

A Prospective Placebo-Controlled Study on the Efficacy of Onion Extract in Silicone Derivative Gel for the Prevention of Hypertrophic Scar and Keloid in Median Sternotomy Wound in Pediatric Patients

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Background: New topical treatments studied in adults have been published to be potentially effective in the treatment of hypertrophic scar and keloids. There is still no study in Thai children.

Objective: To study the efficacy of 10% onion extract in silicone derivative gel for the prevention of hypertrophic scar and keloid in median sternotomy wound from open heart surgery in pediatric patients.

Material and Method: Thirty-nine pediatric patients who had median sternotomy were recruited in this prospective randomized, double-blinded, placebo-controlled split-scar experimental study. The wound in each patient was divided into upper and lower parts, and the treatment with, either onion extract gel or placebo was randomly applied by block randomization onto each part of the wound twice daily after the seventh day postoperatively for six months. The incidence of scars, serial photographs of the wound, Vancouver Scar Scale (VSS), and adverse effect were assessed at each visit.

Results: Thirty patients with the mean age of 4.3 years completed the 6-month study period. Six patients (20%) in onion extract gel group had no scar compared to one patient (3.3%) in placebo group ($p = 0.04$). Of the 27 patients with hypertrophic scar, nine were from onion extract gel group and 18 from the placebo group ($p = 0.02$). Keloid was not statistically significant different in both groups ($p = 0.29$). VSS was not statistically significant different in all visits. One case had a pustule on the part of the onion extract in silicone derivative application at the sixth month.

Conclusion: Onion extract in silicone derivative gel can significantly decreased the incidence of hypertrophic scar from median sternotomy wound in pediatric patients. Keloid did not show statistically significant differences in both groups.

Keywords: Onion extract, Hypertrophic scar, Median sternotomy wound, Pediatric patients

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Median sternotomy wound from open heart surgery has more tension due to underlying bony structure and tend to have scars⁽¹⁾. Scar formation in individual person has various predisposing factors including location and tension of wound, ethnicity, and age⁽¹⁻³⁾. Darker skin phenotypes has higher incidence of keloids. Asian ethnicity is more subject to develop scars after surgery than Caucasian⁽⁴⁾. A review of hypertrophic scar from burns in children confirmed high incidence of scarring in the non-whites⁽⁵⁾. Hypertrophic scar and keloid from median sternotomy wounds, as a result of open heart surgery in pediatric

patients, can cause itching, pain and discomfort⁽⁶⁾. Various treatments such as intralesional corticosteroid, interferon, fluorouracil, radiation, and pulsed-dye laser treatment have shown to be beneficial^(1,5). However, most of these treatments are either painful or may have adverse effects on children. New topical treatments studied in adults and published to show the potential effect in the treatment of hypertrophic scar and keloids⁽⁷⁾. Prevention with topical agents seems to be the best strategy for management of scarring in children. Data from previous studies suggest that silicone gel^(7,8) and 12% onion extracts^(9,10) offer benefits on treatment of scarring in adults while other studies^(11,12) suggest that it was not effective. There is still no study of children.

The authors conducted a prospective, randomized, spit-scar to determine whether 10% onion

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extract in silicone derivative gel can prevent scar formation from median sternotomy in pediatric patients.

Material and Method

The study was conducted at King Chulalongkorn Memorial Hospital, Bangkok, Thailand, with the approval of the Institutional Review Board (IRB) of the Faculty of Medicine, Chulalongkorn University. Sample size was calculated by using the formula for two related groups (dependent samples) to have an 80% chance of detecting a mean difference of scar appearance (SD) by 0.48 (0.95)⁽¹³⁾ at the 95% confidence level. A sample size of 30 subjects was required.

All children who underwent median sternotomy post open heart surgery at King Chulalongkorn Memorial Hospital between November 2009 and February 2011, were enrolled in the study after obtaining informed consent. Exclusion criteria were those who have underlying factors that may influence wound healing such as usage of steroid and immune suppressants.

