Dermatoses like Psoriasis, Vitiligo, and Hand Dermatitis due to structural alterations in the epidermis and dermis. Estrogen and the sympathetic nervous system play a significant role in water immersion-induced wrinkling. The role of estrogen in this phenomenon was a novel observation.

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1. Introduction

As we age, our skin changes in structural composition, structural organization, size, and properties leading to wrinkling formation. One of the earliest visible signs of aging may be found in our hands. Hand aging is described as a three-dimensional process that involves the skin, skeletal and subcutaneous structures.¹ One of the earlier signs of hand aging is wrinkling. It is well known that prolonged exposure to water causes wrinkling of hands called pruney

fingers or water aging. Wrinkling is defined as reversible undulations of the surface skin that occur after 5 to 30 minutes of water immersion. In Water immersion induced wrinkling test subject's hands are kept immersed in water until wrinkling appears over the hand. However, even though it is an interesting phenomenon that occurs mainly over the non-hairy (glabrous) skin of the fingers, palms, and soles, the exact mechanism and significance are not fully understood. The unique anatomical composition of the glabrous skin has a role in the formation of wrinkles. Glabrous or non-hairy skin lacks hair follicles, sebaceous glands, and erector pilori muscles.² It is characterized by

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a thick layer of stratum corneum and an increased number of eccrine sweat glands.³ Glabrous skin wrinkles mainly due to the passive edema of the stratum corneum. Once water enters the digit, the stratum corneum expands to create a larger surface area of the skin and accommodate this expansion skin wrinkles forming ridges and valleys. The other factors that govern wrinkling are eccrine ducts, intact sympathetic function, and the mechanical turgor of the dermal layer. Dermal glands are in intimate contact with a dense dermal neuronal network that plays a significant role in vasomotor control. It is postulated that as water percolates the sweat ducts, it changes the electrolyte composition resulting in the increased firing of the surrounding neurons resulting in further vasoconstriction.

Factors that increase water-induced wrinkling time are temperature, pH, and tonicity.² An increased temperature can facilitate more fluid diffusion into the skin.⁴ However, Cales and Weber et al.⁴ studied the effect of varying temperatures to induce wrinkling and concluded that water temperature had no significant impact on the degree of wrinkling. The temperature of the water did not alter the length of peaks and valleys in the skin. However, it did have a significant effect on how long it took to make them.

Stratum corneum has a fixed isoelectric point of 3.5-5.0 and a pH of 4.5–5.3 at which there is minimal water-binding capacity.⁵ In a hypertonic solution or soapy water, skin wrinkles more rapidly due to change in or tonicity or pH of the immersed medium. Kareklas et al.⁶ experimentally proved that wrinkling is an adaptive mechanism and enables better handling of wet objects as hypothesized by the rain tread hypothesis. Nevertheless, it was Julia Haseleu et al.⁷ who disproved this theory as they could not reproduce the same results as Kareklas et al. The author stated that handling and speed of task completion experimentally proved in the previous study would depend on other factors including motivation and fine motor skills that have an inter-individual variation. These factors are independent of the ability to grip objects reliably. Even though this is a straightforward, non-invasive test,⁸ the implications and utilities of this test are astounding. In 1973 O' Riain et al.⁹ postulated that an area supplied by a denervated nerve does not wrinkle. Once the nerve heals itself, the wrinkling returns proximally to the distal. Hence skin wrinkling can be used as a diagnostic test for detecting early nerve injuries. In a study by Kamran H et al. done in 60 congestive cardiac failure patients versus control water immersion, induced skin wrinkling was significantly reduced. Hence, the role of this test in screening early cardiac failure patients was postulated. This test can also be used in the early detection of peripheral neuropathy in human immunodeficiency virus-infected patients.¹⁰ Water immersion skin wrinkling is an indicator of intact autonomic function and is reduced in leprosy,¹¹ diabetic neuropathy,¹² and nerve injuries. Ricky French et al.¹³ suggested the role of water immersion-

induced skin wrinkling as a predictor of chronological cardiac incompetence by correlating it with Tilt table testing (TTT). Water induced wrinkling test is not commonly employed due to the delay in time taken for the wrinkles to occur, even though it is an inexpensive, reliable and straightforward bedside test.

