Clinical Audit on Management of Vaso-Occlusive Crisis of Sickle Cell Anemic Children Attending Assiut University Children's Hospital

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Abstract

Background: Sickle cell disease could be a common cluster of serious genetic disorders caused by the synthesis of abnormal hemoglobin. It has a wide range of clinical manifestations and complications, one of them being vaso-occlusive crisis (VOC).

The most prominent symptom of VOC is acute episodes of pain. In addition to the pain, there are several clinical consequences, such as acute chest syndrome, hepatic and renal involvement, cerebrovascular accident, and multiorgan failure resulting in death.

Aim: To evaluate the degree of adherence of pediatric physicians of Assiut University Children's Hospital to the international guidelines for the management of acute VOC in patients with sickle cell anemia.

Patients and Methods: A clinical audit prospective study was done in the Hematology Unit at Assiut University Children's Hospital over 1 year, from May 1, 2019, to the end of April 2020.

All children diagnosed with VOC of sickle anemia were enrolled. Data concerning the outline of the management of acute pain were collected in the form of clinical history, examination, investigations, and medications.

Results: All clinical data were asked for in all cases, such as pain, fever, cough, and diarrhea, but skin ulcer was asked only in 19 cases, shortness of breath was asked in 28 cases, abdominal pain in 32, headache in 25, convulsion in 24, and weakness in 26. All physical and general examinations were checked in all cases except skin ulcers. Regarding medications, I.V. fluids, antibiotics, and analgesics were prescribed in all patients; 33 received NSAIDS, and 25 received I.V. paracetamol.

Blood transfusion was needed in 24 cases. Folic acid and hydroxyurea were prescribed for all cases, but prophylactic antibiotics and vaccination were prescribed for 25 and 28 cases, respectively.

Conclusion: The National Heart, Lung, and Blood Institute guidelines were followed by the Hematology Department of Assiut University Children's Hospital for the management of sickle cell disease pediatric patients with VOC.

Keywords: Acute chest syndrome; Sickle cell anemia; Vasoocclusive crisis.

Introduction:

Sickle cell disease (SCD) could be a common cluster of serious genetic disorders caused by the synthesis of abnormal hemoglobin (sickle hemoglobin), which, once deoxygenated, polymerizes and causes the sickling of red blood cells. SCD is characterized by chronic anemia, vaso-occlusion, and progressive vascular injury, inflicting multiorgan injury [1].

The presentation of SCD is somewhat variable and reflects the interactions with

different genetic and environmental factors and might embrace painful vaso-occlusive crises (VOCs), acute chest syndrome, cerebral stroke, and acute and chronic hemolysis. Because of functional hyposplenism, there is an increased incidence of invasive microorganism infection with encapsulated bacterium [2].

Overall complications of SCD can be divided into two main groups: those mainly because of hemolytic disease and functional nitric oxide deficiency, which cause giant vessel vasculopathy (cerebrovascular disease, pulmonary hypertension, nephropathy, priapism, and leg ulcers) and those caused by vaso-occlusive anemia events resulting in painful episodes and progressive organ injury (hyposplenism, osteonecrosis, retinopathy, and liver damage) [3].

VOC constitutes the foremost morbidity in SCD. Fever seems common, even in apparently uncomplicated painful crises, suggesting that the symptom could also be characteristic of the crisis itself and not essentially proof of infection. In fact, SCD is believed to be a quaternion of pain syndromes: anemia and its sequelae, organ failure (including infection), and comorbid conditions, with pain dominating the clinical image, and should either be spontaneous or be triggered by the opposite three parts of the quaternion [4].

The treatment of pain basically involves a serial approach: pain assessment, pain mensuration, and pain management [5].

Patients and Methods

This clinical audit study was done at Assiut University Children's Hospital from May 1, 2019, to the end of April 2020.

All youngsters diagnosed with VOC of sickle anemia were included in this study, and those who met the following criteria were excluded: infants less than 1 year and had splenic sequestration, aplastic crisis, and hyperhemolytic crisis.

Data about the management of acute pain in youngsters who accepted to participate in the study were collected, which included the following:

(1) Clinical history for assessment of the pain, such as onset, length, and severity; symptoms indicating infection; and every one of the symptoms of complications such as abdominal pain, chest pain, shortness of breath or cough, bone pain, and swelling.

