Radiation Exposure Levels in Family Members of Omani Patients with Thyrotoxicosis Treated with Radioiodine (131I) as Outpatients

Ibtisaam Al-Maskery and Haddia Bererhi

ADVANCES IN KNOWLEDGE
1. This study show that, with good radiation safety instructions to patients and relatives, thyrotoxic patients may be treated as outpatients provided the patient is physically and mentally fit to comply with the given instructions and that factors such as travelling distance, socio-economic conditions and family lifestyle are taken into account.

APPLICATION TO PATIENT CARE
Treating thyrotoxic patients, receiving radioiodine therapy, as outpatients will:
1. Avoid the isolation of these patients with all of its complications. Patients will be more comfortable in their own surroundings with their families.
2. Outpatient treatment will reduce waiting lists allowing greater patient throughput. This will lead to greater patient comfort and satisfaction.

Department of Radiology and Molecular Imaging, College of Medicine & Health Sciences, Sultan Qaboos University, Muscat, Sultanate of Oman

*To whom correspondence should be addressed. Email: imaskery@squ.edu.om
Radioiodine therapy, proven to be safe and relatively inexpensive, has been widely used over decades for the treatment of thyrotoxicosis.\(^1,2\) However, there are some radiation protection concerns associated with the treatment. In addition to beta particle emissions, \(^{131}\)I emits penetrating ionizing \(\gamma\)-radiation of 364keV. The therapeutic administration of \(^{131}\)I makes the patient a source of radiation exposure and a potential radiation hazard to individuals in their surroundings.\(^1,2\) Radiation doses received by the public and family members are received through internal contamination as a result of excreted radioiodine or through external exposure which remains the main concern.\(^3,4\) To protect relatives from these radiation exposures, patients are admitted in radioiodine therapy wards for different lengths of time according to local regulations.

Nowadays, most countries treat thyrotoxic patients as outpatients. This is done provided they are given appropriate radiation safety instructions to limit the radiation exposures to their family members, particularly to children and pregnant women and the public, to 1.0mSv per year as recommended by the International Commission of Radiological Protection (ICRP).\(^5\) However, higher radiation doses received by adult family members are acceptable as long as the average dose of five consecutive years does not exceed 5mSv.\(^5\) These limits are also implemented in Oman. The criteria for treating these patients as outpatients are based on the following conditions: a) administered activity should be less than 800MBq (±10%),\(^6,7\) and b) the dose rate should be less than 40\(\mu\)Sv/h at a distance of one meter away from the patient.\(^7\) Unless the above is achieved, to comply with the radiation limits to family members and the public, hospitalisation of patients is necessary.

The advantage of treating these patients as outpatients is that it reduces the burden on the health care systems including treatment expense and waiting list length, with the added benefit of patient comfort and satisfaction. This study was conducted as a follow up study to that of Bererhi and Constable\(^9\) to test thyrotoxic patients as outpatients after radioiodine therapy.

## Methods

Eighty-six family members of 22 self-dependent thyrotoxic patients, treated with \(^{131}\)I as outpatients, participated in this study which was conducted between February 2007 and March 2008. All patients agreed to participate in this study. Patients and family members were monitored for radiation exposure for 10 days using thermoluminescent dosimeters (TLDs). This period was selected as the highest radiation exposure falls within these days. The mean age of the family members was 26.6 years (range 17 months - 75 years) and included 29 children ≤ 16 yrs and 57 adults (11 spouses and 8 parents). Radiation dose rates at one meter from patients were measured following the administration of \(^{131}\)I using a portable calibrated dose rate meter (type PDR1).

Written and verbal local radiation safety instructions [Table 1] were provided to all patients prior to discharge. Patients and their accompanying relatives wore their dosimeters before leaving the hospital. On their journey back home, patients were advised to sit in the back of the car on the opposite side from the driver to keep the distance between them at a maximum.

The selection criteria were based on the following: a) patient and family members had to consent to wearing the dosimeter at all times for 10 days starting from the day the patient returned home; b) patient and family members had to live together in the same house during the whole period the dosimeter was worn. Some patients were called randomly to confirm that they were fulfilling the above criteria.

