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Topical treatment of major omphalocoele: *Acacia nilotica* versus povidone-iodine: A randomised controlled study

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ABSTRACT

Background: Conservative management for major omphalocoele with topical agents as escharotics therapy is well established in practice. Different agents have been used in the past, including mercurochrome and alcohol, proved later to be unsafe. The aim of this study is to evaluate the efficacy and safety of the application of *Acacia nilotica* paste compared to povidone-iodine solution as a primary non-surgical treatment of major omphalocoele. **Patients and Methods:** A double-blind, randomised study was conducted on 24 cases of major omphalocoele where they were randomly divided into two equal groups; Group A treated with topical application of *A. nilotica* paste and Group B treated with topical application of povidone-iodine solution. Cases with gastroschisis, ruptured major omphalocoele or minor omphalocoele were excluded from the study. The evaluating parameters were size of the fascial defect in cm, period of mechanical ventilation if needed, time required for full oral feeding tolerance, duration of hospital stay and any short- or long-term complications. **Results:** There was no statistical significant difference between both groups regarding their gestational or post-natal age, weight and the mean umbilical port defect. Patients from Group A tolerated full oral feeding earlier and had shorter total hospital stay duration than those from Group B, but without a statistical significant difference (P = 0.347 and 0.242, respectively). The overall mortality rate was 33.3% without a statistical significant difference between both groups (P = 0.667). **Conclusions:** Application of *A. nilotica* is a safe and effective treatment of major omphalocoele as it was associated with rapid full enteral feeding tolerance, short duration of hospital stay and low mortality rate.

Key words: Conservative treatment of major omphalocoele, topical treatment of major omphalocoele and *Acacia nilotica*

BACKGROUND AND PURPOSE

Closure of major omphalocoeles constitutes a challenge to most surgeons because of the wide fascial defect size, visceroabdominal disproportion and associated congenital anomalies. The lack of sufficient tissues requires the insertion of prosthetic material to bridge the fascial gap with increased risk of infection. Conservative management of major omphalocele with various local dressings is an established practice.[1-5] Different agents have been used for this purpose, including mercurochrome, alcoholic solutions and silver salts, with reported toxicity. Mercurochrome is associated with fatal mercury poisoning, topical alcohol solutions with alcohol toxicity and silver salts have been also used with reported raised silver serum levels.[6-10]

Acacia nilotica is a spiny tree growing in the Nile Delta, Nile Valley, Sinai and Western desert of Egypt that has been used to treat a variety of conditions, including common cold, bronchitis, diarrhoea, bleeding piles and leucoderma.

The most evident substances in *A. nilotica* are complex phenolic compounds and polysaccharides (gums). Previous study examined the wound healing, anti-inflammatory and antibacterial activities of extracted and formulated bioactive compounds of *A. nilotica* using different topical bases.[11]

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The aim of this study is to evaluate the safety and efficacy of *A. nilotica* paste application as an initial topical treatment of major omphalocoele in comparison to povidone-iodine solution.

PATIENTS AND METHODS

This double-blind, randomised study was conducted at Assiut University Children's Hospital from October 2010 to April 2015 and included 24 cases with major omphalocoele (14 males and 10 females) [Figure 1]. The inclusion criteria were; major omphalocoele where surgical closure was not safe either because of their low birth weight, associated anomalies or large fascial defect with visceroabdominal disproportion. The 24 cases were divided into two equal groups; Group A managed by application of *A. nilotica* paste and Group B managed by application of povidone-iodine 5% solution. Randomisation was done using closed envelope to decide the initial topical treatment option. The antenatal variables included their antenatal diagnosis, mode of delivery, gestational age. The post-natal variables included age at the start of treatment, birth weight size of the defect in cm, associated congenital malformations, the degree of respiratory distress which was evaluated according to Down's score,[12] period of mechanical ventilation if needed, time needed for full oral feeding tolerance, total duration of hospital stay and any short-term (during application of either types of dressings) or long-term complications during the follow-up period. Cases with major omphalocoele that could be closed primary based on the clinical assessment were excluded from the study and also cases with gastroschisis, ruptured major omphalocoele or minor omphalocoele were excluded. A written informed consent was taken from all the parents or guardians for participation in this study with either type of topical dressings. Approval of the Regional Ethical Committee of Faculty of Medicine was obtained to conduct this study.

