Teicoplanin as an anti-methicillin resistant staphylococcus aureus agent in infections of severely poisoned intensive care unit patients/ Tehran- Iran

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Abstract. *Background:* Methicillin-resistant Staphylococcus aureus (MRSA) bacteraemia is related to high morbidity and mortality. Teicoplanin is a semi synthetic glycopeptide antibiotic with a spectrum of activity similar to vancomycin. Our objective is the evaluation of efficacy and safety of Teicoplanin in MRSA infections among severely poisoned intensive care unit (ICU) patients. *Methods:* During a 6 months period, in a prospective cross sectional study, 54 eligible patients were recruited from among 80 who were clinically suspicious for MRSA infections. The efficacy and safety of Teicoplanin by loding dose of 6 mg/kg (maximum 400 mg per dose) for three loading doses 12 hours apart and then every 24 hours was evaluated 5 times. The clinical findings, laboratory data, and bacteriologic responses were categorized as cure, improvement and failure. *Results:* The mean(SD) age was 36.3(13.3) years. 75.9% were male. Suicidal attempts were recorded in 63%. The most common poisoning was TCAs, BZDs, tramadol and opium. 94.4% were unconscious and under mechanical ventilation. Tracheal cultures were positive in 98.1% by VAP diagnosis. ICU length of stay was between 4-54 days. Total clinical effectiveness was 90.4%, and failure 9.6%. Mortality rate was 9/54 (16.6 %). On the fourth visit, the adverse effects included: rash (11.10%), anemia (36.17%), nephrotoxicity (17.02%) and thrombocytopenia < 150000 (100%). Other side effects such as: leucopenia, severe thrombocytopenia (< 50000), pancytopenia and red man syndrome were not detected. *Conclusions:* Teicoplanin can be suggested for use in for MRSA infections among severely poisoned patient, based on its efficacy, safety, half life and tolerance. (www.actabiomedica.it)

Key Words: MRSA infection, Poisoning, Teicoplanin.

Introduction

Methicillin-resistant Staphylococcus aureus (MRSA) bacteraemia is related to a longer length of hospital stay (LOS), higher total treatment cost and higher risk of mortality than bacteraemia due to other bacterial pathogens. Teicoplanin possesses characteristic advantages over vancomycin, such as its prolonged serum half-life, its post antibiotic effect, and a lower frequency of nephrotoxicity and red man syndrome (1-3).

The first-line treatment of choice for invasive MRSA infections is a glycopeptide antibiotic (4,5). Vancomycin (a glycopeptide) and Teicoplanin (a lipoglycopeptide) have bactericidal activity that when mediated by the inhibition of peptidoglycan causes syn-

thesis of the bacterial cell wall. The spectrum coverage of Vancomycin and Teicoplanin are similar; however vancomycin-resistant enteroccie are susceptible to Teicoplaninin.

Teicoplanin is as commonly used in Europe as vancomycin (6,7). Teicoplanin has a long serum half-life which takes time to reach a steady-state concentration (8). For uncomplicated infections, once-daily dosing of teicoplanin is sufficien, an can be administred by intramucscular injection.

Complicated infections need a higher dosing strategy of vancomycin and teicoplanin, which requires monitoring for renal toxicity. Significantly less nephrotoxicity is reported for Teicoplanin (3,6). Histamine-release phenomena such as flushing accompanied by pruritis, hypotension, tachycardia, and even cardiac arrest are much less common with teicoplanin (7,9). Nephrotoxicity was reported as asymptomatic and self-limited in only 8% of patients who did not receive other agents suspected to be nephrotoxic. Ototoxicity with Teicoplanin has been reported as an uncommon side effect.

In large doses of teicoplanin therapy neutropenia or thrombocytopenia has been reported to be less common in comparison to Vancomycin (6,8,10). Vancomycin has been considered the treatment of choice for pneumonia due to MRSA (11). Cross-reactivity between these two glycopeptides is controversial. Teicoplanin is used as an alternative in cases of Vancomycin intolerance (10). An elementary loading dose of Teicoplanin has been recommended for reaching an optimal serum trough level of 10-15 /ml.The exact dose of Teicoplanin in managing the patients with varying renal function levels, however, remains unclear (8). Teicoplanin and Vancomycin show similar clinical and bacteriological efficacy in clinical trials (3,5,7) Overall, Teicoplanin has been reported to have a lower adverse drug reaction (ADR) rate than Vancomycin (11). Available evidence suggests that Teicoplanin as an effective agent against infections has an excellent safety profile (4,5,12).