Thermoluminescent dosimeters (TLD), TLD 200 rods, (6mm x 1mm diameter) made of CaF\(_2\):Dy were used in this study. A Harshow 5500 TLD reader was used to read the TLDs [Figure 1]. The rods were carefully handled with a vacuum tweezer and stored on a numbered plate in order to keep...
track of the individual dosimeters. The dosimeters were annealed at 320°C for 1 min. in a TLD-Oven to clear them from any residual absorbed doses. For individual TLD calibration, all TLDs were irradiated to a dose of 1.0mGy using a 90Sr Irradiator 2000. From the resultant TLD readings, the mean reading was calculated. The ratio of the individual and mean reading was taken to represent a calibration factor known as element correction coefficient (ECC) to compensate for variations in geometry and sensitivity among dosimeters. The reader was calibrated to produce consistent and accurate readings in dosimetrically meaningful units (µGy) by applying a reader calibration factor (RCF).10

For every subject, three rods were inserted into a flexible black tube made of silicon rubber with one sealed end. The open end was sealed with a removable plug of black rubber. The tube was then put into a watertight painted capsule, with a screw-in end piece, and a cord was threaded into two holes at the extremities of the capsule, designed in such a way that, once the cord was in place, the capsule could not be opened. The lengths of the cord were adjusted to bring the capsule to the level of the supra-sternal notch [Figure 2]. The capsules were placed in individually labelled lead pots, which were then fitted into a wooden box [Figure 3] together with a dosimeter for background measurement. The patients were asked to keep the background dosimeter in a place remote from general living activities. After the TLDs were returned, they were preheated in the TLD oven at 100°C for 20 minutes then read out in the TLD reader using a time-temperature profile of 200°C for 100s, 400°C for 300s and 400°C for 200s for preheating, acquisition and annealing, respectively. The average doses from the three TLD rods of each member were recorded after background subtraction.

Results

In compliance with the European Commission (EC) guidelines7 regarding radioiodine therapy patient discharge, our patients left the hospital with mean (±SD) administered doses of 609.8 ±79MBq in the range 520-862MBq and mean radiation exposure dose levels of 23.4 ±6.3µSv/h in the range 13 to 42µSv/h, at one meter from the patient. The cumulative radiation doses (µSv) over 10 days received by the family members are shown in Table 2. All family members, including spouses, received less than the annual dose limit of 1mSv except for four out of 29 children (14%), aged 19 months and 12, 13, 15 years, who received radiation doses of 2.9, 1.2, 1.2 and 1.2 mSv, respectively [Figure 4]. The 19 month-old infant’s mother was treated with 555MBq of 131I and her radiation level at one meter, when leaving the hospital, was 13µSv /h. The 12 and 15 year old children were the younger sisters of a patient who was treated with 585MBq of 131I and her radiation level at one meter, when leaving the hospital, was 13µSv /h. The 12 and 15 year old children were the younger sisters of a patient who was treated with 585MBq of 131I and her radiation level at one meter, when leaving the hospital, was 26µSv/h. The 13 year old child’s mother was treated with 566MBq of 131I and her radiation level at one meter, when leaving the hospital, was 19µSv/h.

Discussion

Although the release criteria limit in this study were less stringent than the recommended limits in some developing countries, where literacy and socio-economical factors were taken into account, such as in India (patient retained activity at discharge ≤ 600 MBq, or dose rate level of 30 µSv/
hr at 1 meter from patient)\textsuperscript{11} and Pakistan (patient retained activity at discharge < 370 MBq, or dose rate level of ∼ 10 µSv/h. at 1 meter from patient).\textsuperscript{12} 95% of family members in this study received radiation dose levels lower than the annual limit of 1mSv [Figure 4]. This proves that the radiation safety instructions given and explained to patients and family members were understood and taken seriously by both patients and family members. The remaining family members who received doses higher than the annual radiation dose limit were children. These doses were received due to socio-economic conditions, i.e. children belonged to homes where they were no person other than the mother to take care of them. This is seen in the case of the 19 month old child who was looked after only by the mother and slept with her in the same bed, although clear radiation safety instructions were given to the mother strictly to avoid contact with her child. However, it is common practice in Oman that mothers sleep with their infants in the same room and children are very much attached to their parents, making the situation difficult to avoid. Living conditions of some families, i.e. number of rooms in the house, was a factor that caused high radiation exposure to the other three children. The 23 year old patient lived in a house with only two rooms and slept with four other family members in the same bedroom exposing her younger sisters aged 12 and 15 years-old to a radiation dose higher than the annual dose limit. The 13 year old girl lived in a house with three rooms and slept in the same bedroom with her mother who received the therapy.