(2) Data about physical examination:

(a) General look and assessment of significant signs (including pulse oximetry and degree of pain).

(b) A general physical examination is needed for evidence of focal infection in the skin and extremities. Signs of all body systems should be assessed: respiratory, GIT, and urinary system.

(3) Investigations:

(a) Full blood count, urea, creatinine, and electrolytes ought to be performed on all patients requiring admission. Any investigation ought to be directed toward specific clinical issues.

(4) Data regarding lines of management of vaso-occlusive pain.

(5) Data on outcome of cases and data on discharge.

Data Collection

(1) Data was collected from the clinical signs of the patients at presentation and from the recent patients' medical records.

(2) A computer software, SPSS Program, version 20, was used to analyze data.

Ethical Considerations

(1) Approval from the Ethics of Scientific Research Committee, Faculty of Medicine, Assiut University, was obtained, IRB NUM: 17100701.

(2) Verbal and written consents were obtained from all the patient's caregivers.

(3) Privacy and confidentiality of all obtained information was observed without intervention in the prescribed treatment.

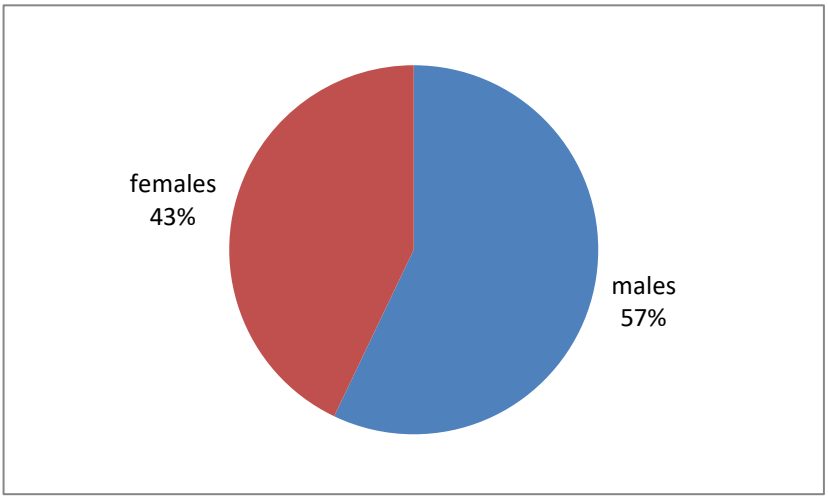
Results

The study included 35 patients with VOC who were admitted to the Hematology

Unit of Assiut University Children's Hospital.

We found that the median age of our studied patients with sickle cell anemia was 12 years old and ranged from 1 year up to 17 years old. Of 35 studied cases, 20 (57%) were males and 15 (43%) were females (Fig. 1).

Figure 1: Sex Distribution



Pain severity was asked in all studied cases. All cases had acute pain onset with a median duration of 5 days and ranged from 1 day up to 7 days. A total of 20 (57%) cases experienced moderate pain severity, and 15 (43%) cases experienced severe pain. Bony pain was the most common site among the studied cases, documented in 89% (65, 29, and 19% had pain in the back, limb, and hip, respectively), followed by chest pain (Figs. 2, 3).