Our study objective is to evaluate the efficacy and safety of Teicoplanin as a recommended agent against MRSA infections among severely poisoned intensive care unit (ICU) patients.

Materials and Methods

Patients and Study Design

In a prospective cross-sectional study during a 6 months period, from September 2012 to March 2013, 66 proven MRSA cases from 80 clinically suspected MRSA ICU patients were recruited. All "poisoned patients" with fever , leukocytosis by bronchial hyperactivity, and new infiltrations on chest X-ray with decreasing respiratory sounds of existence of fine rales while intubated, and under mechanical ventilation at least for 48 hours were selected. All 54 eligible patients with nosocomial infection were studied in the toxicological ICU in Loghman Hakim General Hospital, referral poison center of the Shahid Beheshti University of Medical Sciences (SBMU). The study was approved by the research ethics committee, code number 122.

Blood, urine, and tracheal sample were obtained. We considered colony count > 10^5 as significantly positive culture. The diagnosis of MRSA was based on a fever over 37.5°C tympanic, significantly positive cultures of MRSA, and in accordance to clinical and paraclinical findings which are mentioned above.

Patients who receive Teicoplanin for an MRSA infection were observed during this study after signing an informed consent form. Baseline visit investigator questionnaires were completed. Patient health status, sequence of treatment, and response to treatment was observed during 4 visits and a one-month follow up. Specifically these observations took place according to the following schedule: Day 0 or admission time, day 1or first day of treatment (after positive cultures), day 7 or 3th day of treatment, day 10 or 7th day of treatment and he day 30, one month from the admission day.

The questionnaire included: demographic, clinical, LAB data, treatment, adverse effects and outcomes. Para clinical studies included routine tests (CBC, ESR, CRP, biochemistry, CPK, creatinin and LFT). The disk diffusion for antibiotic susceptibility of microorganisms was used. Disk-diffusion method (Mast London) used inoculums of 0.5 according to the MacFarland standard scale, on Mueller-Hinton Agar plates (Oxoid) and a 30 Lg teicoplanin disk (Oxoid). Chest radiography was done on all patients. Brain and lung Ct-Scan was done as indicated.

Table 1. Efficacy Evaluation

	Cure Up to 7th days of treatmen	Improve Up to 7th days of treatment	Failure Up to 7th days of treatment
1	T° ≤ 37.5	37.5 < T° < 38.5	Persistent T° ≥ 38
2	No positive polymicrobial culture or MRSA culture is negative with 2 or more following data: - No increasing in tracheal discharge - ESR < 30 or CRP < 30 - No progressing infiltration process on CXR or lack of new infiltration - 4000 ≤ WBC ≤ 11000	WBC or other paraclinical data which shows no progress	Positive MRSA or polymicrobial culture with any of the following data: Complication: - ↑Tracheal discharge. - ARDS -Empyema -Pleural Effusion 11000 < WBC or WBC < 4000

Patients who met the following inclusion criteria were evaluated for the clinical study of Teicoplanin in the treatment of MRSA: age ≥14 years, positive culture for MRSA. Cases with hypersensitivity to Teicoplanin, pregnancy and prior antibiotics therapy in the last 2 weeks were excluded from this study. Adequate dosage was defined as based on the manufacturer's instructions. Teicoplanin was given at a loading dose of 6 mg/kg (maximum 400 mg per dose) for three loading doses 12 hours apart and then every 24 hours, adjusted per the patient's renal function. Also we could not avoid using another antimicrobial agent such as Meropenem (1 gr. tds IV) , Ciprofloxacin(400 mg bid IV) or Amikacin (500 mg bid IV) for VAP empirical therapy.

Efficacy evaluation

The efficacy of Teicoplanin was evaluated by the clinical findings, laboratory data, and bacteriologic responses. The efficacy assessment used was as follows: cure, improvement and failure as defined in Table 1 (8,13).

Statistical analysis

Data was reported as mean ± SD, frequency and relative frequency for quantitative and categorical data respectively. Repeated measure analysis was done for evaluating the trend of continuous variables. SPSS version 16 statistical package for Windows (SPSS Inc., Chicago Illinois, USA) was used for all statistical analysis.

