Causes of rhabdomyolysis in acute poisonings

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Abstract

Background/Aim. Rhabdomyolysis (RM) is potentially lethal syndrome, but there are no enough published data on its frequency and characteristics in acute poisonings. The aim of this study was to determine the causes and severity of RM in acute poisonings. Methods. Patients hospital charts were retrospectively screened during a one-year period in order to identify patients with RM among 656 patients treated due to acute poisonings with different agents. All the patients with RM were selected. Entrance criterion was the value of creatine kinase (CK) over 250 U/L. The severity of RM was assessed according to the Poison Severity Score. The patients were divided into three groups: the first one with mild RM (CK from 250 to 1,500 U/L), the second with moderate RM (CK from 1,500 to 10,000 U/L) and the third with severe RM (CK greater than 10,000 U/L). Results. RM occurred in 125 (19%) of the patients with acute poisonings. It was mainly mild (61%), or moderate (30%), and only in 3% of the patients was severe RM. The incidence of RM was the highest in poisonings with opiates (41%), pesticides (26%), anticonvulsants (26%), ethyl alcohol (20%), and gases (19%). Psychotropic agents were the most common causes of poisoning, and consequently of RM. Fatal outcomes were registered in 32 (25.60%) of all RM patients. The incidence of fatal outcomes in poisonings with mild, moderate and severe RM was 19.73%, 31.11% and 75%, respectively. Conclusion. RM syndrome occurs at a relatively high rate in acute poisonings. Although agent’s toxicity is crucial for the outcome, severe RM and its complications may significantly influence the clinical course and prognosis of poisoning. Routine analysis of CK, as a relevant marker for RM may indicate the development of RM in acute poisoning and initiate prompt therapeutic measures in preventing acute renal failure as the most frequent consequence of extensive rhabdomyolysis.

Key words: rhabdomyolysis; poisoning; creatine kinase; diagnosis; pharmaceutical preparations; opiate alkaloids; pesticides; coma.

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Uvod/Gilj. Rabdomioliza (RM) predstavlja potencijalno letalni sindrom, o čijoj učestalosti i karakteristikama u akutnim trovanjima nema mnogo podataka. Gilj rada bio je da se odrede uzročnici i težina RM u ovim stanjima. Metode. Retrospektivno su analizirane istorijs bolesti 656 bolničkih lečenih bolesnika zbog akutnog trovanja različitim agesmima tokom jedne godine. Izdvojeni su bolesnici sa RM, a kriterijum je bio da su imali aktivnost kreatin kinaze (CK) u serumu višu od 250 U/L. Težina RM procenjivana je na osnovu skale težine trovanja (PSS). Bolesnici su bili podeljeni u tri grupe: prvu grupu sa blagom RM (CK od 250 do 1 500 U/L), drugu grupu sa srednje teškom RM (CK od 1 500 do 10 000 U/L) i treću grupu sa teškom RM (CK viša od 10 000 U/L). Rezultati. RM je nađena kod 125 (19%) bolesnika sa akutnim trovanjima, pri čemu je uglavnom bila blaga (61%) ili umjerena (36%), a samo kod 3% bolesnika teška. Učestalost pojave RM bila je najveća kod akutnih trovanja opijatima (41%), pesticidima (38%), neurolepticima (26%), antikonvulzivima (26%), etil alkoholom (20%) i gasovima (19%). Psihotropni lekovi bili su najzastupljeniji uzročnici trovanja, a samim tim i RM. Smrtni ishod je zabeležen kod 25,6% bolesnika sa RM, pri čemu je letalitet iznosio 19,73% u trovanjima sa blagom RM, 31,11% sa srednje teškom i 75% u trovanjima sa teškom RM. Zaključak. Sindrom RM pojavljuje se relativno često u akutnim trovanjima. Za ishod trovanja od presudnog značaja je toksični agen, ali teška RM i njene kompleksije mogu značajno da utiču na tok i prognozu trovanja. Rutinska analiza CK, kao relevantnog pokazatelja RM kod akutnih trovanja, može ukazati na razvoj ovog sindroma i doprinosi pravovremenom preduzimanju terapijskih mera za sprečavanje nastanka akutne bubrežne insufficijencije kao najčešće posledice ekstenzivne RM.
**Introduction**

