# Comparison of Dexpanthenol and Zinc Oxide Ointment with Ointment Base in the Treatment of Irritant Diaper Dermatitis from Diarrhea: A Multicenter Study

Siriwan Wananukul MD*, Wanida Limpongsanuruk MD**,
Srisupalak Singalavanija MD**, Wanee Wisuthsarewong MD***

** Chulalongkorn University,*
*** Queen Sirikit National Institute of Child Health*
**** Siriraj Hospital Bangkok*

***Background:*** *Severity of irritant diaper dermatitis (IDD) from diarrhea varies from patient to patient depending on the nature of feces and the number of bowel movements. The purpose of the present study was to compare the effectiveness of dexpanthenol and zinc oxide ointment with ointment base in the treatment of irritant diaper dermatitis from acute diarrhea in children by measuring transepidermal water loss (TEWL).*
***Material and Method:*** *Forty-six children with diarrhea were prospectively, block randomized, investigator-blinded to receive dexpanthenol and zinc oxide ointment on one side and ointment base on the other side. TEWL was measured before and on days 1, 3, and 7 of treatment together with the assessment of severity score. The efficacy of treatment was defined by complete clearance of the lesion.*
***Results:*** *TEWL in the treated and control side was not different before the application of the topical medication. In the present study, the efficacy of 5% dexpanthenol and zinc oxide ointment on D3 was 39% (18 from 46 patients) compared to 32% in the ointment base side. On D7, the efficacy of the treated side was 58.7% and the ointment base side was 56%. The patients who still had skin lesions were those who had prolonged diarrhea. On the treated side, the mean of TEWL was lower than the control side on D1 ($p = 0.18$) and had significant improvement on D3 ($p = 0.002$). At the end of the present study, TEWL on the treated side was less than TEWL of the control side but it did not have statistical significance ($p = 0.07$). There was no rash or sign of abnormality on the treated side at the end of D7.*
***Conclusion:*** *In the treatment of IDD from acute diarrhea, 5% dexpanthenol and zinc oxide ointment significantly decreased TEWL in the treated side more than the ointment base on day3 but the severity score was not significantly different on days 1, 3 and 7.*

***Keywords:*** *Dexpanthenol, Zinc oxide, Irritant diaper dermatitis, Diarrhea, Transepidermal water loss*

***J Med Assoc Thai 2006; 89 (10): 1654-8***
***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

Irritant diaper dermatitis (IDD) is common in infants with diarrhea. It is caused by friction, maceration, urine, protease, and lipases in fecal content resulting in stratum corneum edema[1,2].

The function of normal skin is to minimize water loss to the environment and prevent toxic substance and microorganisms to penetrate the skin. Skin damage in IDD increases transepidermal water loss (TEWL). Measuring of TEWL is a well-accepted, sensitive, non-invasive assessment method to measure barrier function of the skin. It was also chosen as a parameter to analyze the process of wound healing[3].

Treatment recommendation for IDD is to minimize exposure of urine, feces, and friction. Zinc oxide is generally recommended as the best initial choice for the treatment of diaper dermatitis[4]. Pantothenic acid

*Correspondence to : Wananukul S, Division of Pediatric Dermatology, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Rama IV Rd, Bangkok 10330, Thailand. Phone: 0-2256-4951, Fax: 0-2256-4911, E-mail: siriwanwananukul@yahoo.com*

is a component of coenzyme A. Topical dexpanthenol, an alcoholic analog of pantothenic acid, acts like a moisturizer that improves stratum corneum, hydration and reduces TEWL[5]. It has been used to prevent diaper rash on premature and full-term babies[6]. The purpose of the present study was to compare the efficacy of dexpanthenol and zinc oxide ointment with ointment base in the treatment of irritant diaper dermatitis from acute diarrhea in children by measuring TEWL. The study was done in three medical training centers in Bangkok, Thailand.

## Material and Method

### *Study population*

All infants who had irritant diaper dermatitis from diarrhea aged between 0-24 months were recruited from King Chulalongkorn Memorial Hospital, Queen Sirikit National Institute of Child Health and Siriraj Hospital. Written informed consents were obtained from all of their parents/legal guardians. The institutional ethics committee of each center approved the protocol.