Result

During our prospective study, 12 patients were omitted due to incomplete follow up. A total of fifty-four patients with established and highly suspected MRSA were enrolled. 41 cases (75.9%) were male. The mean age was 36.3 years (range=20-72, SD = 13.3). According to the patient's history, suicidal attempts were recorded in 63% (n = 34) and accidental poisoning in 37% (n= 20). The most common etiologic agent of suicide was substance abuse and poisoning which included: Tricyclic antidepressant (TCAs) in 9 patients, Tramadol and Benzodiazepine (BZD) in 8, and Methadone in 7 patients. Drug toxicity is noted in Table 2. Underlying

Table 2. List of Drug Toxicities

Drug toxicities	Number	(%)
Phenytoin	1	(1.85)
Lidocaine	1	(1.85)
BZD	7	(12.96)
TCA	9	(16.67)
Opium	5	(9.26)
Methadone	7	(12.96)
Tramadol	8	(14.81)
Methanol	3	(5.56)
Baclofen	1	(1.85)
Carbon monoxide	1	(1.85)
Phenobarbital	1	(1.85)
Haloperidol	1	(1.85)
Aluminum phosphate	3	(5.56)
Organophosphorus	2	(3.70)
Sodium valproate	2	(3.70)
TCA &Opium	1	(1.85)
Methanol & Baclofen	1	(1.85)
Total	54	100

diseases such as cardiac disease, epilepsy, hypertension and psychosis were noted in 6 patients. Most of the eligible patients were unconscious (n = 53, 94.4%). All patients were intubated and under mechanical ventilation.

Clinical and paraclinical data is listed in Table 3. Tracheal culture was positive in 53 (98.1%), followed by urine in 12(22.2%) and blood in 7 (13%). It is notable that only one patient had negative tracheal culture and some patients had combinated positive cultures. On day 10, blood cultures were still positive and some polymicrobial agents such as Klebsiella P, Aeruginosa P and Baumannii A in 5 patients with failure of treatment were detected.

Seven patients became septic, with one death on the 3th day of treatment, the patient being post CPR from the first day of admission and having hypoxic sequel. All other patients were treated and cured without any complications or sequels. Complications were recorded in 9 patients, which included: ARDS (n = 7), massive pleural effusion (n = 1) and empyma (n = 1). Length of stay in ICU (LOS) was between 4- 54 days. Tracheostomies were performed on 9 cases in which

Table 3. Clinical and Paraclinical Data

	Day 0		Day 1		Day 3		Day 10		Day 30	
Clinical and paraclinical variable	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
Temperature	37.82	0.69	38.22	0.48	37.63	0.55	37.38	0.37	37.13	0.24
Bp	117.15	19.39	119.55	19.98	115.50	17.18	111.51	13.26	104.78	17.29
HR	106	41	101	19	97	20	87	10	86	12
GCS	7.94	2.61	9.07	3.06	10.60	3.47	12.63	3.52	14.41	1.75
WBC	11185	3972	9722	3912	8780	3457	8202	2924	7262	2897
Poly	78.36	10.48	77.71	11.95	76.55	8.74	73.09	10.16	64.99	10.43
lymph	14.01	7.35	13.43	6.69	16.71	15.75	15.94	6.60	19.83	7.82
Eos	0.85	1.51	0.91	1.50	0.65	1.33	0.73	1.39	1.25	1.77
Monocyte	5.40	3.03	5.84	3.03	7.63	3.72	8.51	4.49	9.65	3.00
Toxic granulation	0.35	0.52	0.17	0.38	0.06	0.24	0.06	0.25	0.03	0.16
ESR	57	27	61	31	56	28	47	23	42	20
Hb	12.38	2.24	11.13	2.03	10.42	2.04	10.85	1.74	11.01	1.31
HCT	38.11	6.65	34.96	5.86	33.34	5.76	34.26	5.19	35.37	3.95
Platelet	173592	65327	169120	89666	197076	78277	219531	105141	205775	103062
Cr	1.43	1.34	1.31	1.48	1.44	2.26	1.01	0.84	1.34	3.37
Ka	3.97	0.68	3.92	(.45)	3.87	0.41	4.74	5.41	4.11	0.21
CPK	2132.36	4288.03	1321.33	(2295.59)	721.17	1141.26	432.51	768.56	183.70	231.69
AST	107.40	189.85	74.96	(77.47)	60.63	64.98	53.06	57.07	37.93	29.04
ALT	71.70	125.47	66.70	(114.57)	50.19	61.78	54.91	107.32	30.33	32.73
ALK	184.24	54.88	187.78	(62.88)	169.77	54.20	164.29	60.45	170.75	68.09
Bill total	0.81	0.47	1.04	(.61)	1.12	1.35	0.87	0.38	0.92	0.62
Bill direct	0.25	0.18	0.36	(.30)	2.33	14.52	0.33	0.19	0.36	0.27
INR	1.33	0.89	1.24	(.42)	1.14	0.29	1.10	0.22	1.02	0.19
PH	7.38	0.08	7.38	(.05)	7.39	0.08	7.36	0.05	7.35	0.03
PO2	98.05	19.62	105.83	(27.37)	100.65	25.03	96.44	18.31	86.66	20.95
Pco2	42.76	11.67	41.18	(8.76)	39.27	8.21	41.76	7.63	42.16	7.28
HCo3	25.01	7.21	23.59	(4.08)	22.79	4.65	23.05	3.29	22.28	0.95
O2 Sat	85.11	10.89	82.61	(13.14)	83.85	10.61	91.20	10.43	95.26	6.11