The literature available on water immersion-induced wrinkling is very little. Even though a few studies have postulated the mechanism of wrinkling and reported this as an evolutionary mechanism, no data is available about the time taken to wrinkle in a patient's hands with any dermatological disease. There is no significant data on the demographic variables of time taken for wrinkling to occur in a healthy adult to the best of our knowledge. Hence this study was undertaken to study more about this unexplained phenomenon and observe if there is a variation in the appearance or disappearance of wrinkling time between Dermatological conditions like Psoriasis, Vitiligo, and Hand dermatitis when compared to wrinkling in a healthy adult.

2. Materials and Methods

An observational study was done on 100 patients who attended the outpatient department of Dermatology in a tertiary care hospital over ten months.

The study was conducted in accordance with Good Clinical Practice guidelines and adhered to the ethical principles of the Declaration of Helsinki. All study documents and procedures were approved by the appropriate institutional review boards and ethics committees at each study site; each patient provided written informed consent before study participation. Patients with a history of neurological diseases, Raynaud's phenomenon, cold urticaria were excluded from the study. Patients with Congestive heart failure and HIV disease with altered hydration responses were also excluded. All consenting patients were evaluated based on their presenting Dermatoses involving their hands (all fingers involved) like Psoriasis, Vitiligo, and Hand dermatitis were included and evaluated regarding duration, treatment taken, co-morbidities, and others, using a Performa. Patients were asked to avoid taking any caffeinated beverages or refrain from using any topicals on their hands one hour before the test. The subjects both hands were placed in $25\pm 1^{\circ}\text{C}$ tap water to elicit wrinkling. Subjects were seated and asked to put their hand (up to wrist) in a trough placed in an adjacent seat. Wrinkling was graded based on a scale from Teoh et al. (2008). Under standard conditions of water (obtained from a common source) filled in a 60*49 cm trough, patients were being asked to immerse their hands in water for a sustained period until they noticed the first appearance of wrinkling. Female participants underwent the study on Day 1 and Day 10 of their menstrual cycle. Following this, the time of early and complete disappearance of wrinkles was documented.

3. Results

3.1. Study population

One hundred patients in the age group 18-60 years were included in the study. Seventy-five patients with dermatoses over their hands were included in the study. Twenty-five patients were included as age-matched controls without any significant dermatoses. The mean age of the study population was 25.96 years. Standard Deviation: 6.898. [Table 1]

3.2. Demographic variation with wrinkling

The formation of wrinkles diminished significantly as the age advanced, with an increased time taken for wrinkles to appear, as shown in [Figure1]. There was a male predominance in the study (52%). Within the normal population, female participants took longer (22 minutes) to develop water immersion-induced wrinkles than males. (11minutes). [Table 2]. Female participants showed an earlier time to wrinkle in their menstrual cycles. [Table 3]

3.3. Time taken for the appearance of water immersion induced wrinkling

The minimum and maximum time taken for hand wrinkling to appear in patients with Psoriasis were 8minutes 36seconds and 27 minutes and 23 seconds, respectively. (Mean= 14 minutes and 57 seconds). The minimum and maximum time taken for hand wrinkling to appear in Vitiligo were 18minutes, 36seconds, and 36 minutes and 20 seconds, respectively. (Mean= 25 minutes and 53 seconds). The minimum and maximum time taken for hand wrinkling to appear in Hand dermatitis were 2minutes 4seconds and 12minutes and 0 seconds, respectively. (Mean= 6 minutes and 30 seconds). The minimum and maximum time taken for hand wrinkling to appear in the normal population was 4minutes, 10seconds and 34 minutes, and 28 seconds respectively. (Mean= 15 minutes and 6 seconds)