Preparation and application technique

For patients from Group A, the commercially available *A. nilotica* powder was mixed with a ratio of 1:1 with gentian violet solution as a solvent to obtain the *A. nilotica* paste. Application of this paste to the intact sac twice daily is done, and then the sac was left exposed without dressing [Figure 2]. For patients from Group B, the povidone-iodine (5% solution) was applied directly to the sac with sterile dressing with the same frequency of *A. nilotica* paste. Routine thyroid function tests were performed for all the cases on admission, repeated on 2 weeks basis after the start of treatment with povidone-iodine and every follow-up visit thereafter. The patients were discharged from the hospital when they are taking full oral feeding and in a stable, general condition. The dressings to all the patients were continued after discharge, until the sac is shed off and skin has covered the defect [Figure 3].

Statistical analysis

The data were analysed using SPSS® (version 16; SPSS Chicago, Illinois, USA) and descriptive statistics (i.e., mean, standard deviation and percentage) was calculated. 'Mann-Whitney Test' and Fisher's exact test were used to compare the means between the groups. The difference was considered as significant if $P \leq 0.05$.

RESULTS

There was no statistical significant difference between both groups regarding their sex, gestational age and

Figure 1: Major omphalocoele containing liver

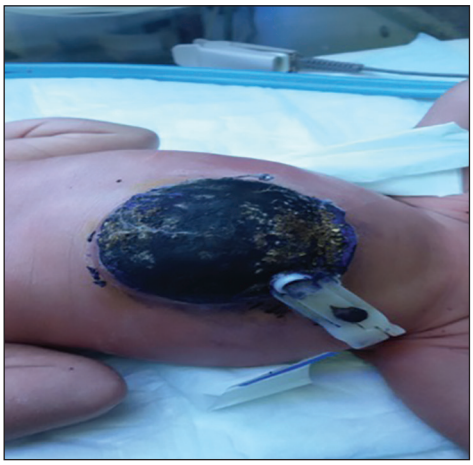

Figure 2: Male baby after the application of *Acacia nilotica* and gentian violet

Figure 3: Female baby after 7 months of the application of *Acacia nilotica* with a ventral hernia and scar at the umbilical port

post-natal age. The mode of delivery and associated anomalies in the 24 cases are listed in Tables 1 and 2. Antenatal diagnosis was made only in 8 cases (3 from Group A and 5 from Group B). The mean birth weight for patients within Group A was 2.37 ± 0.55 kg (range: 1.5-3.1 kg) and for patients within Group B was 2.33 ± 0.65 kg (range: 1.4-3.2 kg) (P = 0.713). Furthermore, the mean fascial defect size in the patients from Group A was 11.75 ± 3.19 cm (range: 7-16 cm) where it was 10.66 ± 3.55 cm in Group B (range: 6-18 cm) (P = 0.410). Patients from both groups had respiratory distress score ranged from 0 to 6. The mean value for respiratory distress score in Group A was 1.97 ± 2.19 and 1.75 ± 1.65 in Group B (P = 0.977). Two cases from Group B developed local infection; one of them progressed to ruptured sac where silo bag was fixed. Both died later because of sepsis and disseminated intravascular coagulopathy. Although patients from Group A reached to full oral feeding tolerance earlier than those from Group B, (7.25 ± 5.04 days ≠ 9.83 ± 8.99 days) this difference did not reach statistical significance (P = 0.347). The mean total duration of hospital stay among patients from Group A was shorter than those from Group B (15.58 ± 8.10 days ≠ 18.66 ± 12.74 days), but the difference did not reach statistical significant difference (P = 0.242).