Study design

The study was designed as a prospective, double-blinded, randomized, split-scar from median sternotomy wound of open heart surgery in pediatric patients.

The wound in each patient was divided into upper and lower parts. Each part of the wound was randomized and assigned to be applied with either 10% onion extract in silicone derivative (Cybele Scagel, Bangkok Botanica, Bangkok, Thailand) or placebo. The placebo gel was a composite of water, acrylate, C10-30 alkyl acrylate crosspolymer, polysorbate 20 and fragrance that was similar in color and consistency as that of active gel. Topical application, twice daily was started from day seven after surgery continuously for six months.

Assessment

Hypertrophic scar was defined if the scar remains within the original wounds while keloids defined as a scar that over grows the boundary of the original wound⁽¹⁾. The Vancouver Scar Scale (VSS), which is composed of scar pigmentation, vascular, pliability, and height⁽¹⁴⁾. Serial photographs of wound, were assessed at baseline, weeks 3, months 2, months 4, and months 6. Any adverse effects were recorded at each visit.

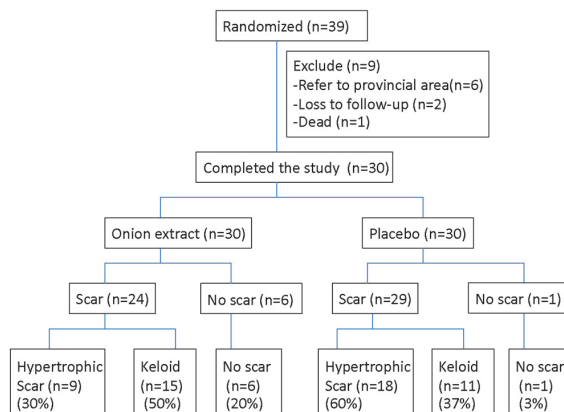


Fig. 1 The flow chart showing number of randomized and result of completed parts of the scar.

Data analysis was performed by Wilcoxon signed rank test and McNemar Chi-square test in SPSS for Windows. A p-value of less than 0.05 was set for statistically significant difference.

Results

Thirty-nine patients were recruited into the study. Thirty patients (17 boys and 13 girls) within mean age of 4.3 years (6 months-15 years) completed the six-month study period.

Nine patients did not complete the study due to referral to provincial area (6 patients), loss to follow-up (2 patients) and one patient died at one month after surgery.

Six patients (20%) in the onion extract gel group had no scar compared to one patient (3.3%) in the placebo group ($p = 0.04$) (Fig. 1).

Hypertrophic scarring in the parts using onion extract in silicone derivative (30%) was significantly lower than in placebo (60%) ($p = 0.02$) (Fig. 2). Keloid in the parts using onion extract in silicone derivative (50%) was not significantly different from placebo (37%) ($p = 0.29$) (Table 1, Fig. 3).

Table 1. Incidence of hypertrophic scar and keloids in onion extract in silicone derivative and placebo groups

Type	Treatment		p-value
	Onion extract in silicone derivative n (%)	Placebo n (%)	
Hypertrophic scar	9 (30)	18 (60.0)	0.02*
Keloid	15 (50)	11 (36.7)	0.29

* $p < 0.05$ McNemar Chi-square test

The Vancouver Scar Scale (VSS), which rate pigmentation, vascular, pliability and height of scar at baseline, 3 weeks, 2 months, 4 months, and 6 months after starting treatment were not significantly different (Fig. 4).

There was no report of any side effects except one case had a pustule on the part of the onion extract

in silicone derivative application at the sixth month. A topical antibiotic was prescribed with good results.