The mean cumulative radiation doses received by spouses of this study was lower than the mean cumulative radiation doses received by spouses in Bererhi and Constable’s\textsuperscript{9} study in 2000. These results were obtained taking into account that the retained mean body activity in our patients when leaving the hospital was about 20 times (609.8 versus 30MBq) more than that reported by Bererhi and Constable\textsuperscript{9}, and the time the dosimeters were worn in our study was longer than in Bererhi and Constable’s study\textsuperscript{9} (10 days versus 7 days). Our outpatients were also strictly advised to sleep separately from their spouses for a period of three weeks post-therapy whereas spouses in Bererhi and Constable’s study slept in the same bed. In the study by Monsieurs et al.,\textsuperscript{13} recommendations for spouses of thyrotoxic patients treated with radioiodine was to sleep separately for a duration of 21 days in order to comply with the annual dose limit of 1mSv. In our study, using the same instructions, the same results were achieved indicating good compliance with the radiation safety instructions given.

### Conclusion

In our institution, thyrotoxic patients treated with radioiodine are hospitalised for a few days. The results of this study show that with good radiation safety instructions to patients and relatives, thyrotoxic patients may be treated as outpatients provided the patient is physically and mentally fit enough to comply with the given instructions. However, the decision of releasing these patients from the hospital should be based on several factors including travelling distance, socio-economic conditions and family life style.

We recommend that: 1) mothers with children below the age of 3 years should not be treated as outpatients unless arrangements can be made for their children to be looked after by someone else other than the mother for a few days as recommended elsewhere\textsuperscript{14}15 2) patients sharing the same room with many other family members should be hospitalised for a few days to avoid unnecessary
Radiation Exposure Levels in Family Members of Omani Patients with Thyrotoxicosis Treated with Radioiodine (131I) as Outpatients

Acknowledgements
The contents of this article were presented at the Annual Scientific Meeting of the Swiss Society of Radiobiology & Medical Physics in November 2008. The authors would like to thank the college of Medicine and Health Sciences and the Hospital at Sultan Qaboos University for supporting this work.

Conflict of Interest
The authors report with no conflict of interest.

References

Figure 4: Dot-plot showing the radiation doses received by family members in reference to annual dose limit. The mean radiation dose is shown in dotted line.

radiation exposure to others.

Effective dose (mSv)

Mean dose

1 mSv dose limit

Age (years)

0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85

0 0.5 1 1.5 2 2.5 3 3.5
The Impact of Chronic Liver Diseases on the Level of Heart-Type Fatty Acid-Binding Protein (H-FABP) Concentrations

Hafidh A Al-Hadi, Brent William, Keith A Fox

Abstract: Objectives: Heart-type fatty acid-binding protein (H-FABP) has been reported to be a potential novel biochemical marker for the early diagnosis of acute myocardial infarction (AMI). The presence of H-FABP in the liver has not been reported. The aim of this study was to compare the effect of chronic liver diseases on the level of H-FABP concentrations. Methods: The effects of chronic liver diseases including infective hepatitis and cirrhosis on the concentration of H-FABP was studied in a small group of patients (n=10, mean age ± SD = 58.33 ± 7.19 years). The serum concentrations of the following markers were measured: H-FABP, alanine aminotransferase (ALT) and bilirubin and compared with a reference control group (20 healthy blood donors, mean age ± SD = 63.8 ± 8.01 years). Results: The serum concentrations of these markers in the control group as compared to patients with chronic liver disease were as follows (mean ± SD): H-FABP = 6.86 ± 2.21 µg/L versus 6.44 ± 3.06 µg/L (p > 0.005), ALT = 29.8 ± 14.7 U/L versus ALT = 198.67 ± 122.89 U/L (p < 0.0005) and bilirubin = 9.6 ± 4.0 µmol/L versus bilirubin = 108.85 ± 87.85 µmol/L (p < 0.0001). Conclusion: These data illustrate clearly that there is no significant interference with the normal concentration of H-FABP in the presence of liver diseases, despite the significant elevation of liver enzymes and proteins. These data may support a useful role of H-FABP for the diagnosis of myocardial injury in patients with liver diseases.

