Risk-Associated Mortality in Patients with Peritonitis Due to *Sandorica Koetjape* Seed Ingestion: A Retrospective Study

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Objective: *To identify the factor associated with the mortality of patients with peritonitis due to Sandoricum koetjape seed ingestion.*
Material and Method: *Thirty patients who presented with peritonitis and had a history of Sandorica seed ingestion between September 2009 and August 2012 were retrospectively reviewed. Gender, age, comorbid, number of ingested seed, duration of symptom, body temperature, shock at initial admission, extent of peritonitis, presence of free air under the dome of the diaphragm, white blood cell count, serum bicarbonate levels, resuscitation time, severity of intraabdominal contamination, perforated wound size, and operation methods were analyzed for their association with the mortality using Fisher's exact test. Odds ratio (OR) and 95% confidence interval (CI) were calculated to determine the strength of association.*
Results: *All patients received a definite diagnosis of Sandorica seed-induced colon perforation intraoperatively. Six of 30 patients died during 28-day hospitalization. The result showed that shock at initial admission (OR 35.0, 95% CI 2.9-411.4, p = 0.002), serum bicarbonate levels less than 15 mmol/L (OR 19.0, 95% CI 1.7-201.6, p = 0.009), and severe intraabdominal contamination (OR 10.0, 95% CI 1.3-74.5, p = 0.029) were the significant factors associated with the mortality.*
Conclusion: *The factor-associated mortality in patients with peritonitis due to Sandorica seed ingestion was consistent with a clinical picture of septic shock. Early recognition and treatment of hypotensive episode accompanying with surgical correction and control of infection is therefore a key to improve the mortality outcome of this group of patients.*

Keywords: *Mortality, Colon perforation, Risk factor, Sandorica seed*

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Peritonitis caused by a perforation in the colon is a serious life threatening condition while the definite diagnosis is usually made intraoperatively. The common etiologies of non-traumatic colon perforation include carcinoma, diverticular disease, and inflammatory or ischemic bowel conditions[1]. Spontaneous perforation could also be found as a rare cause and can be divided into stercoral and idiopathic perforation[1-4]. Stercoral perforation is a perforation of the bowel due to pressure necrosis from hard fecal masses, leading to a round or ovoid perforated ulcer with necrotic and inflammatory edge[3], whereas idiopathic perforation has been defined as a linear tear of the bowel without either inflammatory or ischemic changes[4]. Another cause of bowel perforation is foreign bodies (FBs) i.e., the seeds of fruit such as pickle plum[5]. It seemed that FBs could pass through gastrointestinal tract including pyloric opening and iliocecal valve uneventfully. However, 1% of FBs ingestion caused complications such as peritonitis due to bowel perforation[6].

The seeds of *Sandoricum koetjape* (Sandorica or "Kathon" in Thai) have been reported as a cause of rectosigmoid perforation[7,8] and may be the most common cause of non-traumatic colon perforation in Thailand[8]. Voluntary ingestion of Sandorica seeds is relatively common in the people who live in Thai rural areas. During a half-decade, the authors found a number of patients admitted due to peritonitis (either localized or generalized) with a history of Sandorica seed ingestion. These patients often had a clinical sepsis and required extensive resuscitation prior to emergency surgery. Intraoperative finding showed that the seeds usually presented at (or near) the perforated wound

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and rectosigmoid colon was the only affected site. The mortality rate in this group of patients was high (up to 21.4% as demonstrated in previous report[8]), whereas the factors associated with the mortality was uncertain. To improve the mortality outcome, the present study was then aimed to elucidate the risk-associated mortality in patients with peritonitis due to Sandorica seed ingestion.