LOS was > 20 days. Eight of the patients were hypoxic and vegetative from post CPR position which is recognized as a sequel of poisoning. Mortality rate was 9/54 (16.6%). One death was caused by massive pleural effusion with poly microbial infections in addition to MRSA which did not clinically respond to Teicoplanin, Linezolid and Colistin with Amikacin during a 54 day hospitalization. One death was from empyma, two deaths were from ARDS; death in 3 hypoxic vegetative patients was caused by poly microbial agents. One hypoxic patient died from sepsis, showing a positive blood culture for ARDS. Severe aluminum phosphide toxicity caused the death of one patient within the first day of treatment. Lack of clinical response to Teicoplanin was the reason for the 3 patients death.

We were unable to follow up 14 patients on day 30 of the study, as 5 cases were unavailable and 9 had died. On day 10, total clinical effectiveness (cure and improvement rate) was 90.4% (47/52) and failure reported 9.6% (n = 5). Also on day 10, the adverse effects included were: rash (6/54), anemia (17/47), nephrotoxicity (8/47). Thrombocytopenia < 150000 (47/47) on day 10 was the same as the first of treatment but severe thrombocytopenia (< 5 0000) had been detected in 2 patients in the first day of treatment. Leucopenia was detected in the first day of treatment (n = 2/54), but on day 10 it was seen to be normal. Other side effects such as: leucopenia, severe thrombocytopenia (platelet < 50000), bycytopenia, pancytopenia and red man syndrome were not detected on day 10, although bycytopenia (HB < 10, Platelet < 50000) was seen in 3 patients during the first day of treatment that was omitted in the future visits and follow ups.

Discussion

Teicoplanin is a narrow spectrum antibiotic, which is known as teichmycin A2. It belongs to the glycopeptide group and is similar in structure to vancomycin. Its bioavailability is 90-95% and its half-life is as long as 100 hours in patients with normal renal functions. Therefore, once daily dosage is sufficient for most infections, though we used it twice for the first 3 days as a loading dose (14). Methicillin-resistant Staphylococcus aureus (MRSA) infections are a serious and constantly growing public health consideration. The first line treatment of choice for invasive (MRSA) infections is a glycopeptide antibiotic. In our study 41.5% patients had an LOS in the hospital of more than 20 days, which increases the mortality rate especially in severe and critically poisoned patients. Talaie et al. (15) shows that more than a 5 day hospitalization may increase 3 fold the mortality rate at the surgical sites infected by MRSA, while mortality rate in our study was 16.6% with most of our patients having VAP. Lack of clinical response was seen in 3. In our previous study we found a lower mortality rate in our VAP patients. In the present study, we could not avoid using another antimicrobial agent such as Meropenem or Ciprofloxacin for VAP empirical therapy.