Rhabdomyolysis (RM) is a common and potentially lethal clinical syndrome that results from acute necrosis of myocytes and fiber content releasing into circulation. The first description of RM originates from the Bible – an episode of mass poisoning of Jews who ate quail during their journey from Egypt. Hemlock was eaten by quail, and the poison from this plant, cicutoxin, causes convulsions and RM followed by muscle symptoms and signs on admission. Therefore, the absence of muscle swelling on admission. Therefore, the absence of muscle symptoms and signs on admission does not exclude the diagnosis of RM. In a great number of cases, the clinical picture of RM is covered by the clinical picture of acute poisoning, so the classic triad occurs in only about 10% of patients. Gabow et al. showed that as much as 50% of patients with RM had no muscle pain and only 5% of patients had verified muscle swelling on admission. Therefore, the absence of muscle symptoms and signs on admission does not exclude the diagnosis of RM. In a great number of cases, the clinical picture of RM is covered by the clinical picture of acute poisoning and the diagnosis of RM can easily be missed. To make the diagnosis of RM is more difficult in patients with altered states of consciousness, who cannot point to their problems. For the diagnosis of RM the coma itself may be more important than the cause of coma. Laboratory tests that confirm the presence of RM include elevated creatine kinase (CK) in blood (normally 24 U/L – 195 U/L), typically more than 5 times higher than the upper limit of normal, as well as the presence of myoglobin in urine. However, some authors state lower levels of CK (etc. > 500 U/L) as appropriate for the diagnosis of RM. RM cannot be definitely excluded on the basis of negative myoglobin in urine because it has a very short half-life (2–3 hours).

Major complications of RM are ARF, compartment syndrome, arrhythmias and cardiac arrest, disseminated intravascular coagulation, hepatic dysfunction. An aggressive rehydration is considered to be the standard therapeutic measure in preventing ARF in patients with RM. The role of mannitol and bicarbonate is controversial.

The aim of this study was to determine the causes and the severity of RM in acute poisonings.

**Methods**

Hospital charts of patients were retrospectively screened during a one-year period in order to identify patients with RM among 656 patients treated due to acute poisonings with different agents in the Clinic of Emergency and Clinical Toxicology, Military Medical Academy, Belgrade. We selected all patients with elevated CK (higher than 250 U/L). In poisoning caused by multiple agents, the leading agent was declared as a cause of RM. The severity of RM was assessed according to the Poison Severity Score. The patients were divided into 3 groups: with mild RM (mild pain and tenderness, CK level from 250 U/L to 1,500 U/L); with moderate RM (pain, rigidity, cramping and fasciculation, CK level from 1,500 to 10,000 U/L) and with severe RM (intense pain, extreme rigidity, extensive cramping and fasciculation, RM with complications, CK greater than 10,000 U/L, compartment syndrome). In assessing the increase of CK, the maximum value of each patient during the hospital stay was taken into account.

**Statistical analysis**

The results of variables are expressed as the mean value ± standard deviation or as the frequency (%) from groups total. In order to determine the difference in frequency of appearance of RM in various types of poisoning, χ² test was performed. Differences were considered to be significantly important if the null hypothesis could be rejected with > 95% confidence. The SPSS 17.0 statistical software package was used for all calculations.

**Results**

Elevated level of CK was registered in 125 (19%) among 656 patients hospitalized due to acute poisonings. There were 52.8% males and 47.2% females with the mean age of 40.84 ± 7.53 years. The demographic characteristics of RM patients according to causative agents are shown in Table 1.

**Severity of rhabdomyolysis**

The peak CK values in poisonings caused by different toxic agents are shown in Table 2. In relation to the severity of RM (according to PSS), considering CK as a basic pa-
Mild rhabdomyolysis

In the group of 76 patients with mild RM, the most common toxic agents were drugs – in 33 of the patients. Among the drugs, specific agents included benzodiazepines (diazepam, midazolam, bromazepam, lorazepam and prazepam), anticonvulsants (carbamazepine and phenobarbitone), neuroleptics (haloperidol, chlorpromazine, thioridazine), antidepressant maprotiline, antiparkinson biperiden and antihypertensive drug moxonidine.

