Human & Experimental Toxicology
http://het.sagepub.com/

H-FABP in cases of carbon monoxide intoxication admitted to the emergency room

Ayça Açikalin, Salim Satar, Ahmet Sebe, Ataman Köse and Onur Akpinar

Hum Exp Toxicol 2011 30: 443 originally published online 12 November 2010
DOI: 10.1177/0960327110389836

The online version of this article can be found at:
http://het.sagepub.com/content/30/6/443

Published by:
SAGE
http://www.sagepublications.com

Additional services and information for *Human & Experimental Toxicology* can be found at:

Email Alerts: http://het.sagepub.com/cgi/alerts

Subscriptions: http://het.sagepub.com/subscriptions

Reprints: http://www.sagepub.com/journalsReprints.nav

Permissions: http://www.sagepub.com/journalsPermissions.nav

Citations: http://het.sagepub.com/content/30/6/443.refs.html

>> Version of Record - May 19, 2011

OnlineFirst Version of Record - Nov 12, 2010

What is This?

Downloaded from het.sagepub.com at Uludag Univ Rektorlugu on April 19, 2012

HET

Human and Experimental Toxicology
30(6) 443–447
© The Author(s) 2010
Reprints and permission:
sagepub.co.uk/journalsPermissions.nav
DOI: 10.1177/0960327110389836
het.sagepub.com
SAGE

H-FABP in cases of carbon monoxide intoxication admitted to the emergency room

Ayça Açıkalın[1], Salim Satar[2], Ahmet Sebe[2], Ataman Köse[1] and Onur Akpınar[3]

Abstract

Introduction: Carbon monoxide (CO) intoxication causes cardiovascular problems as a result of diffuse tissue hypoxia. Cardiac biochemical markers and electrocardiographic changes have been reported in CO intoxications. Human fatty acid-binding protein (H-FABP) has been recently used as a reliable marker in identifying early cardiac damage. In this prospective study, we aimed to investigate the advantages of the use of H-FABP, in evaluating the findings of myocardial ischemia in patients with CO intoxication in our region. Methods: Twenty four successive patients admitted to the emergency department with acute CO intoxication were included in our study. Serum traditional markers and H-FABP were also taken in the earliest period for evaluation of cardiac damage. Results: The creatinine kinase MB (CKMB) levels were positive in 11 of the patients; however, H-FABP and troponin T levels were positive in only 3 of them. One of these subjects had elevated level of H-FABP in the short-term and increasing troponin T level increasing level of troponin T during the follow-up period. Conclusion: The obtained data supports the use of H-FABP, a specific indicator in identifying the cardiotoxicity of CO intoxications at an early phase.

Keywords

H-FABP, CO intoxication

Introduction

Carbon monoxide (CO) intoxication, commonly observed in our region, particularly during winter months, is a type of poisoning with serious mortality and morbidity. Since CO is an odorless, colorless, tasteless, and nonirritating gas, patients often do not notice that they are poisoned.[1] CO intoxication leads to a serious decline in tissue oxygenation by decreasing the oxygen carrying-capacity of the blood. As a result of diffuse tissue hypoxia, cardiovascular problems can be seen. It is well-known that the presence of cardiac toxicity in CO poisoning increases short- and long-term mortality.[2] Consequently, it is important to diagnose cardiac involvement rapidly in these patients.

In severe CO intoxications, an increase in cardiac biochemical indicators in blood (creatinine kinase MB [CKMB], troponin I and T, myoglobin) and electrocardiographic (ECG) changes have been reported.[3-5] Human fatty acid-binding protein (H-FABP) is a cytosolic protein abundantly present in myocardial tissue. With small molecular weight, it plays a role in intracellular fatty acid transport.[6] This protein has been recently used as a new marker since it is identifiable in serum by myocardial cell destruction. It is more specific than myoglobin and it can be identified earlier than CKMB and troponins in acute coronary syndromes.[7-10]

In our prospective study, we aimed to investigate the advantages of the use of H-FABP in evaluating the

[1] Department of Emergency Medicine, 25 Aralık Government Hospital, Gaziantep, Turkey
[2] Department of Emergency Medicine, Çukurova University, Adana, Turkey
[3] Department of Cardiology, 25 Aralık Government Hospital, Gaziantep, Turkey

Corresponding author:
Ayça Açikalın, Department of Emergency Medicine, Gaziantep 25 Aralık Hospital, Gaziantep, Turkey
Email: aycaacikalin@yahoo.com

Downloaded from het.sagepub.com at Uludag Univ Rektorlugu on April 19, 2012

findings of myocardial ischemia in patients admitted to the emergency department with medium and severe CO intoxications in our region.