However, for its MIC and limited access to the lung parenchyma, we had acceptable response among our VAP patients (10,11). The effect of teicoplanin was evaluated in terms of the clinical findings, laboratory data, and bacteriologic responses (8), with a total clinical effectiveness of 90.4%. While in the respiratory department of a Chinese hospital it was a 82.1% in different infections such as lower respiratory tract infections, sepsis, catheter-associated infections, endocarditis, leucopenia with fever, bone-joint infectionsv and skin-soft tissue infections. In this toxicological ICU most of our patients tested positive for infection, with 98.1% positive tracheal cultures, , 22.2% positive urine cultures, and 13% positive blood cultures (16). Teicoplanin possesses characteristic advantages over vancomycin, such as its prolonged serum half-life, its postantibiotic effect, and a lower frequency of nephrotoxicity or red man syndrome (8). In a systematic review and meta-analysis survey by Svetitsky et al. (6) red man syndrome was not reported in the teicoplanin group, whereas its incidence was 5% of in the vancomycin group. Also in our study there was no noted red man syndrome. In addition only one hypotensive patient died from severe toxicity with aluminum phosphide.

According to Bibler et al. (17) the most significant adverse reaction to Teicoplanin was an urticarial rash, which required discontinuation of therapy in one

patient. Pruritus and rash were reported by Sato M et al. (8). Likewise, we found rash in 11.1% of patients; rashes were transient and required no treatment.

In several surveys, nephrotoxicity was described as asymptomatic and self-limited in 8% of patients (18-20). Nephrotoxicity was defined heterogeneously as creatinine levels above the normal range (1.1 to 1.5 mg/dl), by an absolute increase of 0.5 mg/dl, or as a 50 to 100% increase from the baseline level which showed in the meta-analysis survey by Svetitsky et al. (6). In the present study, the rising of creatinine (> 30 % based) showed in 8 patients (14.81%) which remained the same range on day 10.

According to the rhabdomyolysis definition, CPK was 5 fold greater than normal in 37% of patients and another 3.7% patients had greater than 10,000 CPK on admission day. On day 10 only 3 patients had elevated CPK.

As it is known well, in rhabdomyolysis which is a common event among poison patients, we have creatinine elevation (21). According to our previous study of poison induced rhabdomyolysis and acute renal failure, 3 out of 180 patients acquired persistent renal failure which needed hemoperfussion dialysis (22).

It is notable that in the present study creatinine increase with rhabdomyolysis was persistent but we cannot disregard the Teicoplanin nephrotoxicity as a side effect. Therefore we concluded Teicoplanin may increase mild nephrotoxicity but not significantly.

Monitoring of the serum level of vancomycin is mandatory in all patients for safety reasons. For Teicoplanin, this monitoring is recommended only in patients who are hemodynamically unstable, and in patients with serious infections (8). Teicoplanin levels or trough in this study was not mentioned.

He et al. (16) reported that the total adverse effects, such as decrease in blood cells and transient abnormal liver functions, occurred only in 1.28% of patients. On the contrary, based on our data, leucopenia, sever thrombocytopenia (< 50000), bycytopenia and pancytopenia were not found at the end of treatment or follow up. However, bicytopenia (anemia and platelet < 150000) is a common transient event in poisoning. Transaminase elevation (mean) averaging 2 or 3 fold greater than the normal was present in the first visit, and decreased by the end of treatment. This may be due to Rhabdomyolysis or liver toxicity from the poisoning, and is transient and reversible (21). Also, I Sato et al. (8) found eosinophilia and transaminase elevation.

Conclusion

Teicoplanin is recommended for MRSA infection among severe critically poisoned patients, base on its efficacy, safety, half life, tolerance and cost.

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References

1. Chang HJ, Hsu PC, Yang CC, Siu LK, Kuo AJ, Chia JH, et al. Influence of teicoplanin MICs on treatment outcomes among patients with teicoplanin-treated methicillin-resistant Staphylococcus aureus bacteraemia: a hospital-based retrospective study. J Antimicrob Chemother 2012; 67: 736-41.
2. Wang JT, Liao HI, Wu Lin FL, Chang SC. Loading dose required to achieve rapid therapeutic teicoplanin trough plasma concentration in patients with multidrug-resistant gram-positive infections. Basic Clin Pharmacol Toxicol 2012; 110: 416-20.
3. Cavalcanti AB, Goncalves AR, Almeida CS, Bugano DD, Silva E. Teicoplanin versus vancomycin for proven or suspected infection. Cochrane Database Syst Rev 2010; 16: CD007022 .
4. Nathwani D, Morgan M, Masterton RG, Dryden M, Cookson BD, French G, et al. Guidelines for UK practice for the diagnosis and management of methicillin-resistant Staphylococcus aureus (MRSA) infections presenting in the community. J Antimicrob Chemother 2008; 61: 976–94.
5. Tobudic S, Poeppl W, Kratzer C, Vychytil A, Burgmann H.Comparative in vitro antimicrobial activity of vancomycin, teicoplanin, daptomycin and ceftobiprole in four different peritoneal dialysis fluids. Eur J Clin Microbiol Infect Dis 2012; 31: 1327-34.
6. Svetitsky S, Leibovici L, Paul M. Comparative efficacy and safety of vancomycin versus teicoplanin: systematic review and meta-analysis. Antimicrob Agents Chemother 2009; 53: 4069-79.