After application of the *A. nilotica* paste, the sac becomes firm and very tough in structure without any signs of infection or other local or systemic complications. The sac gradually came off and skin covered the defect over a mean period of 7.83 ± 4.82 weeks in group A, where it came off over a mean period of 7.42 ± 6.59 weeks in Group B (P = 0.861). No changes were recorded for the thyroid function tests among the patients from Group B either during treatment or follow-up visits.

The overall mortality was 8 cases out of 24; 5 from Group B and 3 from Group A (P = 0.667). All those 8 cases needed mechanical ventilation for a period ranged from 2 to 6 days because of respiratory distress either due to prematurity, lung hypoplasia or pneumonia and died because of respiratory failure and sepsis [Tables 1 and 2].

The mean follow-up period was 15.5 ±3.5 months during this period, the 16 survived babies were gaining weight and were using elastic bandages regularly, to gradually increase the abdominal domain; where 7 cases were subjected to safe fascial closure in one setting based on clinical assessment without the insertion of prosthetic material or postoperative ventilation.

DISCUSSION

In the recent years, an increase in the incidence of omphalocoele has been reported in the different parts of the world with slight male predominance reported in some series.[2,13] This goes with this study where 58% were males.

Most abdominal wall defects are now diagnosed prenatally, which helps to choose the appropriate location, mode and timing of delivery and facilitate post-natal evaluation and management.[14] We had 33.3% of cases in this series diagnosed prenatally. This may be related to the lack of facilities and specialised medical service in the remote health care centres.

Although caesarean delivery is still commonly performed for large omphalocoeles with liver herniation, no difference was found in the survival or complication rates between the infants delivered by normal vaginal delivery or by caesarean section.[15,16] In this study, we had 64% of babies delivered by normal vaginal delivery with no difference in the survival or complication rates between them and those delivered by caesarean section.

Primary fascial closure of large omphalocoeles could raise the intra-abdominal pressure resulting in pulmonary and renal failure. Silastic silo was used to allow gradual return of the abdominal viscera, which may be associated with morbidity, including wound infection and dehiscence, recurrent ventral hernia, bowel obstruction and pulmonary damage, caused by prolonged mechanical ventilation. Furthermore, shock and renal failure from compression and kinking of the inferior vena cava and possibly from abdominal

Table 1: shows mode of delivery, birth weight, defect size, associated congenital anomalies, complications and outcome in patients treated by local application of Acacia Nilotica paste (group A).

No.	Mode of delivery	Weight	Defect size	Associated congenital anomalies	Complications	Outcome
1	NVD	2.447 gm	14 cm	Hypospadias		survived
2	CS	2.500 gm	7 cm			survived
3	CS	1.610 gm	16 cm	VSD, PDA		died
4	CS	2.580 gm	11 cm			survived
5	NVD	2.960 gm	9 cm			survived
6	CS	2.434 gm	12 cm			survived
7	NVD	1.900 gm	14 cm	Lung hypoplasia		died
8	CS	1.500 gm	15 cm	VSD, pulmonary art. Stenosis		died
9	CS	2.800 gm	8 cm			survived
10	NVD	3.104 gm	10 cm			survived
11	NVD	2.900 gm	9 cm			survived
12	CS	1.721 gm	16 cm			survived

CS: caesarean section, NVD: normal vaginal delivery, PDA: patent ductus arteriosus, VSD: ventricular septal defect.

Table 2: shows mode of delivery, birth weight, defect size, associated congenital anomalies, complications and outcome in patients treated by local application of povidone iodine (group B).