### *Study design: Double-blinded block randomization*

The study design of each of the three centers was a prospective, block randomized, investigator-blinded. A subject was to receive either 5% dexpanthenol and 5% zinc oxide as active ingredients (Nivea Baby Panthenol Ointment, Beiersdorf SA, France) or ointment base (liquid paraffin, bee wax, Department of Pharmaceutical, King Chulalongkorn Memorial Hospital) on each side. Both the ointment containing 5% dexpanthenol and the ointment base were repackaged in identical tubes.

### *TEWL - measurement*

Tewameter TM 210 (Courage & Khazaha, Koln, Germany) was used to measure TEWL by a method based on determination of the water vapor pressure gradient in the air layer close to the skin surface[7].

TEWL was measured before treatment, and on days 1, 3, and 7 of the treatment. Before measuring, the preparation residues were removed with a cloth and the skin surfaces were washed with tap water and pat-dried for 30 minutes and before application of the medication. During the measurements, the infants were mostly asleep and showed little motor activity. To avoid errors due to moisture on the investigator's hands, rubber gloves were worn. The skin condition on both sides was clinically graded for severity.

### *Assessment of severity*

The presence of diaper rash was noted daily using the severity score as follows:

Score 0: No erythema;
1: Slight, diffuse or partial erythema;
2: Marked sharply demarcated erythema;
3: Severe erythema without infiltration;
4: Severe erythema with infiltration;
5: Severe erythema with infiltration and vesiculation or epidermal defects

The evaluation was done according to the above criteria. Daily care of the infants on the diaper area consisted of cleansing with water followed by pat-drying. According to the randomization, the skin on each side was followed by either an application of a thin layer of 5% dexpanthenol and 5% zinc oxide ointment or ointment base. The efficacy of treatment was defined by complete clearance of the lesion.

### *Statistical analysis*

Statistical analyses were performed with SPSS 11.5 for Windows software (SPSS Inc., Chicago, IL, USA); TEWL using paired T-test and severity score using Wilcoxon signed ranks test. A p- values of less than 0.05 were accepted as significant.

## Results

Forty-six infants with diarrhea (25 M and 21 F), with an aged ranged from 1-22 months, were recruited. Thirty-eight infants completed this experimental study according to the protocol, eight patients refused to come in and had their TEWL measured at D7. All subjects had diaper dermatitis cleared up (confirmed by telephone calls).

TEWL in the treated and control side was not different before the application of the topical medication (Table 1). TEWL on the treated side decreased significantly from baseline on D1, D3 and D7 with a p-value of 0.002, < 0.001 and < 0.001, respectively. TEWL on the control side also decreased significantly from baseline on D1, D3 and D7 with p-value of 0.034, 0.004 and < 0.001, respectively. In the present study, the efficacy of 5% dexpanthenol and zinc oxide ointment on D3 was 39% (18 from 46 patients) compared to 32% on the ointment base side. On D7, the efficacy of the treated side was 58.7% and the ointment base side was 56%. Patients who still had skin lesions were those who had prolonged diarrhea. On the treated side, the mean of TEWL was lower than the control side on D1 and had significantly decreased on D3 ($p = 0.002$). At the end of the study TEWL on the treated side was less than

**Table 1.** Transepidermal water loss before and after application of ointment containing 5% dexpanthenol and 5% zinc oxide compared with ointment base in irritant diaper dermatitis in children with diarrhea

| | Dexpanthenol and zinc oxide side Mean ± SD (p-value)* | Ointment base side Mean ± SD (p-value)* | p-value between treatment group |
|---|---|---|---|
| D0 (n = 46) | 53.6 ± 19.8 | 53.4 ± 19.9 | 0.872 |
| D1 (n = 46) | 41.6 ± 20.0 (0.002) | 44.1 ± 18.5 (0.034) | 0.187 |
| D3 (n = 43) | 36.0 ± 17.9 (<0.001) | 41.1 ± 17.6 (0.004) | 0.002 |
| D7 (n = 38) | 31.5 ± 14.2 (<0.001) | 34.5 ± 15.2 (<0.001) | 0.072 |