Materials and methods

Twenty-four successive patients admitted to the emergency department with acute CO intoxication were included in our prospective study. Detailed histories were taken from all patients; their physical examinations were performed; and their blood pressures and heart rates were recorded. In the earliest period, serum samples were also taken for creatinine kinase (CK), CKMB, troponin T, H-FABP, and other biochemical examinations. Twelve-derivation ECG was obtained from all patients. Glasgow coma scale (GCS) was calculated for all patients.

Patients were excluded if they had mild CO intoxications, serum creatinine >3 mg/dL, acute transient ischemia, infections, malignancy, acute myocardial infarction, unstable angina pectoris, or acute myocarditis in the last 3 months.

The clinical state of all patients was determined by using poisoning severity index.[11] Accordingly, mild CO intoxication patients, who had minimally headache and vomiting were excluded. Additionally, the patients who had persistent headache, vomiting, and presyncope were described to be moderate CO intoxication and the patients who had cardiotoxicity and neurotoxicity were described to be severe CO intoxication.

All the patients were conventionally treated using high-flow normobaric oxygen and were monitored under intensive care conditions. We were unable to use hyperbaric oxygen therapy due to lack of centre. Consciousness was noted to have improved in all patients and those patients who were discharged with appropriate prescriptions.

Laboratory

CK, CK-MB, troponin T, and H-FABP levels were assessed. CK and CKMB activity in serum was measured by the Olympus Chemistry Analyzer AU640. Point of Care Testing (POCT) systems were used for troponin T assessments and CardioDetect® combi, cardiac infarction test (Rennesens GmbH, Germany) were used for H-FABP assessments. Serum CK-MB $\geq$25 IU/L and troponin T $\geq$0.1 ng/mL were considered as positive. The rapid H-FABP test was calibrated to detect a serum H-FABP concentration of >6.2 ng/mL as a positive line.[12-16]

Statistical analysis

Statistical analysis was performed with SPSS for Windows software program version 13.0 (SPSS, Inc, Chicago, Illinois, USA). All values were expressed as mean $\pm$ SD.

Results

Thirty-seven consecutive patients admitted to emergency department of our hospital with acute CO intoxication between March 2008 and November 2008 participated in the study. The clinical state of all patients was determined by recording their vitals and through local and systemic findings and laboratory results. Thirteen patients, who had mild intoxication, were excluded. Additionally, patients who had a pre-existing neurological disease who were unwilling to participate in the study were excluded.

After excluding these patients, 24 patients, within the age range of 11−86 years (mean 38.5 $\pm$ 20.4 years), who met our study criteria were enrolled. Nine (37.5%) of the patients were male and 15 (62.5%) were female. There was temporary unconsciousness in 14 of the patients and 6 were observed to have Glasgow coma score (GCSs) of 13 or less. Of the patients, five had hypertension, three had DM (diabetes mellitus), and one had chronic obstructive lung disease (COLD). Three of the patients were pregnant. Demographic data, ECG, and laboratory findings of all the patients were displayed in Table 1.

Blood pressure of the patients on arrival was within normal limits (mean 111.5 $\pm$ 20.8/70.0 $\pm$ 13.9 mmHg); however, generally high heart rates were observed (mean 97.3 $\pm$ 19.4 beats/min). An examination of the ECGs of the patients revealed that five patients had ST-segment depression, two had atrial fibrillation, one had right bundle-branch block, and another one had frequent ventricular extrasystole (VES). Serious prolongation of QT interval was not observed in any of the patients. Ten had sinus tachycardia.

Creatinine kinase MB level was positive in 11 of the patients; however, H-FABP levels were positive in only three of them. In these three patients, two patients had positive troponin T levels in the short-term, in the follow-ups third patient's troponin T level increased (Table 1).

Discussion

CO competes with oxygen in tissues and it decreases tissue oxygenation by binding to hemoglobin. As a