Discussion

Onion extract has been marketed for improvement of surgical scar. Quercetin, kaempferol and thiosulfates are active ingredients in onion extract

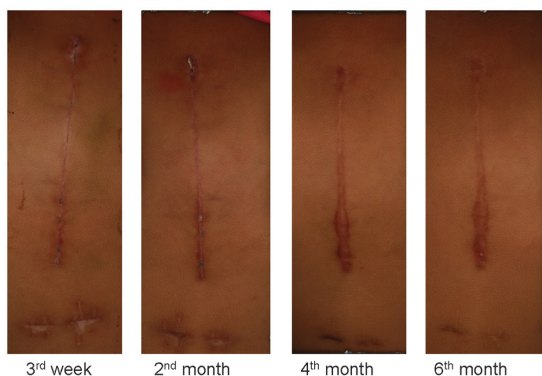


Fig. 2 Photograph of patient No. 13 at 3rd week, 2nd, 4th and 6th month follow-up. Onion extract and placebo were applied on the upper and lower part, respectively. Hypertrophic scar was visibly more elevated in the lower part.

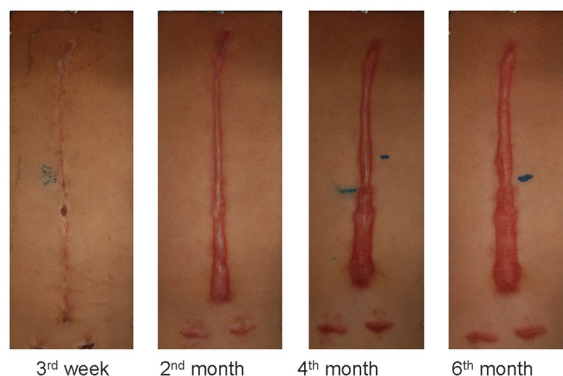


Fig. 3 Photograph of patient No. 19 at 3rd week, 2nd, 4th and 6th month follow-up. Onion extract and placebo were applied on the lower and upper part, respectively. Keloid was visibly detected since the 4th month.

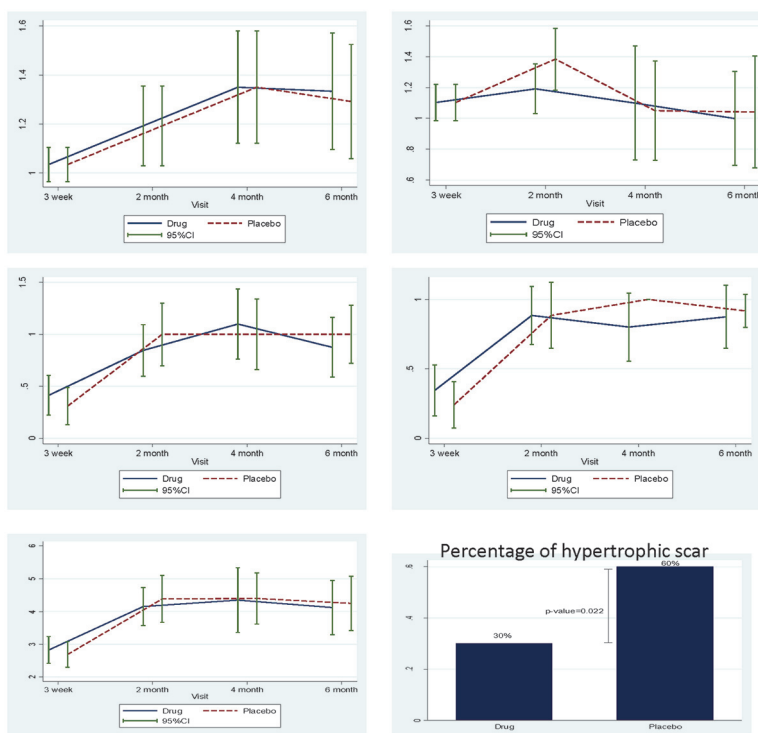


Fig. 4 Vancouver scar score during the follow-up and percentage of hypertrophic scar.