Figure 2: The Severity of Pain

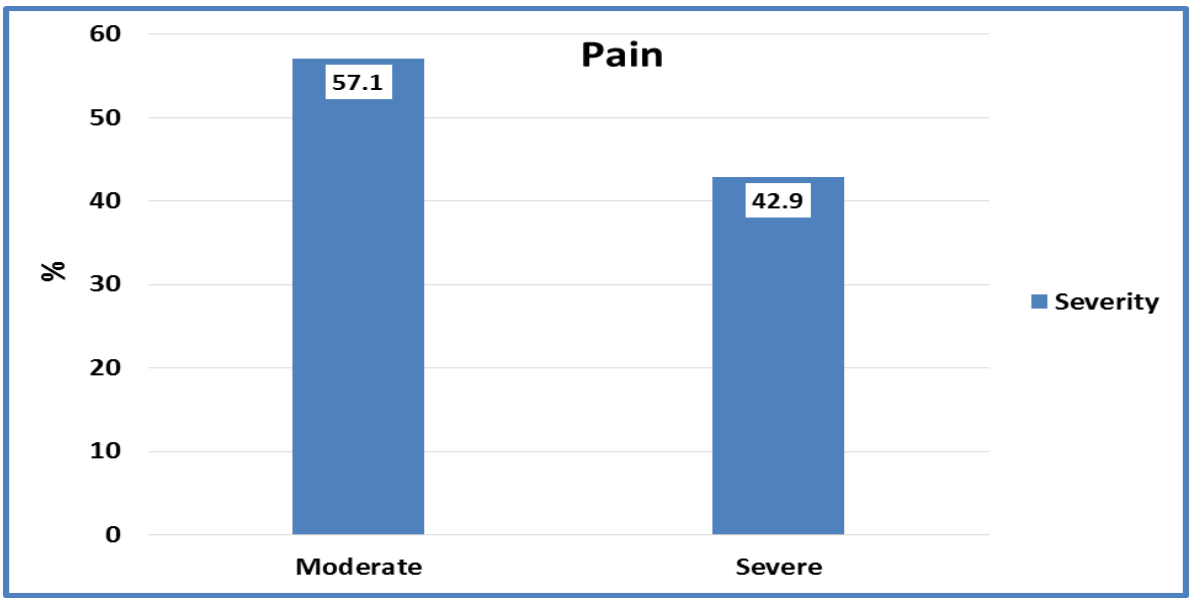
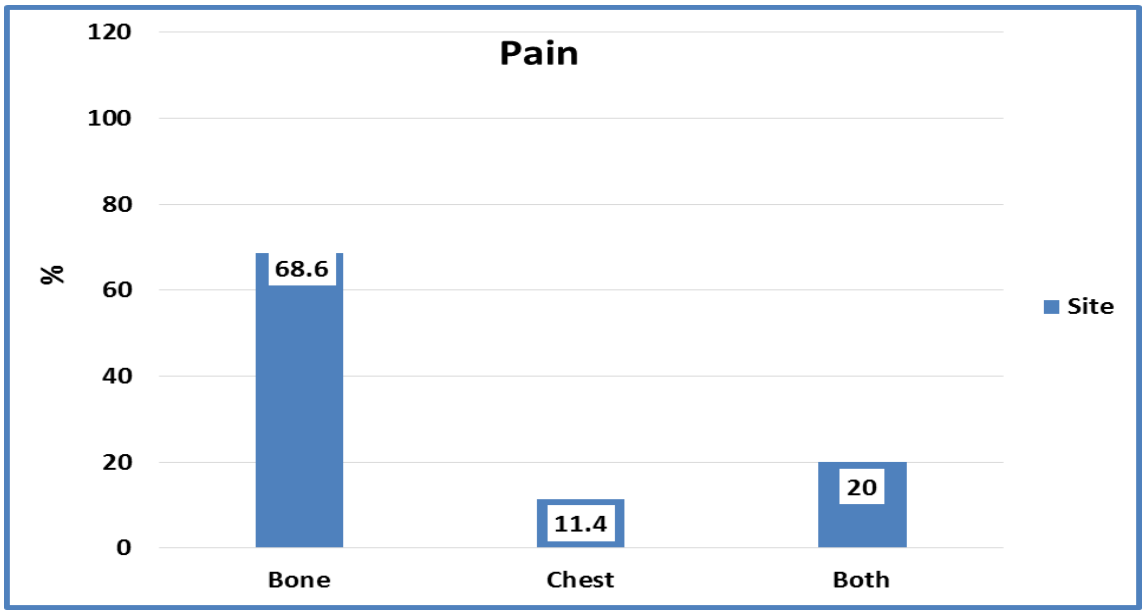
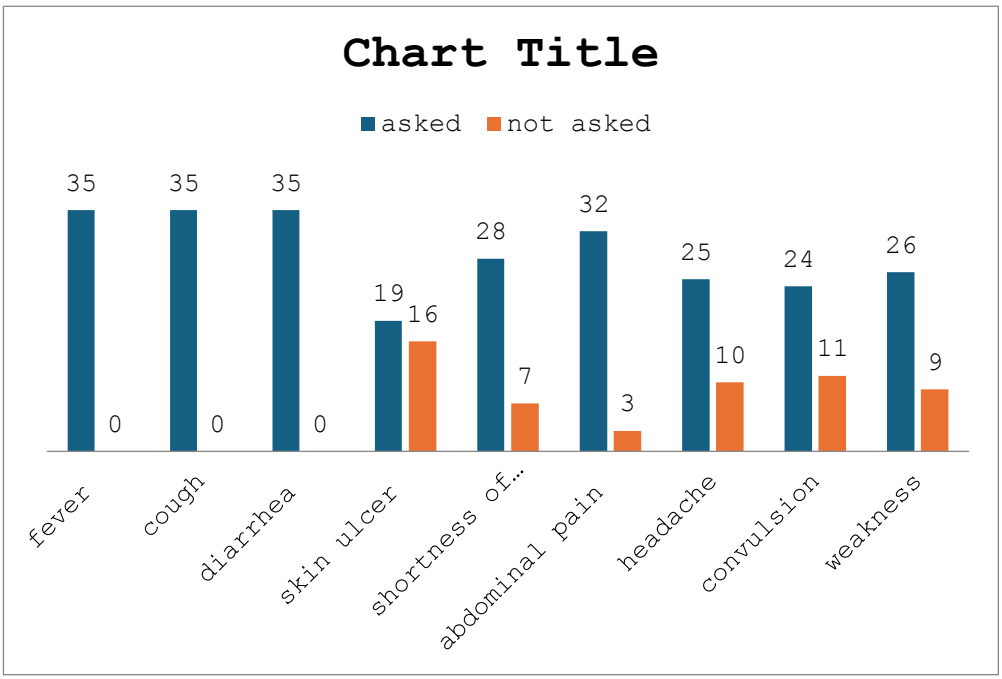


