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# Significance of Continuous Medical Education of General Practitioners about Common Diseases – Iron Deficiency Anemia

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## ABSTRACT

Three years long, prospective study was performed in order to evaluate a possible influence of continuing medical education of general practitioners on managing the patients with common diseases such as iron deficiency anemia (IDA). Altogether 1586 patients that were referred to Hematology Outpatient Clinic, University Hospital Center Rijeka, Croatia due to diagnosis of IDA were examined by clinical hematologist during the first visit and follow up period, were questioned by the means of questionnaire and complete laboratory analyzes were performed in order to: evaluate physical condition and laboratory findings, to assess duration of anemia, possible other specialists' consultation, iron supplementation therapy, and finally, determine the type of anemia present. Initial group of 983 patients was examined during one year period. Following the education campaign the same parameters were analyzed in comparable (final) group of 603 patients during next one year period. Following the education, the number of patients referred to Outpatient Clinic due to diagnosis of IDA was significantly decreased from 983 (61.97%) to 603 (38.02%) ( $p < 0.05$ ) as was the number of patients referred as having IDA but finally established to have a different type of anemia, from 661 (97.24%) to 149 (24.71%) ( $p < 0.001$ ). The number of patients started on iron supplementation therapy before establishing the type of anemia was significantly decreased from 543 (55.24%) to 76 (12.60%) ( $p < 0.001$ ) as well as duration of iron supplementation therapy administered in these cases ( $21 \pm 9.8$  vs.  $6 \pm 8.7$  weeks) ( $p < 0.001$ ). We have detected a significant decrease in: time necessary for definitive diagnosis ( $49 \pm 19.2$  vs.  $28 \pm 9.1$  weeks) ( $p < 0.001$ ), number of visits to other specialists ( $2.9 \pm 1.35$  vs.  $1.1 \pm 0.94$ ) ( $p < 0.05$ ), duration of anemia before treatment initialization ( $41 \pm 29.8$  vs.  $26 \pm 18.7$  weeks) ( $p < 0.001$ ). Average hemoglobin (Hg) level in patients referred to hematologist was significantly lower following education ( $98.9 \pm 15.5$  vs.  $82.6 \pm 14.2$ ) ( $p < 0.05$ ). Continuing medical education of primary care physicians has significant role in diagnosis and treatment of patients with IDA. Education programs result in benefits for the patients and physicians.

**Key words:** general practice, education, iron deficiency anemia

## Introduction

Iron deficiency anemia (IDA) is the most common form of anemia occurring in about 20% of women, 50% of pregnant women and 2–3% of men<sup>1,2</sup>. Iron deficiency results when iron demand by the body is not met by iron absorption from diet. Thus, IDA in patients presenting in primary care may result from inadequate dietary intake, impaired absorption or physiologic losses in a women of reproductive age. It also could result from occult blood loss<sup>1,2</sup>. Generally, IDA is not an end diagnosis, and requires complete work-up until the underlying cause is not discovered.

IDA is classically described as a microcytic anemia and differential diagnosis includes iron deficiency, thalassemia, sideroblastic anemias, some types of anemia of chronic disease, and lead poisoning<sup>2</sup>. Sideroblastic anemia could be easily distinguished due to almost complete saturation of the serum transferrin<sup>2</sup> while patients with lead poisoning display other symptoms resulting from lead accumulation. Differentiating between IDA and anemia of chronic disease could sometimes be difficult, especially when the two conditions coexist or in early iron deficiency.

The symptoms of anemia, such as dyspnea, weakness, tachycardia, depression, and most especially fatigue, can lead to a substantial reduction in functional ability and a decline in general health contributing to patient's feelings of diminished quality of life (QOL). IDA has been suggested to influence cognitive functions<sup>3</sup> and correction of anemia resulted in improvement of cognitive abilities. The level of improvement in cognitive functions depended on duration of anemia emphasizing the importance of early recognition and the treatment of iron deficiency anemia<sup>4–6</sup>.

IDA cannot be reliably diagnosed by clinical presentation and due to variable symptoms and these patients are often referred to different specialists. The most common reason to check hemoglobin in a primary care practice is fatigue<sup>7</sup>. The diagnosis of IDA requires laboratory confirmation of anemia and evidence of iron deficiency and can easily be established in most patients seen by their general practitioner using laboratory tests available to them.