* significant different from day 0 (DO)

**Table 2.** Severity score before and after application of ointment containing 5% dexpanthenol and 5% Zinc oxide compared with ointment base

| | Dexpanthenol and zinc oxide side (Mean rank test) | Ointment base side (Mean rank test) | p-value |
|---|---|---|---|
| D0 (n = 46) | 30.35 | 30.35 | 1.000 |
| D1 (n = 46) | 28.73 | 28.68 | 0.739 |
| D3 (n = 43) | 26.33 | 26.57 | 1.000 |
| D7 (n = 38) | 22.91 | 23.42 | 0.157 |

TEWL on the control side but did not have statistical significance ($p = 0.07$). The severity scores of both sides were significantly decreased from baseline ($p < 0.0001$ in both groups) but there was no significant difference between dexpanthenol and zinc oxide ointment compared to the ointment base side throughout the study period (Table 2). There was neither rash nor sign of abnormality on the treated side at the end of D7.

## Discussion

The severity of IDD may vary from one patient to another patient depending on the nature of feces and the number of bowel movements[7]. The authors studied IDD from diarrhea with block randomized, double-blind placebo-controlled method in the same patient. The TEWL before treatment in the treated side and the control were not different ($p = 0.87$). Dexpanthenol and zinc ointment decreased TEWL significantly better than ointment base on D3 but the severity scores were not different. This finding may be explained by the higher sensitivity of TEWL in the measurement of the barrier function of the skin than the severity scoring system. TEWL is well accepted as a non-invasive assessment method to measure the skin barrier function in contact dermatitis[3,8] in premature infants[9,10]. To minimize the interpersonal variables from the difference in severity and other variables provided by caregivers, the authors set up the treatment and control in the same persons. The difference on the treated sides was not much because the ointment base contains ointment.

The cure for diaper dermatitis occurs when the child no longer needs to wear a diaper. The incidence of diaper dermatitis was 7.35% with a peak of incidence between age 9 and 12 months[11]. Prolonged skin wetness, skin damage from friction, fecal protease and lipase enzymes together with an increase in pH from ammonia increase the activities of enzyme while wearing diapers cause diaper dermatitis[1,12,13]. The type of diaper has been changed from a cloth diaper to disposable diapers, which contain many types of material. Using a disposable diaper, containing super-absorbent gel, markedly reduces IDD compared to other material[14]. Environmental concerns encouraging parents to use cotton nappies instead of disposables, the outcome of diaper dermatitis was not different between the types of diaper worn[12]. Prevention of diaper rash by using proper diapers and proper care are important. Barrier cream is also beneficial in preventing diaper rash.

Dexpanthenol, a derivative of pantothenic acid, is well absorbed through the skin and is rapidly

converted to pantothenic acid[5]. Pantothenic acid is a component of coenzyme A, which serves as a cofactor for enzyme-catalyzed reaction and helps to accelerate the epidermal regeneration process. Topical dexpenthenol acts like a moisturizer, maintaining skin softness and elasticity, improving stratum corneum hydration and reducing TEWL[5]. It has been used in the prevention and treatment of diaper rash including wounds and skin care in Europe[5,6].The side effect of topical dexpanthenol which has been reported is allergic contact dermatitis[15,16].

Zinc oxide is categorized and FDA-approved for the treatment of diaper rash and is the most common ingredient in over-the-counter diaper rash products[17]. Zinc oxide also enhances the healing of the skin[18,19] and has been used as a barrier cream[2].

Other products that have been used for the treatment of diaper rash include petrolatum, titanium, and sucralfate[20]. A short duration of mild topical corticosteroid has been used in moderate to severe cases that have not responded to other topical agents[21].

In conclusion, 5% dexpanthenol and zinc oxide ointment significantly decreased TEWL in the treatment of IDD from acute diarrhea, better than ointment base on day 3 but severity score was not significantly different on days 1, 3, and 7.