Compared to the normal population, water-induced wrinkling time was seen earliest in Dermatitis> Psoriasis>Vitiligo. Out of 100 patients, water-induced wrinkling time was seen earliest in Dermatitis> Normal population > Psoriasis>Vitiligo (5.8952>15.0616>14.5732>25.5304 minutes. seconds). [Table 4]

3.4. Time taken for disappearance of water immersion induced wrinkling

The mean time taken for hand wrinkling to disappear in Psoriasis was 8minutes. The mean time taken for hand wrinkling to disappear in Vitiligo was 11 minutes 69 seconds. The mean time taken for hand wrinkling to disappear in Hand dermatitis was 11 minutes 2seconds. The minimum and maximum time taken for hand wrinkling to

appear in a normal population were 7minutes 6 seconds. [Table 5]

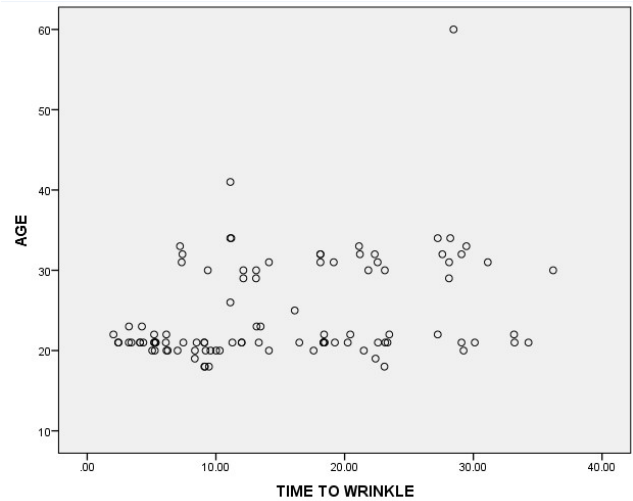


Fig. 1: The inverse association of age with mean wrinkling time on water immersion.

4. Discussion

Water immersion-induced wrinkling is a non-invasive test that involves placing one's hands into the water for a set amount of time. In our study, the formation of wrinkles diminished significantly as the age advanced, with an increased time taken for wrinkles to appear. Our finding is a concordance to C.N. Angel Deepa et al., who found a similar negative inverse relationship between water immersion-induced wrinkling and age. With age, there is a gradual and apparent decrease in sympathetic activity, and hence water-induced wrinkling time increases with age. There was a significant demographic variation regarding gender and time of appearance of wrinkles within the normal population. Females took a longer time to develop water immersion-induced wrinkles compared to males. Our study also showed an early wrinkling time in female participants during their menstrual cycles, thereby hinting at the influence of estrogen in the formation of wrinkles. It is known that a state of hypoestrogenism during menopause is known to accelerate age-related deterioration, which results in thinner skin, and an increase in the number and depth of wrinkles.¹⁴ Hormone replacement therapy (HRT) has been shown to increase epidermal hydration, skin elasticity and also reduces skin wrinkles. Hence we postulate that estrogen has a role in the production of wrinkles, and further studies are needed in the future to elucidate this. The mechanism and significance of Water immersion-induced wrinkling (WIWS) are unclear. However, it was in 1935 that Lewis and Pickering et al.,¹⁵ who studied patients with median nerve palsy, uncovered that wrinkling spared

Table 1: The mean age among subsets of the study population

Study population	Age		P value(ANOVA)
	Mean	Std. Deviation	
Psoriasis	26.52	6.212	0.0001
Vitiligo	28.80	8.382	
Hand dermatitis	22.56	4.134	
Normal Population	20.80	.645	

Table 2: Time taken for the appearance of wrinkling: Sex variation

	Sex		P value (Mann- Whitney Utest)
	Female	Male	
Time to wrinkle	21.68±8.33	11.10±6.61	0.005