Material and Method

Retrospective analysis of medical records was designed for the patients who were admitted due to clinical peritonitis with a history of Sandorica seed ingestion in the Department of Surgery, Chaopraya Yommaraj Hospital, Suphanburi, Thailand between September 2008 and August 2012. Those with other surgical conditions such as ruptured appendicitis or peptic ulcer perforation were excluded. Initially, 31 patients were enrolled in the present study. However, one patient died before surgical operation, so this patient data was excluded due to the uncertain diagnosis. Local Ethic Committee at Chaopraya Yommaraj Hospital approved the present study and waived it necessary to obtain written consent because of its retrospective nature.

The following clinical variables were collected and analyzed as possible factors associated to the mortality: gender, age, comorbidity (detailed in Table 1), number of ingested seeds, duration of symptoms, body temperature, shock at initial admission, peritonitis, free air under the dome of the diaphragm, white blood cell count, serum bicarbonate levels, resuscitation time, severity of intraabdominal contamination, perforated wound size and operation method. Shock was defined as a systolic arterial pressure <90 mmHg and mean arterial pressure <65 mmHg. Resuscitation time was defined as the time period of admission-to-operating room. Severity of intraabdominal contamination was defined as follows; mild, fibrin with exudate; moderate, fecal soiling which intraabdominal lavage was clear; severe, fecal soiling which intraabdominal lavage was not clear[8]. Mortality outcome was defined as the death of the patient within 28-days hospitalization.

Table 1. List of comorbidity

List of comorbid disease
Alcoholism
Asthma
Chronic obstructive pulmonary disease
Cirrhosis
Diabetes mellitus
End stage renal disease (on hemodialysis)
Hypertension
Parkinson disease
Previous history of cerebrovascular accident
Previous history of coronary heart disease
Schizophrenia
Steroid addict

Data were expressed as mean ± standard deviation (range) for continuous data and as percentages for categorical data. Fisher's exact test was used to identify variables possibly correlated with the mortality. Unfortunately, multiple logistic regression was unable to perform due to the limitation of the small number of the study population. Odds ratio (OR) with 95% confidence interval (CI) were calculated as a measure of association. P-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 11.5 (SPSS Inc., Chicago, IL).

Results

Thirty-one patients (14 males and 17 females) presented with peritonitis and had a history of Sandorica seed ingestion were included in the present study. Of these, seven patients died during 28-days hospitalization. However, a female patient died before operation and was therefore excluded from the subsequent analysis. The mean age of the non-survivors was 66.38±12.33 years (range 56-78 years), whereas that of the survivors was 61.33±7.39 years (range 42-85 years). All patients received a definite diagnosis of rectosigmoid perforation intraoperatively, and Sandorica seeds were usually found at (or near) the perforated wound (Fig. 1). According to these, the mortality rate was approximately 20% in the present study. Patients were admitted within the period of April to August each year (which was the harvest season of *Sandoricum koetjape*) (Fig. 2). Clinical data including number of ingested seed, presenting symptom, perforated wound size, method of surgical intervention, causes of death, pathological finding, and length of hospital stay are demonstrated in Table 2. Five patients did not received pathological examination of the surgical specimen due to confident diagnosis of Sandorica seed-induced colon perforation made intraoperatively (in which the seed remained at the perforated wound), so only 25 specimens (in which the

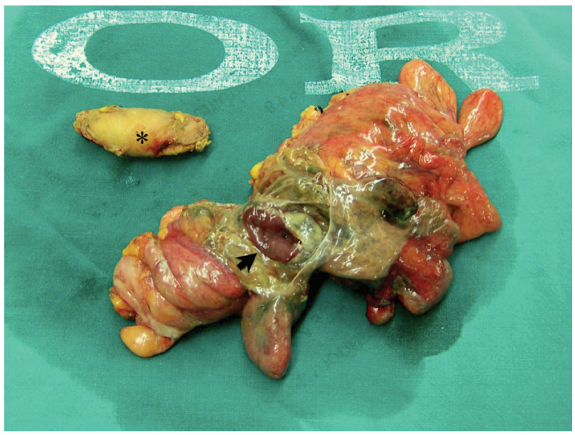

Fig. 1 Colon perforation due to *Sandoricum koetjape* seed ingestion. Labeling; *, Sandorica seed; black arrow, site of perforated wound.