Figure 3: The Site of Pain



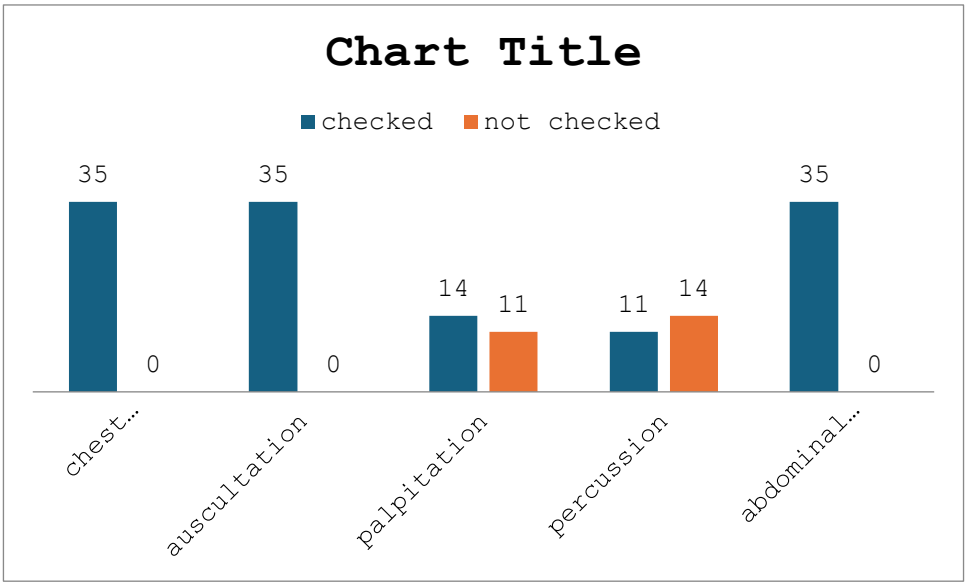
All clinical data were asked for in all cases, such as fever, cough, and diarrhea. Still, skin ulcer was asked only in 19 cases, shortness of breath was asked in 28 cases, abdominal pain in 32 cases, headache in 25 cases, convulsion in 24 cases, and weakness in 26 cases. All physical and general examinations were checked in all cases except skin ulcers (Fig. 4).

Figure 4: Clinical Data



Regarding systemic examination, chest inspection and auscultation were checked in all cases, but palpitation and percussion were checked in 14 and 11 cases receptively. All cases were checked for abdominal examination. There were seven cases with abdominal tenderness, 18 with hepatomegaly, and 10 with splenomegaly (Fig. 5).

