Stability of Adrenaline in Ambulance and Drug Storage Room Narenthorn Center, Rajavithi Hospital

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Background: *The stability and quality of Adrenaline medications were advocated 2 to be stored in temperature labeled at 2℃ to 8℃ at drug storage room. Thailand is located in a tropical area with the average room temperature within 25℃. There was no previous study of adrenaline medication stability and quality in Thailand.*

Objective: *To assess the stability and quality of Adrenaline stored at room temperature in Ambulance and drug storage room of Narenthorn center, Rajavithi Hospital.*

Material and Method: *Forty vials of Adrenaline Bitartrade were stored at the temperature in each season for a period of 4 weeks. Half were stored in one Ambulance and the other half in a drug storage room. Samples were then analyzed for their appearance, pH and using stability indicating High Performance Liquid Chromatography (HPLC).*

Results: *The average temperature in the drug storage rooms were 30℃, 28℃ and 27℃ in hot, rainy and cool seasons respectively; and 34℃, 32℃ and 31℃ in Narenthorn Ambulance. The appearance of adrenaline was not changed as it was still clear. The average pH is 3.18 to 3.36. Adrenaline was found to be stable when storage in both ambulance and drug storage room. The percent drug remaining was 90 Ia% to 115 Ia%. There was no significant difference in between drug quality the two storage places ($p = 0.792$). No significant difference was found in the percent drug remaining between the hot and cool season. There was significant difference in the percent drug remaining between the rainy season from other seasons ($p < 0.005$).*

Conclusion: *Even though the temperature in the drug storage room and Ambulance was higher than recommended storage temperature, adrenaline stability and quality were not changed when testing by HPLC.*

Keywords: *Drug storage, Stability, Drug quality, ACLS drug, Ambulance*

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Thailand is located in South East Asia and has a 69 million population. The weather is tropical, temperature in 2010 ranged from 19°C to 44°C. The Advance Cardiac Life Support (ACLS)[1-5] medications were labeled to be stored at 2°C to 8°C[6]. In 2005, every provinces of Thailand has already serviced for the emergency medical service (EMS). The ground ambulance life support (ALS) ambulance do response to cardiac arrest cases. However, ambulances in Thailand do not have refrigerators, the medications need to be stored at room temperature. ALS ambulance Narenthorn Center. Rajavithi Hospital responded to 1,164 patients in 2010. 39 patients used ACLS drugs and adrenaline 92 ampoules. There is no study of the stability and quality of Adrenaline in Thailand.

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Material and Method

The present study was approved by the Research Ethics Committee of the Rajavithi Hospital. The experience of study was performed in 2010. Forty vials of Adrenaline Bitartrade were stored in a drug box of temperature in each reason for a period of 4 weeks[7]. Half were stored in one ambulance and the other in a drug storage room in Narenthorn Center, Rajavithi Hospital. Samples were then analyzed for their appearance, pH and using stability and in Narenthorn indicating high performance liquid chromatography (HPLC). The temperature in the drug storage room and Ambulance were recorded in hot, rainy and cool seasons respectively.

The objective study to assess the stability and quality of Adrenalin stored of room temperature in Ambulance and drug storage room in Narenthorn Center, Rajavithi Hospital.

Statistical analysis

The Mann-Whitney U test was used to compare the HPLC value between ambulance and Drug

storage room Narenthorn Center Rajavithi Hospital. Analysis the HPLC value in each season used Kruskal Wallis test. Statistical calculations were performed using SPSS version 17.0.

Results

The average temperature in the drug storage rooms were 30°C, 28°C, 27°C in hot, rainy and cool seasons respectively; and 34°C, 30°C, 31°C in Narenthorn Ambulance (Table 1). The appearance of adrenaline is not changed. The average pH is 3.18 to 3.36. Adrenaline was found to be stable when stored in both ambulance and drug storage room. The percent drug remaining was 90 Ia% to 115 Ia%.

There was no significant difference in drug quality, between the two storage places (p = 0.792) (Table 2).

There was significant difference in the percent drug remains which in the rainy season was higher than other seasons (p = 0.005) (Table 3).

Discussion

The process to control drug quality before providing to patients is very important for patient safety. This process is composed of proper packaging, storage and transit handling. The United States Pharmacopeia (USP)[8-14] recommends the standard for medication controlled storage temperature at 2-8°C. Adrenaline drug is one of the High Alert Medications, which must be controlled in use, this drug has been proved to change their stability due to time storage and exposure besides the recommended temperature.