Mild RM was caused by pesticides in 12 of the patients. Organophosphorus insecticides (OPI) malathion, diazinone and dimethoate were the causes of RM in 10 patients. Paraquat and amitraz were toxic agents in single cases.

Ingestion of corrosive agents, hydrochloric or acetic acid, caused mild RM in 12 of the patients. Among the agents producing mild RM were heroin (9 of the patients) and ethyl alcohol (4 of the patients). Mushrooms and gases from fire caused RM each per 3 of the patients.

Moderate rhabdomyolysis

Drugs (27 of the patients) and pesticides (8 of the patients) were the most common causes of poisonings in the group of 45 patients with moderate RM. Neuroleptics (chlorpromazine - 4, thioridazine - 3, haloperidol - 2, clozapine – 2 and fluphenazine 1) were the most frequent among the drugs – in 12 of the patients; then benzodiazepines (diazepam – 4, bromazepam 1) and anticonvulsants (carbamazepine – 4, phenobarbitone 1) each per 5 of the patients. Antidepressants (amitriptyline) caused moderate RM in 2 of the patients. Single cases with beta blocker (propranolol), antihistamine (promethasine) and anticholinergic agent (atropine) poisoning were recorded. Among pesticides, the most common causes were OPI with malathion in 4 of the patients, and diazinone in 1 of the patient. Single cases of poisoning with dinitro-ortho-cresol, paraquat and an unidentified organochlorine pesticide were found.

Table 1

<table>
<thead>
<tr>
<th>Agents of poisoning</th>
<th>Age (years) ± SD</th>
<th>Range</th>
<th>Gender m/f, n (%)</th>
<th>Total patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychoactive drugs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>benzodiazepines</td>
<td>47.3 ± 16.0</td>
<td>19–74</td>
<td>7/12 (36.8/63.2)</td>
<td>19</td>
</tr>
<tr>
<td>neuroleptics</td>
<td>34.9 ± 10.5</td>
<td>22–55</td>
<td>9/9 (50.0/50.0)</td>
<td>18</td>
</tr>
<tr>
<td>anticonvulsants</td>
<td>37.2 ± 13.8</td>
<td>15–64</td>
<td>8/8 (50.0/50.0)</td>
<td>16</td>
</tr>
<tr>
<td>antidepressants</td>
<td>46.7 ± 11.9</td>
<td>29–54</td>
<td>2/2 (50.0/50.0)</td>
<td>4</td>
</tr>
<tr>
<td>antiparkinsons</td>
<td>39.0 ± 0.0</td>
<td>39–39</td>
<td>0/1 (0.0/100.0)</td>
<td>1</td>
</tr>
<tr>
<td>Other drugs</td>
<td>25.2 ± 12.3</td>
<td>15–43</td>
<td>3/1 (75.0/25.0)</td>
<td>4</td>
</tr>
<tr>
<td>Pesticides</td>
<td>46.8 ± 18.4</td>
<td>23–79</td>
<td>8/12 (40.0/60.0)</td>
<td>20</td>
</tr>
<tr>
<td>Corrosives</td>
<td>59.0 ± 17.1</td>
<td>26–78</td>
<td>4/10 (28.6/71.4)</td>
<td>14</td>
</tr>
<tr>
<td>Opiates</td>
<td>24.2 ± 7.5</td>
<td>17–47</td>
<td>11/3 (78.6/21.4)</td>
<td>14</td>
</tr>
<tr>
<td>Ethyl alcohol</td>
<td>29.6 ± 22.1</td>
<td>19–69</td>
<td>5/0 (100.0/0.0)</td>
<td>5</td>
</tr>
<tr>
<td>Mushrooms</td>
<td>50.2 ± 17.9</td>
<td>21–68</td>
<td>4/1 (80.0/20.0)</td>
<td>5</td>
</tr>
<tr>
<td>Gases</td>
<td>31.0 ± 6.4</td>
<td>22–37</td>
<td>5/0 (100.0/0.0)</td>
<td>5</td>
</tr>
<tr>
<td>All groups</td>
<td>40.8 ± 17.5</td>
<td>15–79</td>
<td>66/59 (80.0/20.0)</td>
<td>125</td>
</tr>
</tbody>
</table>

$x$ – mean; SD – standard deviation; m-male; f-female; n – number of patients.