Downloaded from het.sagepub.com at Uludag Univ Rektorlugu on April 19, 2012

Table 1. Demographic data, ECG, and laboratory findings of all the patients

No	Age	Sex	BP	Pulse	GCS	Other	Notes	ECG	QT	CK	CKMB	HFABP	Tr T
1	46	F	140 / 80	92	15	–	–	Normal	421	70	20	0	0
2	26	F	100 / 60	104	10	–	Pregnant	Normal	409	53	28	0	0
3	50	M	110 /60	130	7	COPD	–	Normal	388	88	16	0	0
4	67	F	130 / 90	118	13	DM, HT	–	ST depression	410	344	66	26	0.9
5	52	F	120 / 80	89	14	–	–	Normal	386	53	27	0	0
6	23	F	90 / 60	102	14	–	Pregnant	ST depression	411	74	14	0	0
7	23	M	120 /80	78	15	–	–	Normal	426	169	70	0	0
8	17	F	90 / 60	94	15	–	–	Normal	398	60	12	0	0
9	86	M	130 / 90	136	13	DM, HT	–	AF+ ST depression	–	140	46	9.6	3.4
10	68	F	130 /80	100	13	DM, HT	–	ST depression	412	71	32	100.0	0.7
11	22	M	100 / 60	100	14	–	–	Normal	390	140	32	0	0
12	23	F	80 / 50	106	15	–	–	Normal	388	114	43	0	0
13	21	F	90 / 60	93	15	–	–	Normal	379	74	16	0	0
14	59	F	140 / 80	81	14	HT	–	ST depression	384	125	20	0	0
15	31	F	110 / 60	63	15	–	–	Normal	418	70	11	0	0
16	49	M	130 / 85	61	15	–	–	Normal	412	106	16	0	0
17	15	M	85 / 50	114	14	–	–	Normal	408	146	21	0	0
18	27	F	90 / 60	90	14	–	Pregnant	Normal	400	87	35	0	0
19	41	M	130 / 80	91	14	–	–	VES	412	223	16	0	0
20	11	F	80 / 50	109	13	–	–	Normal	412	188	58	2.1	0
21	43	F	120 / 80	123	14	–	–	AF	389	35	25	0	0
22	29	F	110 / 70	65	15	–	–	Normal	408	47	13	0	0
23	25	M	100 / 60	96	15	–	–	RBBB	391	40	17	0	0
24	70	M	150 / 95	100	15	HT	–	Normal	410	45	12	0	0

Abbreviations: BP: blood pressure, GCS: Glasgow coma scale, ECG: electrocardiography, QT: QT interval (ms), CK: creatinine kinase, CKMB: creatinine kinase MB, HFABP: human fatty acid-binding protein, Tr T: troponin T, M: male, F: female, COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus, HT: hypertension, AF: atrial fibrilation, VES: ventricular extra systole, RBBB: right bundle-branch block.

result, tissue hypoxia-related symptoms occur in CO intoxications.[17,18] Common symptoms due to intoxication include headaches, nausea, vomiting, slumber, and weakness, which may lead to neurological symptoms varying from confusion to coma. If loss of consciousness, syncope, confusion, focal neurological changes, myocardial ischemia, hypertension, and acidosis are detected in a patient with CO toxicity, it should be evaluated as a serious CO intoxicant.[10] Increased carboxyhemoglobin levels during intoxication have been reported to yield inconsistent results in determining the intensity of intoxication.[19,20]

In addition to the central nervous system, the cardiovascular system is also seriously affected by CO intoxication. Hemoglobin will bind with CO 200 times more avidly than with oxygen, leading to hypoxia. Furthermore, it is known to have direct toxicity on myocardial mitochondria. Along with various rhythmic disorders such as sinus tachycardia, atrial fibrillation, and ventricular extrasystoles, it can also lead to ST segment and electrocardiographic T-wave changes.[14] In our study, ST-segment depression was observed in five patients, new atrial fibrillation in two patients, and frequent VES in one patient.

CO intoxication-related myocardial infarction, cardiogenic shock, and cases of death have been reported in the literature.[19-22] Henry et al.[23] have reported increased short- and long-term mortality rates of CO intoxications with acute coronary syndromes. Thus, early identification of findings of myocardial ischemia is highly important. The presence of myocardial ischemia without symptoms is diagnosed by observed ECG variations or increase of cardiac markers. Creatinine kinase and CKMB are biochemical indicators that can be affected by various factors. Since CKMB is present in skeletal muscle, brain, prostate, uterus, and small intestine tissue in addition to myocardium, it may be affected by the dysfunction of these organs.[3,19,20] In our study, ten of the patients had positive CKMB values, while there were only three patients with H-FABP values increasing along with CKMB values. This high incidence of positive CKMB suggests that it may originate from hypoxia

Downloaded from het.sagepub.com at Uludag Univ Rektorlugu on April 19, 2012

Because of high incidences of positive CKMB levels, they may originated from hypoxia present in all tissues.[3,20] These findings were also demonstrated in a study performed by Aslan et al.[20] Another study by Davutoglu et al. showed that level of NT-proBNP was found as a better marker for early detection of cardiotoxicity by CO intoxication compared to conventional methods (ECG, Echo, CK, and CKMB).[24]