The present study is the first investigation of Emergence Medical Services (EMS) pharmaceuticals

Table 1. Temperature measurement

Month	Temperature								
	Bangkok weather (°C)			Drug room storage (°C)			Narenthorn ambulance (°C)		
	Min	Max	Average	Min	Max	Average	Min	Max	Average
Apr	23	39	32	28	32	30	28	40	34
Jul	24	36	29	27	29	28	27	37	32
Nov	21	34	28	26	28	27	26	35	31

Table 2. Comparative high performance chromatogram value of adrenaline drug in Narenthorn ambulance and drug storage room

Place	Mean ± SD	Median	Min-Max	p-value
Narenthorn ambulance	103.85 ± 2.08	104.50	101.50-106.90	0.792
Drug storage room	103.96 ± 2.23	103.80	100.70-106.90	

Normal standard drug concentration value 90 Ia%-115 Ia%
Statistic show p-value from Mann-whitney U test

Table 3. Comparative chromatogram value of adrenaline drug in Narenthorn ambulance and drug storage room

Season	Mean ± SD	Median	Min-Max	p-value
Hot	102.18 ± 0.59	102.20	101.50-102.80	0.003*
Rainy	105.69 ± 1.03	106.00	104.10-106.90	
Cool	102.08 ± 1.41	101.80	100.70-104.00	

Normal Standard drug concentration value 90 Ia%-115 Ia%
Statistic show p-value from Kruskal Wallis test

exposes to thermal environments outside. The study period was one month per season (hot, rainy, cool seasons) due to the turnover rate in adrenalin drug used in ambulance service in Rajavithi Hospital.

The results of our study showed the average temperature in both Rajavithi drug storage room and Rajavithi Narenthorn Ambulance (30°C, 28°C, 27°C in drug storage room 34°C, 30°C, 31°C in Rajavithi Narenthorn Ambulance) were higher than 25°C[15-19]. The average ambulance temperature was higher than average environment temperature (32°C, 29°C, 28°C in Bangkok weather).

The stability and quality of Adrenaline Bitartrade drug were analyzed in their appearance, pH and stability indicated by high performance liquid chromatography (HPLC). The appearance of adrenaline remains clear. The average pH is 3.18 to 3.36 (3.34, 3.35, 3.31, 3.36 in the hot season, 3.20, 3.25, 3.18, 3.26 in the rainy season, 3.18, 3.22, 3.19, 3.22 in the cool season). The average normal standard pH value is 2.2-5.0. Adrenaline was found to be stable when kept in both ambulance and drug storage room. The percent drug remaining was 90 Ia% to 115 Ia%. The averages HPLC $\pm$ 1SD^{w}as 103.85 $\pm$ 2.08 and 103.96 $\pm$ 2.23 in Narenthorn Ambulance and Drug Storage Room in respectively. There was no significant difference in quality between the two storage places ($p = 0.792$).

There was significant difference in percent drug remaining between the rainy season and other seasons ($p < 0.005$).

The present study does have limitations which cannot study more frequently than one time per season because of the high cost of HPLC. The average biological activity of exposed adrenaline drug in humans

Table 4. Show Characteristic of Drug Storage at Ambulance and Drug storage Room

Month	Place/ Batch	Factor					
		Characteristic					Chromatogram (% Ia)
		Sediment		Color		(PH)	
		Clear	sediment	Change color	No change color		
Starting 0							
	Amb/J	Clear	-	-	No change color	3.20	104.80
	Amb/S	Clear	-	-	No change color	3.25	106.90
	Room/J	Clear	-	-	No change color	3.18	104.80
	Room/S	Clear	-	-	No change color	3.26	106.90
April D1-D30							
Hot season	Amb/J	Clear	-	-	No change color	3.34	101.50
	Amb/S	Clear	-	-	No change color	3.35	101.90
	Room/J	Clear	-	-	No change color	3.31	102.50
	Room/S	Clear	-	-	No chang color	3.36	102.80
July D1-D30							
Rainy season	Amb/J	Clear	-	-	No change color	3.20	104.10
	Amb/S	Clear	-	-	No change color	3.25	106.10
	Room/J	Clear	-	-	No change color	3.18	105.80
	Room/S	Clear	-	-	No change color	3.26	106.10
November D1-D30							
Cool season	Amb/J	Clear	-	-	No change color	3.18	101.50
	Amb/S	Clear	-	-	No change color	3.22	104.00
	Room/J	Clear	-	-	No change color	3.19	102.10
	Room/S	Clear	-	-	No change color	3.22	100.70

Normal standard PH value 2.2-5.0
Amb/J: Drug storage at ambulance/bate product J
Amb/S: Drug storage at ambulance/bate product S
Room/J: Drug storage at drug storage room/bate product J
Room/S: Drug storage at drug storage room/bate products

was not study. Moreover, it is still the only one study of adrenaline storage stability in Thailand. The other pre-hospital cardiac arrest drug such as Amiodarone and vasopressin should be future investigated.

Conclusion

Even though the temperature in drug storage room and in the ambulance was higher than the recommended storage temperature, adrenaline stability and quality have not changed when tested by HPLC. Therefore, adrenaline can be stored in room temperature within one month period in each season[20].