Previous studies have shown that continuing medical education in a primary care practice could improve the outcomes of care delivery<sup>8,9</sup>. This prospective study was undertaken in order to analyze a possible influence of continuing medical education of general practitioners on managing the patients with common diseases such as IDA by analyzing: information obtained through detail anamnesis, clinical and laboratory findings in patients referred to hematologist with diagnosis of IDA. Complete laboratory and, if necessary, diagnostic work-up has been performed in patients referred as having IDA in order to determine a type of anemia present and possible underlying illness.

## Materials and Methods

### Patients

Altogether 1586 patients, 294 (18.54%) men and 1292 (81.46%) women, referred to Hematology Outpatient Clinic, University Hospital Center Rijeka, Rijeka, by their general practitioners as having IDA (irrespective of whether they really did have IDA, or were diagnosed previously or not by their general practitioner) were included in this three years prospective study during the period 2003–2006. All referred patients were examined by clinician hematologist during the first visit and follow up period, were questioned by the means of questionnaire and a complete laboratory analyzes were performed in order: to evaluate physical condition and laboratory findings, to assess duration of anemia, possible other specialists' consultation due to different symptoms, iron supplementation therapy, and finally to determine the type of anemia present, IDA or other. In all patients necessary, a complete diagnostic work-up was completed in order to confirm or exclude an underlying illness.

In the first step initial group of 983 patients (»initial group«) was examined during one year period. In the second step, during a one year period, the education campaign regarding the diagnosis and management of IDA

has been undertaken. Project staff used publications, lectures and anemia management guidelines directed to improve the knowledge about symptoms and signs of anemia, possible mechanisms, morphological classification of anemia, diagnostic and therapeutic approach, between primary care physicians. In the third step, following the education project, the same parameters were analyzed, in a comparable group of 603 patients (»final group«) visiting our Outpatient Clinic during the next one year period.

Complete laboratory analyzes of blood samples from all examined patients were undertaken including: iron level, unsaturated iron-binding capacity (UIBC), total iron-binding capacity (TIBC), hemoglobin level (Hg), ferritin level, transferrin saturation (TSAT), red blood cell count (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), white blood cell count (WBC), platelets number. Laboratory analyses performed by general practitioners before and following the education project were compared to determine the possible differences in execution of diagnostic algorithm for IDA in general practice.

### Statistics

The differences in age and sex were analyzed by one-way ANOVA and  $\chi^2$ -test, respectively. The inter-group differences between pre-education (initial group) and after-education (final group) questionnaire results were analyzed using the  $\chi^2$ -test. All statistical analyses were performed using Statistica for Windows (release 6.1, StaSoft. Inc. Tulsa, OK, USA). The level of statistical significance was set at 0.05.

## Results

There was a significant difference in sex distribution of examined patients ( $\chi^2=0.49$ ;  $p<0.001$ ) with predominance of female patients. Average age of the patients was 45.15 years (range 21–81 years) in females, and 67.87 years (range 50–83 years) in males. The female patients were significantly younger as compared to male patients ( $p<0.001$ ).

Following undertaken education the number of patients visiting Outpatient Clinic due to diagnosis of IDA was significantly decreased as compared to the same period of time before the education from 983 (61.97%) to 603 (38.02%) patients ( $p<0.05$ ).

Out of 1586 patients referred to Hematology Outpatient Clinic, Rijeka University Hospital Center, initial diagnosis of IDA has been confirmed in only 776 (48.93%) patients, while other types of anemia were established in altogether 810 (51.07%) patients, as shown in Table 1. Following the education number of patients referred as having IDA but finally established to have a different type of anemia was significantly decreased from 661 (67.24%) patients to 149 (24.71%) patients ( $p<0.001$ ).

Following the education the number of patients started on iron supplementation therapy before establishing

**TABLE 1**  
TYPE OF ANEMIA ESTABLISHED IN PATIENTS REFERRED DUE TO DIAGNOSIS OF IRON DEFICIENCY ANEMIA

Type of anemia	All patients N (%)	Initial group N (%)	Final group N (%)
Referred patients	1586 (100)	983 (100)	603 (100)
Iron deficiency anemia	776 (48.93)	322 (32.76)	454 (75.29)
Anemia of chronic disease	705 (44.45)	570 (57.98)	135 (22.38)
Megaloblastic/macrocytic	24 (1.51)	18 (1.83)	6 (1.00)
Anemia of multiple mechanisms/other type of anemia	81 (5.11)	73 (7.42)	8 (1.32)

the type of anemia, IDA or other, was significantly decreased as compared to the same period of time before the education from 543 (55.24%) to 76 (12.60%) patients ( $p < 0.001$ ). Also, duration of iron supplementation therapy administered in other types of anemia or before confirmation of IDA as a final diagnosis was significantly decreased following the education as compared to the same period of time before the education from  $21 \pm 9.8$  weeks to  $6 \pm 8.7$  weeks ( $p < 0.001$ ).