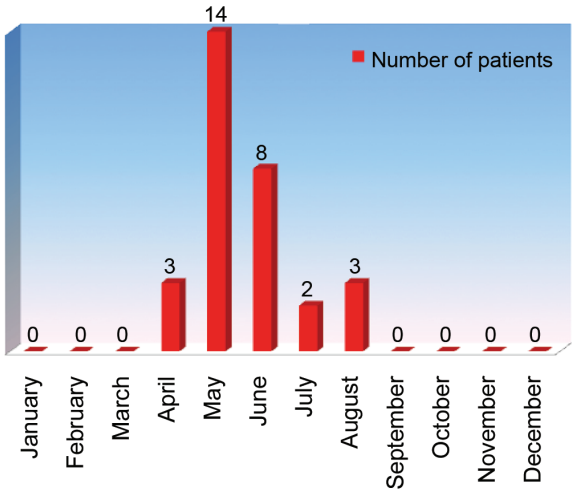

Fig. 2 Annual incidence of patients with peritonitis due to Sandorica seed ingestion. During September 2008-August 2012, a total of 30 patients were admitted into Department of Surgery, Chaopraya Yommaraj Hospital, Suphanburi, Thailand, due to clinical peritonitis with a history of Sandorica seed ingestion. Interestingly, patients only visited within the period of April to August each year, which was the harvest season of *Sandoricum koetjape* fruits.

seed was expelled through the perforation site into peritoneal cavity) were examined for pathological findings (Table 2).

Comparisons of 15 clinical variables between survivors and non-survivors are presented in Table 3. As a result, shock at initial admission (OR 35.0, 95% CI 2.9-411.4, p = 0.002), low serum bicarbonate levels (OR 19.0, 95% CI 1.7-201.6, p = 0.009), and severe intraabdominal contamination (OR 10.0, 95% CI 1.3-74.5, p = 0.029) were significantly correlated with the mortality (Table 4). These significant factors were consistent with a clinical picture of septic shock.

Discussion

Two previous studies emphasized Sandorica seed as a serious cause of bowel perforation, but no study demonstrated the mortality risk associated with this condition. Somboonpanya P[7] reported nine cases of patients with peritonitis due to Sandorica seed ingestion as the descriptive clinical data and did not report the non-survival case. Suradom C et al[8]

Table 2. Pertinent clinical data of patients with peritonitis due to sandorica seed ingestion

Clinical data	Numbers of patient (%)
Number of ingested seed (n = 30)	
1	9 (30.00)
2	5 (16.67)
3	10 (33.33)
4	4 (13.33)
≥5	2 (6.67)
Presenting symptom (n = 30)	
Severe abdominal pain	24 (80.00)
Lower gastrointestinal bleeding	1 (3.33)
Abdominal pain with diarrhea	5 (16.67)
Perforated wound size (cm) (n = 30)	
1	7 (23.33)
2	14 (46.67)
3	9 (30.00)
>3	1 (3.33)
Method of surgical intervention (n = 30)	
Hartmann procedure	21 (70.00)
Repair with proximal loop colostomy	5 (16.67)
Resection and re-anastomosis with loop colostomy	4 (13.33)
Causes of death (n = 6)	
Septic shock with renal failure	3 (50.00)
Septic shock with metabolic acidosis	2 (33.33)
Congestive heart failure with pulmonary edema	1 (16.67)
Pathological finding (n = 25)	
Necrotizing inflammation	11 (44.00)
Diverticulitis	13 (52.00)
Adenocarcinoma	1 (4.00)
Length of hospital stay (days) (n = 24)	
≤15	13 (54.17)
16-30	5 (20.83)
≥31	6 (25.00)