Table 3: Change in time to wrinkle during and after menstrual cycles in females

S.No	Time to wrinkle during menstruation	Time to wrinkle after menstruation (minutes/seconds)	Variation
1	21.2	25.8	Increased
2	17.59	23.12	Increased
3	18.45	19.16	Increased
4	21.84	24.14	Increased
5	27.23	19.22	Increased
6	23.47	25.12	Increased
7	28.48	29.45	Increased
8	28.21	24.45	Decreased
9	28.12	29.10	Increased

Table 4: Time taken for the appearance of wrinkling: Based on Dermatological condition compared with normal population

Study population	Time to wrinkle		p value (Kruskal Wallis Test)
	Mean	Std. Deviation	
Psoriasis	14.5732	4.33834	0.0001
Vitiligo	25.5304	4.58873	
Hand dermatitis	5.8952	2.54877	
Normal population	15.0616	9.34616	

Table 5: Time taken for the first disappearance of wrinkling Based on Dermatological condition compared with normal population

Study population	Time of first Disappearance (minutes/secs)		P value (Kruskal Wallis Test)
	Mean	Std. Deviation	
Psoriasis	2.8928	1.32209	0.0001
Vitiligo	7.4420	1.33787	
Hand dermatitis	3.4520	1.82914	
Normal population	4.1888	4.69983	

Table 6: Time taken for the complete disappearance of wrinkling Based on Dermatological condition compared with normal population

Study population	Time of complete disappearance (minutes/secs)		P value (Kruskal Wallis Test)
	Mean	Std. Deviation	
Psoriasis	8.0716	5.04128	0.0001
Vitiligo	11.6984	1.28079	
Hand dermatitis	11.2852	7.61295	
Normal population	7.6368	5.05176	

Table 7: Interval time between first and Complete disappearance of wrinkling Based on Dermatological condition compared with normal population

Study population	Interval time		p value (Kruskal Wallis Test)
	Mean	Std. Deviation	
Psoriasis	5.1788	5.07469	0.084
Vitiligo	4.2932	.76230	
Hand dermatitis	7.6780	7.04569	
Normal population	3.3216	1.73629	

the areas innervated by a damaged nerve, thus postulating that there is a role of the nervous system in the wrinkling phenomenon. Many others supported this theory in subsequent years.^{16–23} Vasudevan¹⁷ et al. demonstrated that by blocking the sympathetic response, either temporarily via lumbar epidural infusion or permanently via chemical or surgical cervical sympathectomy, water immersion induced wrinkling response can be terminated. Cales and Weber¹⁶ in 1997 proposed that fingers and toes wrinkle if soaked in water for around five minutes and attributed the same to local osmotic reactions. Wilder-Smith et al.²⁴ hypothesized that the finger-wrinkling mechanism might be due to digit pulp vasoconstriction. The author postulated that vasoconstrictive agents could induce wrinkles.²⁵ Water immersion-induced wrinkling (WIWS) is caused due to the rigidification of both stratum corneum and dermis, along with the weakening of the upper dermis with loss of echogenicity.²⁶ It was earlier postulated that when water gets absorbed into the keratin content of the skin, it expands to a larger surface area causing it to fold, creating wrinkling lines. Our study participants who had significant dermatoses such as contact dermatitis on their hands subjected to the study showed an earlier appearance and later disappearance of wrinkling compared to those without any dermatoses. In Dermatitis, especially Atopic Dermatitis, it is well established that there is an altered expression of keratin and filaggrin protein leading to a structural alteration.^{27,28} Even though the reason for the early wrinkling time is unclear, it can be postulated that in patients with Dermatitis, there is an altered expression of epidermal differentiation molecules such as filaggrin, keratohyalin granules, transglutaminase I.²⁹ This alters the epidermal desquamation and the capacity of stratum corneum to retain water due to an altered water-binding capacity of keratins. In wrinkles caused by aging, it has been established that the dermo-epidermal junction is significantly transformed by a decrease of collagen IV and VII, along with fewer oxytalan fibers under wrinkles, weakening the interface.²⁹ Hence, we postulate a role in the breakdown of collagen, leading to an increased and earlier appearance of wrinkling in eczematous conditions. A similar mechanism is associated with aquagenic wrinkling of palms (AWP) characterized by a rapid formation of wrinkles upon limited exposure to water, i.e., as early as 2minutes. The pathomechanism of this entity is due to an increase in the water-binding capacity of

keratins, mediated by increased salt concentrations in the epidermis.³⁰ In children with marasmus, a form of protein-energy malnutrition has been observed to have excessive skin wrinkling similar to that seen in patients with Cystic Fibrosis.