Table 2

<table>
<thead>
<tr>
<th>Agents of poisoning</th>
<th>CK (U/L) ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychoactive drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>benzodiazepines</td>
<td>2151.3 ± 2968.1</td>
<td>261–10608</td>
</tr>
<tr>
<td>neuroleptics</td>
<td>3627.4 ± 2973.9</td>
<td>302–11420</td>
</tr>
<tr>
<td>anticonvulsants</td>
<td>1249.4 ± 1124.9</td>
<td>315–3602</td>
</tr>
<tr>
<td>antidepressants</td>
<td>2382.0 ± 2670.9</td>
<td>347–6270</td>
</tr>
<tr>
<td>antiparkinsons</td>
<td>865.0 ± 0.0</td>
<td>865–865</td>
</tr>
<tr>
<td>Other drugs</td>
<td>2880.2 ± 2435.6</td>
<td>362–5986</td>
</tr>
<tr>
<td>Pesticides</td>
<td>1633.9 ± 1811.7</td>
<td>276–7314</td>
</tr>
<tr>
<td>Corrosives</td>
<td>907.8 ± 739.7</td>
<td>258–2843</td>
</tr>
<tr>
<td>Opiates</td>
<td>3115.4 ± 3949.5</td>
<td>277–10306</td>
</tr>
<tr>
<td>Ethyl alcohol</td>
<td>888.6 ± 1022.3</td>
<td>275–2665</td>
</tr>
<tr>
<td>Mushrooms</td>
<td>1460.8 ± 1593.6</td>
<td>447–4160</td>
</tr>
<tr>
<td>Gases</td>
<td>2516.8 ± 3229.4</td>
<td>520–8180</td>
</tr>
<tr>
<td>All groups</td>
<td>2091.3 ± 2545.2</td>
<td>258–11420</td>
</tr>
</tbody>
</table>

$x$ – mean; SD – standard deviation.
The rest of the causes of moderate RM were opiates (heroine) – 3 of the patients, corrosives (acetic acid) 2 of the patients, Amanita phaloides 2 of the patients, gases (carbon monoxide and intoxication from inhaled fumes in fire – each per one of the patients), and ethyl alcohol – 1 patient.

### Severe rhabdomyolysis

In four cases of severe RM, heroin overdose and combined drug poisonings were present, each per two patients. In one drug-overdosed patient, the causes of poisoning were benzodiazepines diazepam and alprazolam, but the clinical course included prolonged coma before admission, pneumonia and sepsis with multiorgan failure. The second case was multi-drug poisoning by neuroleptics (chlorpromazine and haloperidol), antiparkinson drug (trihexyphenidyl) and anticonvulsant drug (carbamazepine).

### The frequency of rhabdomyolysis

A total of 370 acute drug poisonings were registered in the observed period; 301 were caused by psychotropic drugs and 69 by the other drugs. Overall, psychotropic drugs were the most common causes of RM. RM was present in 58 (19.27%) of the cases out of all psychotropic drug poisonings. Out of a totally 73 acute pesticides poisonings, RM was registered in 20 (27.39%). RM was recorded in 14 (18.42%) out of 76 patients with corrosive ingestion and in 14 (41.17%) among 34 opiate overdosed patients. Out of 25 patients hospitalized due to acute ethyl alcohol intoxication, 5 (20%) had RM. RM occurred in 5 (18%) out of 28 mushroom poisoning. Out of totally 27 patients hospitalized for acute poisoning with harmful gases, RM was noted in 5 (18.51%). Two patients had carbon monoxide or toxic fumes in fire as the causative agent, while a single had chlorine.

The highest frequency of RM was found in patients poisoned with opiates, then pesticides, neuroleptics and anticonvulsants (Figure 1).

There was a significantly higher rate of RM occurrence in patients with acute opiate poisoning than in patients poisoned by corrosives, benzodiazepines and antidepressants. Among the other analysed agents, there were no significant differences in RM incidence.