Out of 1586 patients only 89.29 (5.63%) patients have had an underlining hematological illness. Since, IDA is, generally, not a final diagnosis other patients were, during the diagnostic process, diagnosed for other underlined illnesses. In examined patients underlining diseases were most commonly detected in gastrointestinal system in 948 (59.77%) patients, followed by gynecological diagnosis in 507 (31.9%) patients, previously mentioned hematological illnesses, diseases of immune system in 27 (1.70%) patients, and diseases of respiratory system in 5 (0.31%) patients, while in 8 (0.50%) cases no underlining cause have been determined.

Statistically significant results of performed questionnaire in initial and final patient groups as well as statistical analyses regarding duration of IDA, time necessary for determining a definitive diagnosis of anemia type and initialization of treatment as well as number of other specialists' consultation were summarized and shown in Table 2. Comparison between execution of laboratory analyses in general practice before and following the education was summarized and shown in Table 3. Obtained values of performed laboratory analyses in general practice and outpatient clinic were shown in Table 4. The differences between laboratory results obtained in primary

care practice and outpatient clinic were, probably, due to different number of patients examined, since only in Clinical Hospital a complete laboratory workup of blood samples of all examined patients was performed, as well as the differences in laboratory equipment used.

## Discussion

According to our knowledge, this is the first study evaluating the significance of continuous medical education of general practitioners about IDA by assessing the possible changes and improvements in managing these patients in general practice through patient follow-up, analyzes of anamnesis information, clinical and laboratory finding in patients referred to hematologists as having IDA. The results of this study clearly show that continuing medical education of general practitioners improves management of patients with common diseases such as IDA in their general practice. In contrast to this study, based on evaluating changes in clinical practice, most of the studies evaluating the influence of continuous medical education assess the improvement and obtained theoretical as well as practical knowledge through different testing methods of target trainee groups before and/or following the education program. At this point we should stress out that the aim of this study was not to analyze the reasons for referrals. Besides adequate reasons for referral such as inability of general practitioner to establish the diagnosis, treatment failure and the need for transfusion, we suspect that some patients were referred for inadequate reasons, due to patient persistence for unnecessary referral, inadequate treatment or insufficient

**TABLE 2**  
RESULTS OF QUESTIONNAIRE REGARDING DURATION AND CONFIRMATION OF IRON DEFICIENCY ANEMIA AND SPECIALIST CONSULTATIONS

Clinical questions	Initial group $\bar{X} \pm SD$	Final group $\bar{X} \pm SD$	p-value*
Duration of anemia before treatment (weeks)	41 $\pm$ 29.8	26 $\pm$ 18.7	$p < 0.001$
Number of visits to other specialists per patient	2.9 $\pm$ 1.35	1.1 $\pm$ 0.94	$p < 0.05$
Hemoglobin (Hg) level before referral to hematologist	98.9 $\pm$ 15.5	82.6 $\pm$ 14.2	$p < 0.05$
Time necessary for definitive diagnosis and treatment (weeks)	49 $\pm$ 19.2	28 $\pm$ 9.1	$p < 0.001$

\* $\chi^2$ -test –  $p < 0.05$  was considered significant

**TABLE 3**

EXECUTION OF DIAGNOSTIC ALGORITHM BY GENERAL PRACTITIONERS IN PATIENTS REFERRED DUE TO DIAGNOSIS OF IRON DEFICIENCY ANEMIA

Laboratory analyzes	Initial group (N=983)	Final group (N=603)	p-value*
	N <sup>†</sup> (%)	N <sup>†</sup> (%)	
Fe	671 (68.26)	586 (97.18)	p<0.05
UIBC	532 (64.12)	520 (86.23)	p<0.05
TIBC	510 (51.88)	516 (85.57)	p<0.01
Hg	906 (92.17)	603 (100.0)	p>0.05
Ferritin	9 (0.92)	374 (62.02)	p<0.001
TSAT	ND	ND	ND
RBC	925 (94.09)	603 (100.0)	p>0.05
MCV	683 (69.48)	540 (89.55)	p<0.05
MCHC	558 (56.76)	476 (78.94)	p<0.01
WBC	827 (84.13)	574 (95.19)	p<0.05
PLT	790 (80.36)	552 (91.54)	p<0.05

\* $\chi^2$ -test – p<0.05 was considered significant; N<sup>†</sup> – patients with laboratory analyzes, ND – not done

knowledge or/and involvement of general practitioner to manage the patient.