Human fatty acid-binding protein, a cytosolic protein found in large amounts in the myocardium, plays a role in intracellular transport of fatty acid.[6] Human fatty acid-binding protein is rapidly released into the circulation when the myocardium is injured. It starts to increase in 1.5 hours in the plasma, reaches a peak in 5–6 hours, and starts declining in the 24th hour. H-FABP is a new and valuable diagnostic instrument in identifying patients with myocardial injury, it is more specific for myocardium than myoglobulin and it increases in ischemia in the early phase like myoglobulin.[7-10]

As far as is known, some patients with CO intoxication cannot describe chest pain upon arrival at the hospital due to their problems about their altered levels of consciousness. Thus, indicators pointing to cardiac involvement are significant. In our study, H-FABP levels of three patients were observed to be positive at the early phase when they applied to the emergency clinic. However, troponin T was positive in two patients at the same time. During the second-hour follow-up of the patient with positive H-FABP and negative troponin, troponin T level increased. Traditional methods were shown to yield misleading negative results at an early phase. Consequently, the H-FABP examination used in our clinic was determined to be useful in identifying cardiac involvement in CO intoxications.

It is well-known that in pregnant women exposed to CO intoxication, the fetus is much more sensitive to CO gas and has exposure to intoxication over a longer period of time. It has been reported that fetus returns to its normal state approximately 40 hours later than the mother does.[25,26] Severe CO intoxication-related stillborn baby with sequel of cerebral palsy has been reported in the literature.[27] This is caused by higher fetal hemoglobin affinity of CO. Our study included three pregnant patients, one of whom was 26 weeks pregnant and she had serious toxicity. The fetus was alive in the fetal ultrasonography performed upon her admittance to the clinic and during discharge. In the two other pregnant women with slight toxicity, the fetuses were seen to be alive in the fetal ultrasonographies performed before discharge. Both H-FABP and other cardiac enzymes of these patients were within the normal limits.

Study limitation

Our study has some limitations. (1) The small sample size may be regarded as a limitation. (2) Since we did not follow up our study groups, we cannot provide any information on mortality and morbidity. (3) If the carboxyhemoglobin levels of the patients had been investigated, it would be better.

Conclusion

The obtained data supports the use of H-FABP, a specific indicator in identifying the cardiotoxicity of CO intoxications at an early phase. In elderly patients with systemic diseases such as diabetes mellitus and hypertension, findings of cardiac toxicity are more commonly observed. Positive H-FABP values obtained to identify cardiotoxicity should be supported by other cardiac enzymes during the follow-up and these patients should be followed and treated more carefully since cardiotoxicity increases mortality.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not for-profit sectors.

References

1. Handa PK and Tai DYH. Carbon monoxide poisoning: a five–year review at Tan Tock Seng Hospital, Singapore. *Ann Acad Med Singapor* 2005; 34: 611–614.
2. Satran D, Christopher R, Cheryl A, Caren IN, Yiscah B, and Timothy D. Cardiovascular manifestations of moderate to severe carbon monoxide poisoning. *JACC* 2005; 45: 1513–1516.
3. Fiorista F, Casazza F, and Comolatti G. Silent myocardial infarction after acute exposure to carbon monoxide. *G Ital Cardiol* 1993; 23: 583–587.
4. Gandini C, Castoldi AF, Candura SM, Priori S, Locatelli C, Butera R, et al. Cardiac damage in pediatric carbon monoxide poisoning. *Clin Toxicol* 2001; 39: 45–51.
5. Aslan Ş, Erol MK, Karcıoğlu Ö, Meral M, Çakır Z, and Katırci Y. Karbonmonoksit zehirlenmeli hastalarda iskemik miyokardiyal hasarın araştırılması. *Anadolu Kardiyol Derg* 2005; 5: 189–193.
6. Paulussen RJ, van Moerkerk HT, and Veerkamp JH. Immunochemical quantitation of fatty acid-binding proteins. Tissue distribution of liver and heart FABP