Table 3. Comparison of 15 clinical variables between survivors and non-survivors

	Numbers of patient (%)		p-value
	Survive (n = 24)	Death (n = 6)	
Gender			
Male	12 (50.00)	2 (33.33)	0.657
Female	12 (50.00)	4 (66.67)	
Age (year)			
≤65	15 (62.50)	3 (50.00)	0.660
>65	9 (37.50)	3 (50.00)	
Comorbid			
Absence	7 (29.20)	2 (33.33)	1.000
Presence	17 (70.80)	4 (66.67)	
Number of ingested seed			
≤2	11 (45.80)	3 (50.00)	1.000
>2	13 (54.20)	3 (50.00)	
Duration of symptom (day)			
≤1	19 (79.20)	3 (50.00)	0.300
>1	5 (20.80)	3 (50.00)	
Body temperature (°C)			
<38	10 (20.80)	1 (16.67)	0.372
≥38	14 (79.20)	5 (83.33)	
Shock at initial admission			
Absence	21 (87.50)	1 (16.67)	0.002
Presence	3 (12.50)	5 (83.33)	
Peritonitis			
Localized	8 (33.30)	2 (33.33)	1.000
Generalized	16 (66.70)	4 (66.67)	
Free air under the dome of diaphragm			
Absence	19 (79.20)	3 (50.00)	0.300
Presence	5 (20.80)	3 (50.00)	
White blood cell count (cell/mm^3)			
>5,000	17 (70.80)	2 (33.33)	0.156
≤5,000	7 (29.20)	4 (66.67)	
Serum bicarbonate levels (mmol/L)			
>15	19 (79.20)	1 (16.67)	0.009
≤15	5 (20.80)	5 (83.33)	
Resuscitation time (hr)			
≤6	14 (37.50)	5 (83.30)	0.372
>6	10 (62.50)	1 (16.70)	
Severity of intraabdominal contamination[a]			
Mild-to-moderate	20 (83.30)	2 (33.33)	0.029
Severe	4 (16.70)	4 (66.67)	
Perforated wound size (cm)			
≤2	18 (75.00)	3 (50.00)	0.329
>2	6 (25.00)	3 (50.00)	
Operation method			
Hartman procedure	18 (75.00)	3 (50.00)	0.329
Others	6 (25.00)	3 (50.00)	

[a] Mild, fibrin with exudate; moderate, fecal soiling which intraabdominal lavage was clear; severe, fecal soiling which intraabdominal lavage was not clear

Table 4. Univariate analysis of 3 significant factors related with the mortality

Variable	Odds ratio (95% CI)	p-value
Shock at initial admission	35.00 (2.98-411.46)	0.002
Serum bicarbonate levels ≤15 mmol/L	19.00 (1.79-201.68)	0.009
Severe intraabdominal contamination	10.00 (1.34-74.51)	0.029

demonstrated that 14 of 42 patients with non-traumatic perforation of colon were affected by Sandorica seed ingestion. They also analyzed the factors related to the mortality; however, it was performed on several causes of non-traumatic colon perforation but not focused on Sandorica seed. This present study then aimed to identify the risk-associated mortality in patients with peritonitis due to Sandorica seed. Fifteen clinical variables were analyzed by Fisher's exact test to determine the correlation between each variable and the mortality and OR and 95% CI were also calculated to examine the strength of association. The result showed that three clinical factors including shock at initial admission, low serum bicarbonate levels, and severe intraabdominal contamination were significantly related to the mortality (Table 3, 4). These significant variables were consistent with a clinical picture of septic shock.