No.	Mode of delivery	Weight	Defect size	Associated congenital anomalies	Complications	Outcome
1	NVD	2.300 gm	8 cm	ASD	Sepsis	died
2	CS	1.850 gm	18 cm	Lung hypoplasia		died
3	NVD	1.400 gm	9 cm			died
4	CS	2.410 gm	10 cm	UDT		survived
5	NVD	2.785 gm	8 cm			survived
6	NVD	1.670 gm	11 cm			died
7	NVD	2.350 gm	6 cm			survived
8	CS	1.780 gm	14 cm	VSD	Sepsis and rupture	died
9	CS	2.910 gm	10 cm			survived
10	NVD	3.120 gm	15 cm			survived
11	CS	3.240 gm	12 cm	Limb anomaly		survived
12	CS	2.750 gm	7 cm	-		survived

CS: caesarean section, NVD: normal vaginal delivery, UDT: undescended testes, ASD: atrial septal defect, VSD: ventricular septal defect

compartment syndrome besides its need to general anaesthesia are all known associated risks.[17,18] Other options for the closure of large omphalocoeles, including the mobilisation of large skin flaps and skin closure only, placement of prosthetic material and in folding of the amniotic sac without resection, have been tried.[19,20] All these methods have some advantages and are indicated in certain situations; however, none of these methods allow closure of the abdominal wall defect without the use of prosthetic material or multiple operations.

Conservative management of giant omphalocoeles was first described in 1899 by Ahlfeld using alcohol as a topical agent.[21] In the 1950s and 1960s, escharotics therapy was popularised by Grob.[22] This therapy allowed the sac to desiccate, contract and eventually the defect was epithelialised, which left a ventral hernia that could be repaired later in life. This approach has the general advantage of completely avoiding the major abdominal surgery in the neonatal period with the risks of tight abdominal closure with its morbidity and mortality as well as the complications of silon placement. This conservative escharotic therapy is also used for the high-risk infants with large omphalocoeles and prematurity, respiratory insufficiency, congenital heart disease or chromosomal abnormalities who cannot tolerate the surgery with low complication rates.[23] Although different agents have been used in the past, they proved to be potentially toxic and should be avoided.[6-9] The use of topical silver sulphadiazine (SSD) cream to provide initial sac coverage was first reported in 1987 by Hatch and Baxter.[24] Lee *et al.*,[25] and Ein and Langer,[4] reported in their series the safety and efficacy of SSD as it provides a moist wound healing environment that promotes epithelialisation and simultaneously minimises the risk of infection. Although the reported risks of silver toxicity, including seizures, peripheral neuropathy, ocular pathology, nephrotic syndrome, raised liver enzymes and leucopenia, are well documented in the literature, the duration of exposure and dosage leading to this toxicity are not well established as there are no reports of the long-term outcome of elevated silver serum levels in

neonates yet.[10] Even topical application of povidone-iodine has been associated with a known risk of hypothyroidism.[9] In this study, we did not encounter any case of hypothyroidism among Group B either during treatment or follow-up period.

The use of plants for healing purposes predates human history and forms the origin of much modern medicine. Many conventional drugs originate from plant sources; including acetylsalicylic acid from willow bark,[26] digoxin from foxglove[27] and morphine from the opium poppy.[28]

A. nilotica is one of about 135 thorny African Acacia species.[29] The presumed mechanism of action after the application of *A. nilotica* paste that it induces coagulation of the protein contents of the sac (Wharton jelly), preventing protein fermentation, changing the sac to a very tough structure, which prevents fluid losses from the sac and acts as a barrier against invasion by microorganisms.[11]

Some authors reported that conservative approach in major omphalocoele was associated with prolonged time for full oral feeding tolerance and requires a long duration of hospital stay.[3,23] In this series, patients treated with either topical application of *A. nilotica* paste or povidone-iodine solution have relatively rapid tolerance to full oral feeding and short total hospital duration compared to those reports.