Keywords: Heart-type fatty acid-binding protein (H-FABP); Chronic liver diseases; Bilirubin; Alanine aminotransferase.

Advances in Knowledge
1. Heart-type fatty acid-binding protein is a useful early marker for the diagnosis of acute myocardial infarction.
2. The effect of chronic liver diseases on the diagnostic potential of this marker is not known.
3. This article illustrates the lack of interferences of the various types of chronic liver diseases on the ability to use heart-type fatty acid-binding protein as an early cardiac marker for the early diagnosis of acute myocardial infarction.

Application to Patient Care
1. The information provided in this article will help health institutions caring for patients with acute myocardial infarction on how best to use, interpret and apply the results obtained with heart-type fatty acid-binding protein in patients presenting with acute chest pain suggestive of evolving acute myocardial infarction who also have various co-existing types of chronic liver diseases.

*To whom correspondence should be addressed. Email: halhadi@hotmail.com

1Department of Medicine, Sultan Qaboos University Hospital, Muscat, Sultanate of Oman. 2Department of Medical Sciences, Faculty of Medicine, University of Edinburgh, UK. 3University of Edinburgh, Cardiovascular Research Unit, Royal Infirmary of Edinburgh, UK.
Heart-type fatty acid binding-protein (H-FABP) is a small soluble non-enzyme protein composed of 132 amino acids. It is one of the most abundant proteins in the heart and comprises 5-15% of the total cytosolic protein pool. H-FABP exists in high concentrations in the heart; however, this protein is not totally cardiac specific and occurs in other tissues although in a much lesser concentrations. H-FABP was introduced by Glatz et al. in 1988 as a potential novel biochemical marker for the early diagnosis of acute myocardial infarction (AMI). This was soon confirmed in many other studies. Some of the more recent studies have questioned the value of these early markers (H-FABP and myoglobin) when compared with specific markers like cardiac troponin I (cTnI).

H-FABP is released into plasma within 2 hours after symptom onset and is reported to peak at about 4-6 hours and return to normal base line value in 20 hours. Within the period of 30-210 minutes after symptom onset, H-FABP has > 80% sensitivity for the diagnosis of AMI. Within the interval of 0-6 hours after symptom onset, the other cardiac markers such as creatine kinase (CK), CK-MB mass or activity, cTnI and T (cTnT) will only be starting to accumulate in the plasma, and their sensitivity has been reported to be around 64%.

The exact route(s) of excretion of H-FABP from the circulation is not fully understood. As suggested by previous studies, the kidney may be the major route of excretion of H-FABP from circulation. A rise in serum and urine H-FABP concentration above normal values is seen in patients who present with AMI as early as 1.5 hours after symptom onset. Studies in animals have also shown decreased myocardial tissue content and rising plasma and urine concentrations of H-FABP very early after coronary artery ligation. H-FABP circulates for a longer time (> 25 hours) after AMI in the presence of renal failure.

The presence of H-FABP in the liver has not been reported. However, an isoform specific to the liver called liver-type FABP exists. The interferences of this protein and chronic liver diseases on the concentration of H-FABP has not been studied before. Also, the effect of chronic liver diseases on the release of H-FABP from other tissues has not yet been fully evaluated. Therefore, the aim of the study was to compare the effect of chronic liver diseases on the serum levels of H-FABP.

Methods

The effects of disease states in particular chronic liver diseases on the normal concentration of H-FABP was studied in 2003-2004 a small group of patients with a mixture of chronic liver disorders (n=10, mean age ±SD = 58.33 ±7.19 years, range 45-70 years, median = 59 years) These patients had a range of conditions including infective hepatitis and cirrhosis (chronic hepatitis B = 2, chronic hepatitis C = 2, chronic alcoholic hepatitis = 3, other cirrhosis = 3). They were recruited from the Liver Unit at the Edinburgh Royal Infirmary, UK. Ethical approval was obtained from the local ethical committee (Lothian Research Ethics Committee, Edinburgh) and informed consent was obtained from each patient before beginning the study. The study complies with the Declaration of Helsinki. The serum concentrations of the following markers H-FABP, ALT and bilirubin were measured in the study group and compared with the concentrations of these markers in a normal reference control group of healthy blood donor controls (n=20, mean age ±SD = 63.8 ±8.01, range 53-75 years, median = 65 years). Peripheral blood samples for serum analysis were collected in white Starstedt Monovette vacutainer tubes by venepuncture. The blood samples (5mls) were taken through a peripheral line (intravascular access). The extracted samples were allowed to clot at room temperature for 1 hour and then centrifuged at 4°C, and the resulting serum was divided into small aliquots and frozen at -70°C until analysis. H-FABP was analysed by an enzyme linked immunosorbent assay method using commercially available assays (Hycult, Cambridge). Bilirubin and ALT were measured in the Biochemistry Department of the Edinburgh Royal Infirmary on an automated analyser machine using commercial assays.