### Clinical course and outcome of rhabdomyolysis

A total of 21 (16.8%) of the patients with RM developed ARF. In cases with mildly and moderately elevated CK, nephrotoxicity of agents such as acetic acid, Amanita

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**Discussion**

In this study CK was chosen for assessment of RM severity in acute poisonings because it is a reliable biological parameter. High CK concentrations suggest the presence and damage of myocytes in a proper way. CK is slowly and totally degraded and removed from circulation, so concentrations in serum remain elevated much longer than myoglobin concentration in urine.

Data on the incidence of RM in acute poisonings are unreliable, as it often goes unnoticed. CK elevation was noted in many of our patients – even 19% of the total number of those hospitalized for acute poisoning. Because of predominant clinical manifestations of acute poisonings and without the presence of the usual characteristics of RM, its subclinical course may be overlooked. According to Elzadi-Mool et al., the most frequent grade of RM in patients poisoned with various agents presenting in coma, was the moderate one (55%). Our observation included all poisoned patients, and in the majority of patients with RM, it was mild (60.80%). This disorder was diagnosed only based on biochemical indicator (CK), without clinical signs and symptoms. It was easier to recognize the cases of moderate to severe RM, which were manifested by clinical disorders (pain in the muscles, rigidity or swelling, changes in colour and the amount of urine, the development of renal failure). In such cases, RM contributed to the severity of poisoning.

More than 150 medications and toxins have been described as a cause of RM, but drugs and alcohol are the most common. Underlying mechanisms are different, such as immobilization, increased psychomotor activity, or direct toxic effects which may act via altering myocyte function by inhibition of calcium metabolism, due to impairment of adenosine phosphate production, or alterations in carbohydrate metabolism.

Psychotropic drugs were the most prevalent causes of poisoning, and consequently of RM, in our study, as well as in a report of Mousavi et al. Though the incidence of RM in acute benzodiazepine poisonings is not high (14.5%), benzodiazepines were the most frequent cause of RM in our patients, simply because they were the most common cause of poisoning. These drugs were involved in 13 patients with mild, 5 with moderate, and 1 with severe RM and fatal outcome due to septic and cardio-circulatory complications. Benzodiazepines primarily cause RM due to secondary mechanism, mainly because of local muscle compression and ischemia during prolonged immobilization in prolonged consciousness depression.

Neuroleptics were the second among the drugs causing RM in our patients. Considering the incidence (26%) and severity (mainly moderate to severe), RM was the most pronounced in poisonings with these prescription drugs. Phenothiazines haloperidol and flufenazin, were the causes of neuroleptic malignant syndrome (NMS) in one patient, with agitation, hyperthermia and fatal outcome.

RM is a manifestation, as well as one of diagnostic criteria for NMS. It could be subclinical, only with increased activity of CK, or could cause massive myoglobinuria and ARF. However, haloperidol can cause RM even without NMS.

Convulsions caused by cyclic antidepressants are very frequent causes of RM. In this study, maprotiline and amitriptyline caused mild to moderate RM in 4 of the patients in the absence of manifested convulsions.

In this study, RM developed most frequently (41%) in opiates overdoses. Heroin was the most common opiate. Two of heroin overdosed patients (one combined with "ecstasy") with severe RM developed ARF and other complications resulting in fatal outcomes. Severe RM is reported as very frequent complication of opiate intoxication – even in 22 of 188 consecutive patients in a study by Larpin et al. Except for heroin, RM with extremely high CK level, up to 100,000 U/L, or higher, may occur in other opiates overdoses, like methadone or morphine. Opiate-induced RM ensues secondary, by muscle compression in coma and consciousness disorders in general, but a short period before severe RM manifestation indicates that direct myotoxic effect probably has the most important role in these cases.

The patient who except for heroin allegedly ingested only two "ecstasy" tablets developed severe clinical picture including also fulminate hyperthermia. Very serious complications after ingestion of relatively small amounts of 3,4-methylenedioxyamphetamine (MDMA) may indicate to a direct pharmacological interaction effects (disturbances that are characteristic of serotonin syndrome) and individual susceptibility.

Even severe acute poisonings with ethyl alcohol rarely need admitting to the hospital or do not require long hospitalization. In our series of 5 patients which had to be admitted for hospital treatment due to prolonged coma or complications like aspiration pneumonia, all had mildly to moderately elevated CK.