**Acknowledgements**

The authors wish to thank the Department of Pharmaceutics, King Chulalongkorn Memorial Hospital for repackaging 5% dexpanthenol and zinc oxide ointment and the Dermatology Unit, Department of Medicine, Faculty of Medicine, Ramathibodi Hospital for providing the Tewameter.

**References**

1. Atherton DJ. A review of the pathophysiology, prevention and treatment of irritant diaper dermatitis. Curr Med Res Opin 2004; 20: 645-9.
2. Wolf R, Wolf D, Tuzun B, Tuzun Y. Diaper dermatitis. Clin Dermatol 2000; 18: 657-60.
3. Levy JJ, von Rosen J, Gassmuller J, Kleine KR, Lange L. Validation of an in vivo wound healing model for the quantification of pharmacological effects on epidermal regeneration. Dermatology 1995; 190: 136-41.
4. Siegfried EC, Shah PY. Skin care practices in the neonatal nursery: a clinical survey. J Perinatol 1999; 19: 31-9.
5. Ebner F, Heller A, Rippke F, Tausch I. Topical use of dexpanthenol in skin disorders. Am J Clin Dermatol 2002; 3: 427-33.
6. Putet G, Guy B, Pages S, Gibaud C, Andres P, Sirvent A, et al. Effect of bepanthen ointment in the prevention of diaper rash on premature and full-term babies: open pilot study. Real Pediatr 2001; 63: 33-8.
7. Jordan WE, Lawson KD, Berg RW, Franxman JJ, Marrer AM. Diaper dermatitis: frequency and severity among a general infant population. Pediatr Dermatol 1986; 3: 198-207.
8. Pinnagoda J, Tupker RA, Agner T, Serup J. Guidelines for transepidermal water loss (TEWL) measurement. A report from the Standardization Group of the European Society of Contact Dermatitis. Contact Dermatitis 1990; 22: 164-78.
9. Nopper AJ, Horii KA, Sookdeo-Drost S, Wang TH, Mancini AJ, Lane AT. Topical ointment therapy benefits premature infants. J Pediatr 1996; 128: 660-9.
10. Wananukul S, Praisuwanna P, Kesorncam K. Effects of clear topical ointment on transepidermal water loss in jaundiced pretermm infants receiving phototherapy. J Med Assoc Thai 2001; 84: 837-41.
11. Ward DB, Fleischer AB Jr, Feldman SR, Krowchuk DP. Characterization of diaper dermatitis in the United States. Arch Pediatr Adolesc Med 2000; 154: 943-6.
12. Philipp R, Hughes A, Golding J. Getting to the bottom of nappy rash. ALSPAC Survey Team. Avon Longitudinal Study of Pregnancy and Childhood. Br J Gen Pract 1997; 47: 493-7.
13. Berg RW, Buckingham KW, Stewart RL. Etiologic factors in diaper dermatitis: the role of urine. Pediatr Dermatol 1986; 3: 102-6.
14. Campbell RL, Seymour JL, Stone LC, Milligan MC. Clinical studies with disposable diapers containing absorbent gelling materials: evaluation of effects on infant skin condition. J Am Acad Dermatol 1987; 17: 978-87.
15. Jeanmougin M, Manciet JR, Moulin JP, Blanc P, Pons A, Civatte J. Contact allergy to dexpanthenol in sunscreens. Contact Dermatitis 1988; 18: 240.
16. Stables GI, Wilkinson SM. Allergic contact dermatitis due to panthenol. Contact Dermatitis 1998; 38: 236-7.
17. Boiko S. Treatment of diaper dermatitis. Dermatol Clin 1999; 17: 235-40, x.
18. Tarnow P, Agren M, Steenfos H, Jansson JO. Topical zinc oxide treatment increases endogenous gene expression of insulin-like growth factor-1 in granulation tissue from porcine wounds. Scand J

Plast Reconstr Surg Hand Surg 1994; 28: 255-9.
19. Agren MS. Studies on zinc in wound healing. Acta Derm Venereol Suppl (Stockh) 1990; 154: 1-36.
20. Markham T, Kennedy F, Collins P. Topical sucralfate for erosive irritant diaper dermatitis. Arch Dermatol 2000; 136: 1199-200.
21. Gupta AK, Skinner AR. Management of diaper dermatitis. Int J Dermatol 2004; 43: 830-4.