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS™, Pittsburgh, Version 15). Continuous variables were presented as mean ± standard deviation. Comparisons between the study group and control group variables were conducted by the Mann-Whitney U test for continuous variables. Significant results were indicated by probability values less than or equal to 0.05.
Results

The analytical sensitivity of H-FABP assay (mean ± 2SD) was 0.206 ±0.047 g/L. The normal concentrations of these markers in the normal reference control group of healthy blood donor controls were as follows: H-FABP = 6.86 ±2.21 µg/L; ALT = 29.8 ±14.7 U/L and bilirubin = 9.6 ±4.0 µmol/L. The study group consisted of 10 patients. The concentration of these markers in patients with chronic liver diseases were as follows: H-FABP = 6.44 ±3.06 µg/L, (range 2-11 µg/L, median = 7 µg/L); ALT = 198.67 ±122.9 U/L, (range 73-500 U/L, median = 114 U/L) and bilirubin = 100.89 ±87.85 µmol/L, (range 17 - 337 µmol/L, median = 66 µmol/L). There was no significant difference between the concentration of H-FABP in the study group and controls; however, the concentrations of liver enzymes and protein (ALT and Bilirubin) were significantly elevated in the study group [Table 1].

Discussion

Under normal conditions H-FABP is present in plasma in very low concentrations (< 5 µg/L), but it is significantly elevated upon cellular injury. This makes the plasma estimation of H-FABP suitable for the early detection and quantification of myocardial tissue injury. However, this protein is not totally cardiac specific as it occurs in skeletal muscle in concentrations varying between 0.05-0.2 mg/g wet weight of tissue, depending on muscle fibre type studied. It has also been reported in very low concentrations in tissues like the kidney, aorta, testes, mammary glands, placenta, brain, adrenal glands, adipose tissue, and stomach. The concentration of H-FABP in the study group was not statistically different from the control group. This finding leads to several assumptions. First, the Liver-FABP (L-FABP) is a separate factor with no or negligible cross-reactivity with H-FABP assays. Indeed, the cross-reactivity between these two proteins has been reported to be < 0.005. Second, the release of H-FABP from other tissues containing this protein (see above) is at best minimal in patients who have chronic liver diseases. Our study was the first of its kind to address the interference of chronic liver diseases on the normal concentrations of H-FABP. There are no data on this issue in the literature hence it is difficult to correlate our findings.

In a previous study, we have shown major limitations for the use of H-FABP concentration for the diagnosis of myocardial injury in the presence of renal failure. The liver contains only L-FABP, but co-expression of H-FABP and L-FABP occurs in the kidney. Similarly, intestinal-type FABP (I-FABP) and L-FABP are found in intestines, and brain-type FABP (B-FABP) and H-FABP occur in the brain. Preliminary but promising applications of these proteins have been demonstrated for liver rejection, viability selection of kidneys from non-heart-beating donors (NHBD), inflammatory and ischaemic bowel disease, traumatic brain injury and in the prevention of muscle injury in trained athletes. Measurement of H-FABP in the first 24 hours after onset of symptoms may be potentially useful for the diagnosis of AMI; identification of patients who need reperfusion treatment early; identification of patients who reperfuse their infarct related artery; detection of re-infarction if it occurs early, and estimation of infarct size.

Conclusion

These data illustrate clearly that there is no significant interference with the normal concentration of H-FABP in the presence of chronic liver diseases, despite the significant elevation of liver enzymes and proteins. This is consistent with the reduced cross-reactivity between H-FABP and other FABP
including L-FABP. These findings may support a useful role of H-FABP for the diagnosis of myocardial injury in patients with chronic liver diseases.

**Source of Funding:**
The research was funded by a grant from the Cardiovascular Research Unit at the University of Edinburgh.

**Conflict of Interest:**
The authors report no conflict of interest.

**References**