7. Davey PG, Williams AH. A review of the safety profile of teicoplanin. J Antimicrob Chemother 1991; 27 Suppl B: 69-73.
8. Sato M, Chida K, Suda T, Muramatsu H, Suzuki Y, Hashimoto H, et al. Recommended initial loading dose of teicoplanin, established by therapeutic drug monitoring, and outcome in terms of optimal trough level. J Infect Chemother 2006; 12: 185-9.
9. Southorn PA, Plevak DJ, Wright AJ, Wilson WR. Adverse effects of vancomycin administered in the perioperative period. Mayo Clin Proc 1986; 61: 721-4.
10. Wilson AP. Comparative safety of teicoplanin and vancomycin. Int Antimicrob Agents 1998; 10: 143–52.
11. Ramirez P, Fernández-Barat L, Torres A. New therapy options for MRSA with respiratory infection/pneumonia. Curr Opin Infect Dis 2012; 25: 159-65.
12. Davies JM. A survey of the use of teicoplanin in patients with haematological malignancies and solid tumours. Infection 1998; 26: 389-95.
13. Talaie H, Jabari HR, Shadnia S, Pajouhmand A, Nava-Ocampo AA, Youssefi M. Cefepime/clindamycin vs. ceftriaxone/clindamycin for the empiric treatment of poisoned patients with aspiration pneumonia. Acta Biomed 2008; 79: 117-22.
14. Salaria M. Teicoplanin. Indian Pediatr 2001; 38: 372-5.
15. Talaie H, Sabeti S, Mahdavinejad A, Barari B, Kamalbeik S. A survey on microorganisms and their sensitivity by E-test in ventilator-associated pneumonia at Toxicological-Intensive Care Unit of Loghman-Hakim Hospital. Acta Biomed 2010; 81: 210-6.
16. He LX, Pan J, Chen SY, Wang AX, Xie CM, Shen ZY. Clinical study of teicoplanin in the treatment of patients with gram-positive cocci the Chinese experience. Zhonghua Nei Ke Za Zhi 2005; 44: 337-41.
17. Bibler MR, Frame PT, Hagler DN, Bode RB, Staneck JL, Thamlikitkul V, et al. Clinical evaluation of efficacy, pharmacokinetics, and safety of teicoplanin for serious gram-positive infections. Antimicrob Agents Chemother 1987; 31: 207–12.
18. Cooper GL, Given DB . Vancomycin: a comprehensive review of 30 years clinical experience. San Diego: Park Row Publishers; 1986. Pharmacokinetics of vancomycin; p. 23-38.
19. Van Laethem Y, Hermans P, De Wit S, Goosens H, Clume N. Teicoplanin compared with vancomycin in methicillin-resistant Staphylococcus aureus infections: preliminary results. J Antimicrobial Chemotherapy 1988; 21 Suppl A: 81–7
20. Bartlett JG. Clinical practice. Antibiotic-associated diarrhea. N Engl J Med 2002; 346: 334-9.
21. Talaie H, Pajouhmand A, Abdollahi M, Panahandeh R, Emami H, Hajinasrolah S, et al. Rhabdomyolysis among acute human poisoning cases. Hum Exp Toxicol 2007; 26: 557-61.
22. Talaie H, Emam-Hadi M, Panahandeh R, Hassanian-Moghaddam H, Abdollahi M. On the mechanisms underlying poisoning-induced rhabdomyolysis and acute renal failure. Toxicol Mech Methods 2008; 18: 585-8.

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