The outcome for a neonate with exomphalos is dependent on different variables such as the severity of associated anomalies and degree of prematurity.[3] In the previous series,[30-32] the incidence of congenital anomalies ranged from 45% to 77%. This is nearly similar to our study where the associated anomalies were encountered in 43.4% of patients. There was no statistical significant difference between both groups regarding the associated congenital anomalies or other risk factors in this study, which were the low birth weight and umbilical port size with visceraabdominal disproportion. In spite of the presence of all these risk factors, the patients from Group A had low mortality rate (25%) compared to the patients from Group B (41.7%) $P = 0.667$. Vachharajani *et al*.,[33] reported an overall mortality rate of 33% in all the cases with major omphalocoele treated by a different method; primary surgical closure and silo placement. Ein and Langer,[4] reported nearly the same mortality rate (30%) in cases with major omphalocoele treated conservatively by SSD. Both attributed their mortality to prematurity and pulmonary hypoplasia. In this study, the overall mortality rate was 33.3% and was also related to prematurity, lung hypoplasia and sepsis.

External compression with bandages have been used as a treatment option either early during neonatal period[34,35] or delayed during infancy.[20] We choose to use the elastic external compression in a stabilised infant, where seven patients had single safe fascial closure of their ventral hernias without prosthetic materials insertion or postoperative mechanical ventilation.

CONCLUSION

Both *A. nilotica* paste and povidone-iodine solution are safe and effective initial topical treatments of major omphalocoeles. Application of *A. nilotica* paste was associated with rapid full enteral feeding tolerance, short duration of hospital stay and low mortality rate. Furthermore, it is cheap, natural, easy to apply and non-toxic preparation.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Minkes RK. Abdominal wall defects. In: Oldham KT, Colombani PM, Foglia RP, Skinner MA, editors. Principles and Practice of Pediatric Surgery. Philadelphia (PA): Lippincott Williams & Wilkins; 2005. p. 1103-19.
2. Gudrun A, Jacob CL. Abdominal wall defects. J Curr Pediatr 2006;16:192-8.
3. Rijhwani A, Davenport M, Dawrant M, Dimitriou G, Patel S, Greenough A, *et al*. Definitive surgical management of antenatally diagnosed exomphalos. J Pediatr Surg 2005;40:516-22.
4. Ein SH, Langer JC. Delayed management of giant omphalocele using silver sulfadiazine cream: An 18-year experience. J Pediatr Surg 2012;47:494-500.
5. Luijendijk RW, Hop WC, van den Tol MP, de Lange DC, Braaksma MM, IJzermans JN, *et al*. A comparison of suture repair with mesh repair for incisional hernia. N Engl J Med 2000;343:392-8.
6. Wakhlu A, Wakhlu AK. The management of exomphalos. J Pediatr Surg 2000;35:73-6.
7. Mullins ME, Horowitz BZ. Iatrogenic neonatal mercury poisoning from Mercurochrome treatment of a large omphalocele. Clin Pediatr (Phila) 1999;38:111-2.
8. Gough DC, Auldist AW. Giant exomphalos — Conservative or operative treatment? Arch Dis Child 1979;54:441-4.
9. Festen C, Severijnen RS, vd Staak FH. Nonsurgical (conservative) treatment of giant omphalocele. A report of 10 cases. Clin Pediatr (Phila) 1987;26:35-9.
10. Lewis N, Kolimarala V, Lander A. Conservative management of exomphalos major with silver dressings: Are they safe? J Pediatr Surg 2010;45:2438-9.
11. Abdallah IK, Fetouh MI, Mostafa MM, Ibrahim I: The Use of Parts