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Potential conflicts of interest

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การคงตัวของยาอะดรีนาลินที่เก็บไว้ในรถพยาบาลและห้องเก็บยาของศูนย์กู้ชีพนเรนทร โรงพยาบาลราชวิถี

นพมณี ตันติเวทเรืองเดช

ภูมิหลัง: *ความคงตัวและคุณสมบัติของยาอะดรีนาลินตามใบกำกับยา แนะนำให้เก็บยาอะดรีนาลินไบตราเตรทไว้ที่อุณหภูมิอยู่ในช่วง 2 องศาเซลเซียส ถึง 8 องศาเซลเซียส ประเทศไทยตั้งอยู่ที่ลักษณะภูมิอากาศอยู่ในเขตโซนร้อน อุณหภูมิเฉลี่ยน้อยกว่า 25 องศาเซลเซียส และยังไม่มีการศึกษาเกี่ยวกับความคงตัวและคุณสมบัติของยาอะดรีนาลินในประเทศ*

วัตถุประสงค์: *เพื่อศึกษาความเข้มข้นและคุณสมบัติด้านสีตะกอนรวมทั้งวัดค่าความเป็นกรด-ด่างของยาอะดรีนาลินที่เก็บในรถพยาบาลกู้ชีพ และตัวยาที่เก็บไว้ที่ห้องเก็บยาของศูนย์กู้ชีพนเรนทร ว่ามีการเปลี่ยนแปลงของตัวยาอะดรีนาลินหรือไม่*

วัสดุและวิธีการ: *โดยนำยาอะดรีนาลินไบตราเตรทที่ผลิตโดยองค์การเภสัชกรรมประเทศไทย ที่ได้รับการตรวจสอบแล้วว่ายายังไม่หมดอายุการใช้งานมาจำนวน 40 หลอด แบ่งเป็น 2 กลุ่ม นำกลุ่มที่ 1 ไปเก็บไว้ที่กล่องยารถพยาบาล และกลุ่มที่ 2 ไปไว้ที่ห้องจัดเก็บยาอุณภูมิห้องจริงของศูนย์กู้ชีพนเรนทร โรงพยาบาลราชวิถี เป็นเวลาหนึ่งเดือนของฤดูร้อนฤดูฝนและฤดูหนาว เมื่อครบกำหนดจัดเก็บยาดังกล่าว ไปวิเคราะห์ด้วยเทคนิคโครมาโทกราฟีของเหลวสมรรถนะสูง (HPLC) เพื่อทดสอบความเข้มข้นของตัวยา และคุณสมบัติภายนอกของยาด้านสีตะกอน รวมทั้งวัดค่าความเป็นกรด-ด่างของยา*

ผลการศึกษา: *อุณหภูมิห้องเก็บยาศูนย์กู้ชีพนเรนทรโรงพยาบาลราชวิถี มีอุณหภูมิเฉลี่ย ฤดูร้อน 30 องศาเซลเซียส ฤดูฝน 28 องศาเซลเซียส และ ฤดูหนาว 27 องศาเซลเซียส อุณหภูมิที่รถพยาบาลโรงพยาบาลราชวิถี มีอุณหภูมิเฉลี่ย ฤดูร้อน 34 องศาเซลเซียส ฤดูฝน 32 องศาเซลเซียสและฤดูหนาว 31 องศาเซลเซียส การศึกษาพบว่าด้านคุณสมบัติภายนอกไม่มีการเปลี่ยนสีตะกอนของตัวยาทั้งหมดและค่าความเป็นกรด-ด่าง (pH) ของยาเฉลี่ย 3.18-3.36 เปรียบเทียบค่า HPLC ที่วัดได้ของรถพยาบาลกับอุณหภูมิห้องเก็บยาศูนย์กู้ชีพนเรนทรโรงพยาบาลราชวิถี พบว่าค่า $p = 0.792$ ตามสถิติ Mann-Whitney U test ค่าการวิเคราะห์ HPLC ตามระยะเวลาและฤดูที่กำหนดแล้วพบว่าในฤดูร้อนมีค่าไม่แตกต่างจากฤดูหนาว แต่ในฤดูฝนแตกต่างจากฤดูร้อนและฤดูหนาวค่า $p < 0.05$ ตามสถิติ Kruskal Wallis test*

สรุป: *การศึกษานี้พบว่ายาอะดรีนาลินไบตราเตรทที่เก็บไว้ในรถพยาบาล และห้องเก็บยาศูนย์กู้ชีพนเรนทร โรงพยาบาลราชวิถี ที่มีอุณหภูมิสูงกว่าค่าอุณหภูมิที่กำหนด แต่พบว่าไม่มีการเปลี่ยนแปลงความเข้มข้นและคุณสมบัติของยาเมื่อนำมาทดสอบโดย HPLC*