In patients with Vitiligo who had depigmented macules over the hands relatively higher time to wrinkle was observed in our study. Vitiligo is a melanopenic disorder and is unknown to cause any structural alterations in the epidermis or dermis. Most of the patients showed an increased time to wrinkle, which could be hypothesized for the following reasons.

Firstly, "Neural Theory" was one of the earliest theories proposed in Vitiligo by Sir Lerner³¹ in 1959 and later supported by others.^{32,33} The role of the sympathetic nervous system in Vitiligo has been established in the past. There is a dysfunction in sympathetic nervous systems in Vitiligo that affects melanin production leading to depigmentation. Water-induced wrinkling is an indicator of the sympathetic nervous system. Hence an altered sympathetic activity might have led to the delay in time to wrinkle in Vitiligo patients.

Secondly, studies in vitiliginous skin with iontophoresis and laser Doppler flowmetry have revealed an increased microcirculation level in lesions with Vitiligo.³⁴ This leads to a nearly threefold increase in cutaneous blood flow in Vitiligo compared to contralateral normal skin leading to an increased duration for recovery from vasoconstriction than control groups.³⁴ Further, it has been stated by Einar P.V. Wilder-Smith et al.,³⁵ that water-immersion wrinkling is directly linked to vasoconstriction. There is a significant reduction in blood flow velocity in all vessels during the wrinkling test. The maximum velocity is found in digital vessels. Hence it is proposed that the water-immersion wrinkling test is a function of digit pulp vasoconstriction and alters with abnormalities in the blood flow. Hence combining the data from the above points and applying it to our study, it can be hypothesized that the increased time to wrinkle in our study is due to the increase in cutaneous blood flow in vitiliginous skin compared to the normal skin.

Lastly, all these patients were on NBUVB phototherapy treatment. Prolonged UVB causes hardening, and this may be the reason for the increased time to wrinkle. The mechanism of action of phototherapy and photo chemotherapy-induced artificial "hardening" is not

fully understood. However, it is postulated that over time, increased exposure to phototherapy stratum corneum thickens and rigidifies.^{36–38} It also causes hyperpigmentation and alteration of cellular immunity. UVB radiation has several effects on the skin, such as induction of alteration in cytokine production, local immunosuppression, stimulation of melanocyte-stimulating hormone, increased melanocyte proliferation, and melanogenesis.

The time to wrinkle was considerably higher in patients with psoriatic lesions over their hands compared to the normal population. Hyperkeratosis, parakeratosis, and thickening of the stratum corneum are the major histopathological features of Psoriasis. The proposed mechanism of wrinkling is postulated in Psoriasis due to the stratum corneum's thickness, which creates a mechanical barrier preventing the water percolation in the water immersion test. The stratum corneum is thick or hyperkeratotic in Psoriasis, creating less extensibility, decreased deep tissue turgor, preventing contraction of myoepithelial cells in the absence of sebaceous glands in the glabrous skin.³⁹

5. Limitations of the study

1. Single observer study: Observer bias.
2. The diurnal variation in the water immersion induced wrinkling was not tested for, owing to circadian variations observed in the autonomic nervous system functioning.
3. The constancy of environmental factors and hardness of water was not taken into account.

6. Conflict of Interest

The authors declare they have no conflict of interest.

7. Source of Funding

No financial support was received for the work within this manuscript.

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Cite this article: Ravindran S, Criton S. A comparative analysis of water immersion induced hand wrinkling in dermatological diseases. *IP Indian J Clin Exp Dermatol* 2022;8(1):32-38.