---

## *การศึกษาเปรียบเทียบขี้ผึ้งเด็กแพนทีนอลและซิงค์ออกไซด์กับขี้ผึ้งเบสในการรักษาในเด็กที่เป็นผื่นผ้าอ้อมจากการถ่ายเหลว: การศึกษาจากหลายสถาบัน*

***ศิริวรรณ วนานุกูล, วนิดา ลิ้มพงศานุรักษ์, ศรีศุภลักษณ์ สิงคาลวณิช, วาณี วิสุทธิ์เสรีวงศ์***

***บทนำ**: ความรุนแรงของผื่นผ้าอ้อมจากการถ่ายเหลวในผู้ป่วยแต่ละคนไม่เท่ากัน ขึ้นกับลักษณะและจำนวนครั้งของการถ่าย*

***วัตถุประสงค์**: เพื่อเปรียบเทียบประสิทธิภาพของขี้ผึ้งเด็กแพนทีนอลและซิงค์ออกไซด์กับขี้ผึ้งเบส ในการรักษาภาวะผื่นผ้าอ้อมจากการถ่ายเหลวในเด็กโดยการวัดการระเหยของน้ำผ่านผิวหนัง (transepidermal water loss, TEWL)*

***วัสดุและวิธีการ**: การศึกษาไปข้างหน้าโดยรวบรวมผู้ป่วยเด็กที่มีผื่นผ้าอ้อมจากการถ่ายเหลว 46 คน จาก 3 สถาบัน แบ่งเป็นกลุ่มโดยไม่ให้ผู้วิจัยทราบว่าผู้ป่วยได้รับการทาขี้ผึ้งเด็กแพนทีนอลและซิงค์ออกไซด์กับครีมเบสที่ด้านใดของผื่นในผู้ป่วยคนเดียวกัน ทำการวัด TEWL ก่อนทาและในวันที่ 1, 3 และ 7 ของการทา ประสิทธิภาพของการรักษาดูจากการที่ผื่นหายหมด*

***ผลการศึกษา**: TEWL ก่อนการรักษาในแต่ละข้างไม่แตกต่างกัน ประสิทธิภาพของการรักษาผื่นผ้าอ้อมในข้างที่ทาขี้ผึ้งเด็กแพนทีนอลและซิงค์ออกไซด์ ในวันที่ 3 ของการรักษาเท่ากับร้อยละ 39 เปรียบเทียบกับข้างที่ทาขี้ผึ้งเบสซึ่งเท่ากับ 32 ส่วนในวันที่ 7 ข้างที่ทาขี้ผึ้งเด็กแพนทีนอลและซิงค์ออกไซด์เท่ากับร้อยละ 58 ส่วนข้างที่ทาขี้ผึ้งเบสเท่ากับ 56 ผู้ป่วยที่ยังมีผื่นอยู่เป็นผู้ป่วยที่มีการถ่ายเหลวนาน ส่วนค่า TEWL ในข้างที่ทาขี้ผึ้งเด็กแพนทีนอลและซิงค์ออกไซด์ในวันแรกต่ำกว่าข้างที่ทาขี้ผึ้งเบส ($p = 0.18$) และในวันที่ 3 ต่ำกว่าอย่างมีนัยสำคัญทางสถิติ ($p = 0.002$) ส่วนในวันที่ 7 ของการรักษาค่า TEWL ไม่แตกต่างกัน ($p = 0.07$) ไม่พบผลข้างเคียงจากการทายา*

***สรุป**: ขี้ผึ้งเด็กแพนทีนอลและซิงค์ออกไซด์ลด TEWL อย่างมีนัยสำคัญทางสถิติในวันที่ 3 ของการรักษาภาวะผื่นผ้าอ้อมจากการถ่ายเหลว แต่เมื่อเปรียบเทียบคะแนนความรุนแรงพบว่าไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติในวันที่ 1, 3 และ 7*

---