Underlying mechanisms of RM caused by ethyl alcohol include a combination of ischemia due to immobilization, or agitation and other movement disorders, hypokalemia, hypophosphatemia and direct myotoxicity. Different levels of
CK in RM due to acute ethyl alcohol intoxications can be found in data published \(^8\) and except for cases of heavy ethyl alcohol abuses with coma, muscular swelling, myoglobinuria and ARF, there are also reports on chronic alcoholics with a high level of CK \(^9\) not connected with compression and ischemia.

RM is not rare in acute pesticide poisonings \(^1\). We noted elevated CK in 38% of the patients admitted due to pesticide ingestion. Acute poisonings with OPI were most frequent in our patients. Their manifestations include coma and/or convulsions as a central toxic phenomena. OPI also lead to disturbances in the neuromuscular junction, causing muscle fasciculation and fibrillation, which is another cause of RM in poisoning with these substances. However, only a few cases of OPI poisoning complicated by severe RM have been reported \(^2\). We noted mild RM in one patient with paraquat poisoning and moderate RM in paraquat and dinitro-orthocresol poisonings, per one patient each. In addition to the effects on the kidney, liver, adrenal, and, in the case of paraquat, the subsequent effects on the lungs, dipyridyl compounds paraquat and diquat lead to local caustic action on the exposed skin and mucous membranes. However, Park et al. \(^3\) reported that among 1,420 patients with acute paraquat intoxication, none had rhabdomyolysis. Dinitrophenol ingestion leads to disruption of the process of oxidative metabolism and overproduction of heat to which the CNS is particularly sensitive. For this reasons, tonic-clonic convulsions and coma quickly perform as severe poisoning manifestations \(^4\).

We noticed elevated CK, mainly of mild level, in acute poisonings with corrosive substances. This is probably due to the releasing of this enzyme from the damaged muscle of the digestive tract, and restlessness of these patients.

In this study, mild to moderate elevation of CK was recorded in 5/28 patients with clinical picture of poisoning by hepatotoxic mushrooms, probably *Amanita phalloides*. Some humans edible wild mushrooms like *Russula subnigricans* can cause severe RM due to mycotoxin effects \(^5\). Mushrooms *Tricholoma equestre* or *Tricholoma flavovirens* can cause RM, even with fatal outcomes \(^6\). *Amanita phalloides* is not reported to be myotoxic, so elevation of CK in blood may be due to co-ingestion of other mushrooms or the consequence of severe clinical disturbances including hypotension and prolonged inactivity.

RM due to carbon monoxide poisoning is not reported frequently \(^7\) though hypoxia causes cerebral and muscle metabolism disorders, manifesting as coma and convulsions in severe cases. In addition to myocardial necrosis, a manifestation of poisoning is necrosis of skeletal muscle. One patient from our series had mildly elevated CK, with MB fraction within normal value.

Burns and heat stroke are known physical factors that induce RM \(^8\). Because of their thermal effect, fumes in fire lead to burn of the upper respiratory tract mucosa, and therefore may cause RM, like in our patients. In such cases, one should bear in mind an increased muscle activity of the participants in fire.

**Conclusion**

In this study, RM occurred at a relatively high incidence in acute poisonings – in even 19% of all the cases. The majority of the patients had mild or moderate RM, while severe RM occurred in only 0.6% of the total number of patients. Psychotropic drugs were the most frequent causative agents of poisoning, and therefore of RM. Among the prescription drugs, we noticed the highest incidence and severity of RM in poisoning with neuroleptics. Though limited by a small number of patients, the results of this study show the highest frequency of RM in opiate (heroin) and OPI poisonings. Although agent’s toxicity is crucial for the outcome, severe RM and its complications may significantly influence the clinical course and prognosis of poisoning. Routine analysis of CK, which is a relevant marker for RM, may indicate the development of RM in acute poisoning and initiate prompt therapeutic measures for preventing ARF as the most frequent consequence of extensive RM.

**REFERENCES**


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33. Shen CH, Hung CJ, Wu CC, Huang HW, Ho WM. Rhabdomyolysis-induced acute renal failure after morphine over-