that have shown in vitro studies to have anti-inflammatory effect^(15,16). Quercetin affects cell proliferation by decreasing cell protein contents as well as the reduction of mitotic index depending on the concentration and cell exposure time to the compound⁽¹⁷⁾. Onion extract and quercetin have a dose-dependent up-regulation of MMP-1 expression⁽¹⁶⁾. These data suggest that onion extract is a promising material for reducing scar formation. A randomized, controlled, blinded-investigator study of onion extract gel versus no treatment on new scars found that onion extract gel improved the appearance of new scars⁽¹³⁾. A recent prospective double-blind, split-scar study showed that early use of 12% onion extract gel on Pfannenstiel's cesarean section scars in Asians resulted in improvement of scar height and symptoms⁽¹⁸⁾. In another study using 12% onion extract in silicone derivative gel for preventing the hypertrophic scar after median sternotomy, the VSS score was not significantly different, only pigmentation, pain and itch scores were significantly different ($p < 0.05$)⁽¹⁹⁾. Most of the product market at 12% onion extract is for adults, while 10% onion extract is proposed to be used in children.

The authors conducted a prospective, randomized, placebo-controlled, split-scar to minimize other factors that might affect scarring. From the present study, the incidence of hypertrophic scar and keloid from median sternotomy in pediatric patient in the part that applied 10% onion extract in silicone derivative gel was lower than in the placebo. Incidence of hypertrophic scar was significantly lower than placebo but incidence of keloid did not show statistically significant difference with placebo. VSS were not significantly different throughout the follow-up period from baseline, weeks 3, month 2, month 4, and month 6. Pain and itching were not evaluated in our patients because the authors think that it was subjective and it was hard to be addressed in small children. Even though the active ingredient can decrease the incidence of hypertrophic scar, compared to placebo but VSS was not significantly different. The Vancouver Scar Scale (VSS) that was used to rate burn scars on pigmentation, vascular, pliability and height⁽¹⁴⁾ may not be suitable for the evaluation of non-burn scars⁽³⁾. Limitations in this study are small sample size and the need for longer follow-up periods. A larger sample size and tools that can differentiate scar clinically and objectively for color and measure height in range such as colorimeter, volume meter or 3D imaging technologies are essential to provide assessing scars accurately.

From the present study, 10% onion extract in silicone derivative gel on median sternotomy wound in pediatric patient early after stitch removal can prevent hypertrophic scar. It is easy to use and less painful than other treatments for scars and has less adverse effects on children. In patients who did not respond to 10% onion extract, 12% onion extract may be beneficial especially in older children as in vivo study shows that onion extract and quercetin had a dose-dependent effect on scar formation and in studies using 12% onion extract showed that it has benefits on scar symptoms^(18,19), height⁽¹⁸⁾, pigmentation⁽¹⁹⁾, and scar softening⁽¹³⁾.

In conclusion, during the six-month follow-up period, the evidence demonstrates that 10% onion extract in silicone derivative gel can prevent or decrease severity of hypertrophic scars. However, 10% onion extract in silicone derivative gel cannot prevent keloids formation, which is more severe.

Potential conflicts of interest

The present study was supported by Bangkok Botanica, Bangkok, Thailand. The sponsor had no influence on study design, data collection, and data analyses.

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การศึกษาไปข้างหน้าเพื่อเปรียบเทียบประสิทธิภาพระหว่างสารสกัดจากหัวหอมในสารซิลิโคนกับยาหลอกในการป้องกันการเกิดแผลเป็น hypertrophic และ keloid จากแผลผ่าตัดที่หน้าอกในผู้ป่วยเด็ก

ศิริวรรณ วนานุกูล, สุชีรา ฉัตรเพริศพราย, ดนยวรรณ พึ่งสุจริต, พรเทพ เลิศทรัพย์เจริญ