Downloaded from het.sagepub.com at Uludag Univ Rektorlugu on April 19, 2012

types in human and porcine tissues. *Int J Biochem* 1990; 22: 393–398.
7. Ishii J, Ozaki Y, Lu J, Kitagawa F, Kuno T, Nakano T, et al. Prognostic value of serum concentration of heart-type fatty acid–binding protein relative to cardiac Troponin T on admission in the early hours of acute coronary syndrome. *Clinical Chem* 2005; 51: 1397–1404.
8. Alhadi A and Fox KA. Do we need additional markers of myosite necrosis: the potential value of heat fatty acid binding protein. *QJ Med* 2004; 97: 187–198.
9. Suzuki M, Hori S, Noma S, and Kobayashi K. Prognostic value of a qualitative test for heart-type fatty acid-binding protein in patients with acute coronary syndrome. *Int Heart J* 2005; 46: 601–606.
10. Nakata T, Hashimoto A, Hase M, Tsuchihashi K, and Shimamoto K. Human heart-type fatty acid-binding protein as an early diagnostic and prognostic marker in acute coronary syndrome. *Cardiology* 2003; 99: 96–104.
11. Ellenhorn JM, Schonwald S, Ordog G, Wasserberger J. Respiratory toxicology. Carbon monoxide. Ellenhorn's Medical Toxicology, 2nd ed. Baltimore: Williams & Wilkins, 1997, p. 1465–1476.
12. Seino Y, Ogata K, Takano T, Ishii J, Hishida H, Morita H, et al. Use of a whole blood rapid panel test for heart-type fatty acid-binding protein in patients with acute chest pain: Comparison with rapid troponin T and myoglobin tests. *Am J Med* 2003; 115: 185–190.
13. Watanabe T, Ohkubo Y, Matsuoka H, Kimura H, Sakai Y, Ohkaru Y, et al. Development of a single whole blood panel test for detection of human heart-type fatty acid-binding protein. *Clin Biochem* 2001; 34: 257–263.
14. Tanaka T, Hirota Y, Sohmiya K, Nishimura S, Kawamura K. Serum and urinary human heart fatty acid-binding protein in acute myocardial infarction. *Clin Biochem* 1991; 24: 195–201.
15. Tsuji R, Tanaka T, Sohmiya K, Hirota Y, Yoshimoto K, Kinoshita K, et al. Human heart-type cytoplasmic fatty acid-binding protein in serum and urine during hyperacute myocardial infarction. *Int J Cardiol* 1993; 41: 209–217.
16. Ohkaru Y, Asayama K, Ishii H, Nishimura S, Sunahara N, Tanaka T, et al. Development of a sandwich enzyme-linked immunosorbent assay for the determination of human heart-type fatty acid-binding protein in plasma and urine by using two different monoclonal antibodies specific for human heart-type fatty acid-binding protein. *J Immunol Methods* 1995; 178: 99–111.
17. Tintinalli, JE, Kelen, GD, Stapcyzynski, SJ. Carbon monoxide poisoning. Emergency Medicine: A Comprehensive Study Guide. 5th ed. North Carolina: McGraw-Hill, 2000, p. 1302–1306.
18. Choi IS. Carbon monoxide poisoning: systemic manifestations and complications. *J Korean Med Sci* 2001; 16: 253–261.
19. Gorman DF and Runciman WB. Carbon monoxide poisoning. *Anaesth Intensive Care* 1991; 19: 506–511.
20. Aslan S, Uzkeser M, Seven B, Gundoğdu F, and Acemoğlu H. The evaluation of myocardial damage in 83 young adults with carbon monoxide poisoning in the East Anatolia region in Turkey. *Human Exp Toxicol* 2006; 25: 439–446.
21. Gandini C, Castoldi A, and Candura MS. Carbon monoxide cardiotoxicity. *Clinical Toxicol* 2001; 39: 35–44.
22. Nunez M. Miyocardial Infarction with normal coronary arteries after acute exposure to carbon monoxide. *Chest* 1990; 97: 491–494.
23. Henry CR, Satran D, Lindgren B, Adkinson C, Nicholson CI, and Henry TD. Myocardial injury and long-term mortality following moderate to severe carbon monoxide poisoning. *JAMA* 2006; 295: 398–402.
24. Davutoglu V, Gunay N, Kocoglu H, Gunay NE, Yildirim C, Cavdar M, et al. Serum levels of NT-ProBNP as an early cardiac marker of carbon monoxide poisoning. *Inhal Toxicol* 2006; 18: 155–158.
25. Greingor JL, Tosi JM, Ruhlmann S, and Aussedat M. Acute carbon monoxide intoxication during pregnancy. One case report and review of the literature. *Emerg Med J* 2001; 18: 399–401.
26. Hutter CD and Blair MD. Carbon monoxide–does fetal exposure cause sudden infant death syndrome? *Med Hypotheses* 1996; 46: 1–4.
27. Alehan F, Erol I, Onay OS. Cerebral palsy due to nonlethal maternal carbon monoxide intoxication. *Birth Defects Res A Clin Mol Teratol* 2007; 79: 614–616.

Downloaded from het.sagepub.com at Uludag Univ Rektorlugu on April 19, 2012