According to the presented data and experience, the principle of surgical intervention in this group of patients is suggested as follows; 1) early recognition, resuscitation and treatment of septic shock, and 2) surgical source control of fecal peritonitis and correction of the affected part of the colon. When peritonitis due to Sandorica seed ingestion is suspected, clinical sign of sepsis and septic shock should be recognized at the time of initial admission. In severe cases, early goal-directed therapy for septic shock[9] should be applied together with resuscitation process to prepare patients before on-going surgery. Surgical source control and massive saline irrigation should be performed to decrease the bacterial load in peritoneal cavity. The methods of operation depended on the patient situation and severity of intra-abdominal contamination. Segmental resection of the affected part with end colostomy (Hartmann procedure) was recommended as a treatment of choice in many studies of spontaneous or stercoral perforation with the low mortality[10-12]. Some surgeons prefer colonic repair and proximal loop colostomy[2,7], which is simple and time sparing. One-stage resection with primary anastomosis has been claimed to provide a good outcome, safe and cost effective when performed by experienced colorectal surgeons[13-15]. In the present study, four patients received resection with re-anastomosis. However, diversion of fecal stream by proximal loop colostomy was still performed. Hartmann procedure was the most common procedure in the present study because of the unknown underlying pathogenesis of the perforation. It is safe to remove the affected part of the colon and complete diversion of the fecal stream to prevent further contamination in the peritoneal cavity. Since the method of surgical intervention provided non-significant difference based on the mortality outcome (Table 3), surgeons can choose any suitable procedure depending on clinical situation and experience.

Pathogenesis of colon perforation due to Sandorica seed ingestion has remained unknown. However, the perforation usually found at rectosigmoid colon (as observed in the present study and previous reports[7,8]), which was similar to that of stercoral perforation[2,4,16]. In addition, pathological finding in 11 of 25 examined specimens (44%) were necrotizing inflammation of colonic wall as that found in stercoral perforation (Table 2). Therefore, it was possible that Sandorica seed-induced and stercoral perforation shared some common pathogenic mechanism. The authors hypothesized that the ingested seeds were digested and/or processes during passing through the gastrointestinal tract and then be transformed into the hard "fecaloma" mass, which pressed over the colonic wall, leading to acute pressure necrosis. Another mechanism might be related to diverticular disease, since 13 of 25 examined specimens (52%) were acute diverticulitis with rupture (Table 2). The authors postulated that the seeds might act as a hard solid stool that is difficult to pass through the anal canal, causing sudden increase in the intraluminal pressure. Diverticulosis may be considered as the weak point of sigmoido-rectal wall, which probably ruptures under high colonic pressure[16]. Direct irritation of diverticulosis colon by the seed was also possible and may lead to acute diverticulitis with subsequent rupture.

The major limitation of the present study was a relative small number of study populations, particularly the non-survivor group (n = 6), that was

not allowed for multivariate analysis. Although it is relatively common in Thailand, Sandorica seed induced bowel perforation is still considered as a rare condition. At least, the authors successfully identified three significant factors related to the mortality in patients with peritonitis due to Sandorica seed ingestion. These factors could be used to estimate the study population for multivariate analysis, which by a rough estimation were 30 patients in each survivor and non-survivor group. Multicenter study may be required to achieve those numbers of patients. Another limitation was that, the diagnosis of Sandorica seed-induced perforation was made during surgical operation, but not preoperatively. In any cases that the diagnosis was uncertain, high-resolution computed tomography (HRCT) could be used to detect sign of colonic perforation with a higher sensitivity[1,17]. This imaging study would help to achieve the preoperative diagnosis if Sandorica seed was detected at that time. However, the authors did not apply HRCT because all patients presented with localized or generalized peritonitis (which was considered as an emergency condition), so the decision for exploratory laparotomy was made in all cases. According to this, the definite diagnosis of Sandorica seed-induced rectosigmoid perforation was therefore achieved intraoperatively. Beside these limitations, the present study may be the biggest case series of bowel perforation due to the plant seed at the present.

In conclusion, the present study revealed that shock at initial admission, low serum bicarbonate levels and severe intraabdominal contamination were the significant factors associated with the mortality. Early recognition and management to intervene septic shock episode, in accompanying with surgical source control and correction, is a key to improve the mortality outcome in patients with peritonitis due to Sandorica seed ingestion.