ภูมิหลัง: มีการศึกษาถึงยาทาใหม่ที่ใช้ในการรักษาแผลเป็นในผู้ใหญ่ แต่ยังไม่มีการศึกษาในเด็กไทย

วัตถุประสงค์: เพื่อศึกษาเปรียบเทียบประสิทธิภาพในการป้องกันการเกิดแผลเป็นนูน (hypertrophic scar) และ keloid หลังการผ่าตัดโรคหัวใจพิการแต่กำเนิดในผู้ป่วยเด็ก ระหว่างเจลสารสกัดจากหัวหอม (onion extract) และสารอื่นๆ กับยาหลอก (placebo)

วัตถุประสงค์และวิธีการ: เป็นการศึกษาแบบ prospective randomized double-blinded split-scar experimental study ทำการศึกษาในผู้ป่วยเด็กที่มีแผล median sternotomy หลังจากผ่าตัดโรคหัวใจพิการแต่กำเนิด ที่เข้ารับการรักษาที่โรงพยาบาลจุฬาลงกรณ์ จำนวนผู้ป่วยเด็ก 39 ราย ตั้งแต่เดือนพฤศจิกายน พ.ศ. 2552 ถึง เดือนกุมภาพันธ์ พ.ศ. 2554 หลังจากผ่าตัดวันที่ 7 ผู้ป่วยจะได้ยาทาโดยวิธีสุ่มแบ่งแผลเป็นแผลครึ่งบนและแผลครึ่งล่าง ให้ทาเจลสารสกัดจากหัวหอมในสารซิลิโคนหรือยาหลอกในผู้ป่วยรายเดียวกัน ทำการตรวจติดตามการเกิดแผลเป็นทั้งหมด 6 เดือน โดยผู้ประเมินและผู้ป่วยไม่ทราบชนิดของยาที่ใช้ การประเมินแผลเป็นใช้อัตราการเกิดแผลเป็น, Vancouver Scar Scale (VSS) เปรียบเทียบแผลครึ่งบนและครึ่งล่าง และถ่ายรูปแผลเป็นรวมทั้งบันทึกผลข้างเคียงจากยา

ผลการศึกษา: มีผู้ป่วย 30 ราย ที่เข้าร่วมตลอดการศึกษา 6 เดือน พบว่าในกลุ่มเจลสารสกัดจากหัวหอมในสารซิลิโคน มีจำนวนผู้ป่วยที่ไม่เกิดแผลเป็นเลย 6 ราย (ร้อยละ 20) มากกว่ากลุ่ม placebo ที่มี 1 ราย (ร้อยละ 3.3) อย่างมีนัยสำคัญทางสถิติ ($p = 0.04$) และในกลุ่มเจลสารสกัดจากหัวหอมในสารซิลิโคนมีจำนวนผู้ป่วยที่เป็น hypertrophic scar 9 ราย ซึ่งน้อยกว่ากลุ่ม placebo ที่มี 18 ราย อย่างมีนัยสำคัญทางสถิติ ($p = 0.022$) อัตราการเกิด keloid ในกลุ่มทั้งสองกลุ่มไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ คะแนน VSS ของยาทั้ง 2 กลุ่มไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติในการตรวจติดตามแผลเป็นทั้งหมดเป็นระยะเวลา 6 เดือน มีผู้ป่วย 1 ราย ที่มีตุ่มหนองขนาดเล็กขึ้นในบริเวณที่ทาเจลสารสกัดจากหัวหอมในสารซิลิโคน

สรุป: เจลสารสกัดจากหัวหอมในสารซิลิโคนสามารถช่วยป้องกันการเกิดแผลเป็นในแผล median sternotomy ในผู้ป่วยเด็กได้ส่วนหนึ่ง และช่วยลดอัตราการเกิด hypertrophic scar ลงได้มากกว่ากลุ่ม placebo อย่างมีนัยสำคัญทางสถิติ แต่ไม่ได้ช่วยลดการเกิด keloid