from Medicinal Plants in Different Pharmaceutical Dosage form in Treatment of Some Surgical Cases. Master Degree of Pharmaceutical Sciences, Al-Azhar University, Assiut; 2009.
12. Wood DW, Downes JJ, Lecks HI. A clinical scoring system for the diagnosis of respiratory failure. Preliminary report on childhood status asthmaticus. Am J Dis Child 1972;123:227-8.
13. Cooney DR. Defects of the abdominal wall. In: O'Neill JA Jr, Rowe MI, Grosfeld JL, Fonkalsrud EW, Coran AG, editors. Pediatric Surgery. 5th ed. St. Louis: Mosby; 1998. p. 1045-69.
14. Crombleholme TM, D'Alton M, Cendron M, Alman B, Goldberg MD, Klauber GT, *et al*. Prenatal diagnosis and the pediatric surgeon: The impact of prenatal consultation on perinatal management. J Pediatr Surg 1996;31:156-62.
15. Adra AM, Landy HJ, Nahmias J, Gómez-Marín O. The fetus with gastroschisis: Impact of route of delivery and prenatal ultrasonography. Am J Obstet Gynecol 1996;174:540-6.
16. Strauss RA, Balu R, Kuller JA, McMahon MJ. Gastroschisis: The effect of labor and ruptured membranes on neonatal outcome. Am J Obstet Gynecol 2003;189:1672-8.
17. Nakayama DK, Mutich R, Motoyama EK. Pulmonary dysfunction after primary closure of an abdominal wall defect and its improvement with bronchodilators. Pediatr Pulmonol 1992;12:174-80.
18. Adam AS, Corbally MT, Fitzgerald RJ. Evaluation of conservative therapy for exomphalos. Surg Gynecol Obstet 1991;172:394-6.
19. Gross RE. A new method for surgical treatment of large omphaloceles. Surgery 1998;24:277-92.
20. Brown MF, Wright L. Delayed external compression reduction of an omphalocele (DECRO): An alternative method of treatment for moderate and large omphaloceles. J Pediatr Surg 1998;33:1113-5.
21. Tran DA, Truong QD, Nguyen MT. Topical application of povidone-iodine solution (Betadine) in the management of giant omphaloceles. Dermatology 2006;212(Suppl 1):88-90.
22. Grob M. Conservative treatment of exomphalos. Arch Dis Child 1963;38:148-50.
23. Nuchtern JG, Baxter R, Hatch EI Jr. Nonoperative initial management versus silon chimney for treatment of giant omphalocele. J Pediatr Surg 1995;30:771-6.
24. Hatch EI Jr, Baxter R. Surgical options in the management of large omphaloceles. Am J Surg 1987;153:449-52.
25. Lee SL, Beyer TD, Kim SS, Waldhausen JH, Healey PJ, Sawin RS, *et al*. Initial nonoperative management and delayed closure for treatment of giant omphaloceles. J Pediatr Surg 2006;41:1846-9.
26. Bisset NG. Herbal Drugs and Phytopharmaceuticals. Stuttgart, Germany: Medpharm Scientific Publishers; 2004. p. 534-6.
27. Al-Qura'n S. Ethnopharmacological survey of wild medicinal plants in Showbak, Jordan. J Ethnopharmacol 2009;123:45-50.
28. Morimoto S, Suemori K, Moriwaki J, Taura F, Tanaka H, Aso M, *et al*. Morphine metabolism in the opium poppy and its possible physiological function. Biochemical characterization of the morphine metabolite, bismorphine. J Biol Chem 2001;276:38179-84.
29. Brenan JP. Manual on taxonomy of Acacia species: Present taxonomy of four species of *Acacia* (*A. albida, A. senegal, A. tortilis and A. nilotica*). Rome, Italy: FAO; 1983. p. 47-54.
30. Boyd PA, Bhattacharjee A, Gould S, Manning N, Chamberlain P. Outcome of prenatally diagnosed anterior abdominal wall defects. Arch Dis Child Fetal Neonatal Ed 1998;78:F209-13.
31. Yazbeck S, Ndoye M, Khan AH. Omphalocele: A 25-year experience. J Pediatr Surg 1986;21:761-3.
32. Dunn JC, Fonkalsrud EW. Improved survival of infants with omphalocele. Am J Surg 1997;173:284-7.
33. Vachharajani AJ, Rao R, Keswani S, Mathur AM. Outcomes of exomphalos: An institutional experience. Pediatr Surg Int 2009;25:139-44.
34. Barlow B, Cooper A, Gandhi R, Niemirska M. External silo reduction of the unruptured giant omphalocele. J Pediatr Surg 1987;22:75-6.
35. DeLuca FG, Gilchrist BF, Paquette E, Wesselhoeft CW, Luks FI. External compression as initial management of giant omphaloceles. J Pediatr Surg 1996;31:965-7.