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Potential conflicts of interest

None.

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การศึกษาย้อนหลังเพื่อหาปัจจัยที่สัมพันธ์กับอัตราตายในผู้ป่วยที่มีภาวะเยื่อบุช่องท้องอักเสบจากการกินเมล็ดกระท้อน

สมเดช แจ้งศรีสุข, สมชาย ชุติพงศ์ธเนศ

วัตถุประสงค์: *เพื่อหาปัจจัยที่สัมพันธ์กับอัตราตายในผู้ป่วยที่มีภาวะเยื่อบุช่องท้องอักเสบเนื่องจากการกินเมล็ดกระท้อน*

วัสดุและวิธีการ: *ทำการศึกษาย้อนหลังจากข้อมูลของผู้ป่วย 30 ราย ที่มาโรงพยาบาลด้วยภาวะเยื่อบุช่องท้องอักเสบร่วมกับการมีประวัติกินเมล็ดกระท้อน ปัจจัยต่าง ๆ ได้แก่ เพศ อายุ โรคประจำตัว จำนวนเมล็ดที่กิน ระยะเวลาที่มีอาการก่อนมาโรงพยาบาล อุณหภูมิกาย ภาวะช็อกตั้งแต่แรกรับเข้ารักษาในโรงพยาบาล ความรุนแรงของภาวะเยื่อบุช่องท้องอักเสบ การพบลมใต้ช่องกะบังลมจากฟิล์มเอกซเรย์ ปริมาณเม็ดเลือดขาว ระดับไบคาร์บอเนตในเลือด เวลาที่ใช้ในการเตรียมผู้ป่วยก่อนผ่าตัด ความรุนแรงของการปนเปื้อนของสิ่งสกปรกในช่องท้อง ขนาดแผลทะลุและวิธีการผ่าตัด ได้รับการศึกษาวิเคราะห์หาความสัมพันธ์กับอัตราตายโดยใช้การทดสอบ Fisher's exact และหาความเข้มแข็งของความสัมพันธ์โดยวิธี odds ratio (OR) และ 95% confidence interval (CI)*

ผลการศึกษา: *ผู้ป่วยทั้งหมดได้รับการวินิจฉัยยืนยันครั้งสุดท้ายในห้องผ่าตัดว่าเป็นภาวะลำไส้ใหญ่ทะลุเกี่ยวเนื่องจากการกลืนเมล็ดกระท้อนในผู้ป่วย 30 ราย มี 6 ราย ที่เสียชีวิต จากศึกษาพบว่าภาวะช็อกตั้งแต่แรกรับเข้ารักษาในโรงพยาบาล (OR 35.0, 95% CI 2.9-411.4, p = 0.002) ระดับไบคาร์บอเนตในเลือดต่ำกว่า 15 mmol/L (OR 19.0, 95% CI 1.7-201.6, p = 0.009) และการปนเปื้อนของสิ่งสกปรกในช่องท้องรุนแรง (OR 10.0, 95% CI 1.3-74.5, p = 0.029) เป็นปัจจัยที่มีความสัมพันธ์กับอัตราตายอย่างมีนัยสำคัญ*

สรุป: *ปัจจัยที่สัมพันธ์กับอัตราตายในผู้ป่วยที่มีภาวะเยื่อบุช่องท้องอักเสบเนื่องจากการกินเมล็ดกระท้อนสอดคล้องกับลักษณะทางคลินิกของภาวะช็อกจากการติดเชื้อในกระแสเลือด การเฝ้าระวังและให้การรักษาตั้งแต่ระยะแรกของการช็อกร่วมกับการผ่าตัดเพื่อแก้ไขความผิดปกติและควบคุมการติดเชื้อ ถือเป็นกุญแจสำคัญในการลดอัตราตายในผู้ป่วยกลุ่มนี้*