Figure 5: Systemic Examinations



Regarding the lines of management recommended by the unit's protocol, it was advised to use those four lines of treatment in all cases (analgesia, intravenous fluids, and antibiotics ± blood transfusion). This was followed in 100% of cases. All cases received analgesia; among them, 33 (94.3%) received NSAIDs' Ketorolac, and 25 (71.4%) received I.V. paracetamol, intravenous fluids, and antibiotics). However, blood transfusion was needed in 24 (68.6%) studied cases (Tables 1–3).

Table 1: Medication received by 35 cases with sickle cell anemia.

Medication	N	(%)
Management of acute painful crisis		
1. Analgesia		
• Not prescribed	0	(0.0)
• Prescribed	35	(100.0)
▪ **NSAIDS "Ketolac"**	33	(94.3)
▪ **IV Paracetamol**	25	(71.4)
▪ **Oral Opioids**	0	(0.0)
▪ **IV Opioids**	0	(0.0)
2. Intravenous fluid		
• Not prescribed	0	(0.0)
• Prescribed	35	(100.0)
3. Blood		
• Not needed	11	(31.4)

• Needed	24	(68.6)

Table 1: Medication received by 35 cases with sickle cell anemia ***(Cont.)***

Medication	N	(%)
4. Antibiotics		
• Not prescribed	0	(0.0)
• Prescribed	35	(100.0)
Long term therapy		
• Not prescribed	0	(0.0)
• Prescribed	35	(100.0)
▪ **Folic acid**	35	(100.0)
▪ **Hydroxy urea**	35	(100.0)
▪ **Prophylactic antibiotics**	25	(71.4)
▪ **Vaccinations**	28	(80.0)

Table 2: Outcome of 35 patients with sickle cell anemia

Medication	N	(%)
❖ **Analgesic "on discharge"**		
• Not prescribed	5	(14.3)
• Prescribed	30	(85.7)
❖ **Advice "for follow-up"**		
• Not advised for FU	0	(0.0)
• Advised for FU	35	(100.0)
❖ **Complication**	5	(14.3)
• Septic hip	3	(60)
• Septic knee	2	(40)
❖ **Death**	0	(0)

Table 3: The unit's protocol as compared and contrasted to National Heart, Lung, and Blood Institute guidelines for the management of pediatric vaso-occlusive crisis-sickle cell disease

Item	Unit protocol	Checklist	NHLBI protocol
History:	• Present History of pain	100%	✓
	• Symptoms of focal infection: - **Fever**, **Cough**, **Diarrhea,** and **Vomiting** - **Skin ulcer**	100% 54.3%	✓
	• Symptoms of complications - **Shortness of breathing** - **Abdominal pain** - **Bone swelling** - **Severe headache** - **Convulsions** - **Weakness of limbs**	 80% 91.4% 100% 71.4% 68.6% 74.3%	✓

Table 3: The unit's protocol as compared and contrasted to National Heart, Lung, and Blood Institute guidelines for the management of pediatric vaso-occlusive crisis-sickle cell disease. ***(Cont).***

Item	Unit protocol	Checklist	NHLBI protocol
Examination:	Pulse	100%	✓
	blood pressure	100%	✓
	Respiratory rate	100%	✓
	oxygen saturation	0%	✓
	General examination:	**100%**	✓
Systemic examination:	*Chest examination:* *Inspection* *Palpitation* *Percussion* *Auscultation*	 100% 40% 31.4% 100%	✓
	Abdominal examination:	**100%**	✓
	Genitalia examination for painful erection	95%	✓
	CNS examination	17.1%	✓
Laboratory investigations:	CBC, Bilirubin, Electrolytes and Kidney function	**100%**	**CBC is only recommended**
Imaging:	Chest X-ray (CXR)	68.6%	Not recommended
	Abdominal sonar	60%	✓
Management:	Initial management of acute painful crisis	100%	✓
	recent analgesic use within 30 minutes of triage or 60 minutes of registration (opioid and nonopioid)	100%	✓
	For mild to moderate pain who report relief with NSAIDS, continue with NSAIDS	100%	✓
	VOC associated with severe pain rapidly initiates treatment with parenteral opioids.	0%	✓
	Reassess pain and re-administer opioids if necessary for continued severe pain every 15–30 minutes until pain is under control per patient report.	100%	✓
	Administer oral NSAIDS as an adjuvant analgesic in the absence of contraindications.	100%	✓
	Oral antihistamine agents prescribe for itching secondary to opioid administration	0%	✓
	In adults and children with VOC, use adjunctive nonpharmacologic approaches to treat pain, such as local heat application and distraction	0%	✓

Table 3: The unit's protocol as compared and contrasted to National Heart, Lung, and Blood Institute guidelines for the management of pediatric vaso-occlusive crisis-sickle cell disease. ***(Cont).***

Item	Unit protocol	Checklist	NHLBI protocol
	In euvolemic children who are unable to drink fluids, provide intravenous hydration	100%	✓
	In children treated with opioids, monitor for excessive sedation by measuring sedation with objective measurement sedation scale and oxygenation levels.	0%	✓
	Don't dive into blood transfusion unless there is a need for that	68.6 %	✓
	✓ If oxygen saturation is < 95 percent on room air, administer oxygen	0%	✓
	Analgesia on discharge	85.7%	✓
	Advise for follow-up	100%	✓

Discussion

In the present study on 35 children with SCD with VOC, we found that the median age of our studied patients was 12 years and ranged from 1 year up to 17 years old.

This is consistent with the study of Smith and colleagues, which aimed to understand the equilibrium between endothelin-mediated vasoconstriction and apelin-mediated vasodilation in the modulation of pain in pediatric SCD on 47 children with SCD. It found that the mean age of the studied participants was 9.98 ± 4.78 years and ranged from 2 to 18 years old [6].

There is no sex predilection among studied children with SCD. Of 35 studied cases, 20 (57%) were males and 15 (43%) were females. This comes in agreement with the study of Hagag *et al.* [7], who reported that 18/30 (60%) were males.

In the current study, we found that all cases had acute pain onset with a median duration of 5 days and ranged from 1 day up to 7 days. A total of 20 (57%) patients experienced moderate pain severity, and 15 (43%) had severe pain. Bony pain was the most common site (89%), followed by chest pain (31.4%). In line with our study, Abd El-Ghany and colleagues reported that the children most studied presented with limb and back pain, with a significantly higher frequency among children between 7 and 14 years old. Most children with SCD are presented with painful crises of variable severity and frequency by the age of 6 years [8].

In the current study, we found that 26 (74%) cases had fever, six (17%) cases had cough, three (9%) cases had diarrhea, and seven (20%) cases had vomiting. However, skin ulcers were documented in only one (5%) case.

In agreement with our study, a previous study reported that infections were the second cause of hospitalizations recorded in 24.5% of cases in the form of herpetic stomatitis, viral upper respiratory tract infections, severe gastroenteritis, encephalitis, and osteomyelitis [8].

Based on these results, we could say that our institution successfully follows international standards for the management of VOC in children with SCD, as we found that analgesia was prescribed for all studied cases in the management of acute painful crises. Among them, 33 (94.3%) patients

received NSAIDs 'Ketorolac' and 25 (71.4%) received I.V. paracetamol. In all studied cases received intravenous fluids, blood transfusion was needed in 24 (68.6%) of studied cases, and all studied cases received antibiotics [9].

Regarding long-term therapy, all studied cases received folic acid, hydroxyurea, prophylactic antibiotics, and special vaccinations, which were received by most of the studied cases, that is, ~28 (80.0%). At discharge, analgesia medication was prescribed for 30 (85.7%), and advice for follow-up was given for all SCD studied cases.

Folic acid administration, which was received in all our studied cases, is the only drug that was not recommended by the aforementioned international guidelines (National Heart, Lung and Blood Institute 2014; Pediatrics 2014). In line with our study, the recent double-blind, randomized controlled trial concluded that a high dose was given with 1–5 mg/d folic acid, and synthetic folate has been the standard recommendation for children with SCD. This is because SCD is a genetic disorder that causes dysfunctional red blood cells and is thought to increase requirements for folate, an essential B vitamin, due to increased red blood cell production and turnover in the disease [10].

Conclusion

The National Heart, Lung, and Blood Institute guidelines were followed by the Hematology Department of Assiut University Children's Hospital for the management of SCD pediatric patients with VOC.

Limitations: (a) Our unit does not use spirometry to reduce the risk of ACS. (b) Our unit does not use opioids to control severe painful VOC among patients with SCD. (c) Our unit does not use nonpharmacologic approaches to treat pain, such as local heat fomentation.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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