The most commonly used definitions of anemia are suggested by the Centers for disease Control and Prevention and the World Health Organization (WHO). The diagnosis of IDA requires that a patient be anemic and show laboratory evidence of iron deficiency. Still, initial diagnosis of IDA was very often considered by primary care physicians in cases of iron deficiency with no real ev-

idence of anemia or in other types of anemia, especially before the education project.

The serum ferritin level is considered the most accurate initial diagnostic test for IDA, reflecting iron storage and absolute iron deficiency, but we have found that it is rarely performed by primary care physicians before patient referral to hematologist. Following the education program this diagnostic test was performed significantly more commonly in general practice (0.9% vs. 60%). Ferritin level, as determined during the diagnostic procedures, was decreased in majority of referred patients. In patients with IDA the amount of iron available to bind to the iron-caring protein transferrin is reduced, causing a decrease in the transferrin saturation (TSAT) and an increase in the unsaturated iron-binding capacity (UIBC). Absolute iron deficiency is defined by TSAT<20% or serum ferritin <10  $\mu\text{g/L}$ <sup>10-12</sup>.

Although, TSAT and serum ferritin have been suggested as simple and favorable markers for assessment of iron status due to their widespread availability, extensive literature base, and familiarity<sup>12-15</sup>, TSAT values were not determined during laboratory analyzes undertaken in general practice before, but also after the education of general practitioners.

It is clear that diagnostic procedure for IDA could easily be made in most patients seen by their general practitioners using laboratory tests available to them. But, especially before education, laboratory analyzes performed in a primary care practice in patients referred to hematologist as having IDA were, often, inadequate to clearly confirm this diagnosis or, in some cases, blood analyses were not performed at all before referral. Thus, incomplete diagnostic procedures could lead to unnecessary iron supplementation therapy usage and administration of oral iron supplement therapy before confirmation of

**TABLE 4**

VALUES OF LABORATORY ANALYZES OBTAINED IN GENERAL PRACTICE AND CLINICAL HOSPITAL

Laboratory analyzes	Initial group (N=983)		Final group (N=603)	
	General practice	Hospital	General practice	Hospital
	$\bar{X}\pm\text{SD}$	$\bar{X}\pm\text{SD}$	$\bar{X}\pm\text{SD}$	$\bar{X}\pm\text{SD}$
Fe ( $\mu\text{mol/L}$ )	8.4±4.8	6.8±3.2	5.9±3.7	5.5±3.4
UIBC ( $\mu\text{mol/L}$ )	59.1±14.6	64.2±15.1	64.1±6.2	66.2±9.1
TIBC ( $\mu\text{mol/L}$ )	77.9±16.3	82.3±10.3	81.9±12.5	84.3±10.3
Hg (g/L)	98.9±15.5	91.6±12.4	82.6±14.2	81.0±12.4
Ferritin ( $\mu\text{mol/L}$ )	ND	19.7±16.9	6.8±14.1	13.7±18.9
TSAT (%)	ND	24±13.1	ND	18±8.6
RBC ( $\times 10^{12}/\text{L}$ )	3.1±0.8	2.9±1.4	3.0±1.3	2.7±0.9
MCV (fL)	78.9±11.3	65.9±16.3	78.9±11.3	65.9±16.3
MCHC (g/L)	318.6±15.5	271.6±19.7	311.6±16.1	283.6±14.7
WBC ( $\times 10^9/\text{L}$ )	6.4±1.9	6.2±2.1	6.7±2.1	6.4±2.5
PLT ( $\times 10^9/\text{L}$ )	198.9±45.5	182.0±37.9	185.9±32.8	187.0±39.8

ND – not done



IDA, in cases with no real evidence of iron deficiency present or in other types of anemia.

The majority of general practitioners were not familiar with a diagnostic algorithm of IDA and their knowledge was significantly improved following education project, resulting in improved management of patients with IDA and increased usage of generally suggested diagnostic algorithm. Standard laboratory analyzes for assessment of IDA were more commonly performed in general practice including: serum iron, Hb and ferritin level, UIBC, TIBC, RBC, MCV, and MCHC, resulting in shorter period of time necessary to determine a type of anemia present. Following confirmation of IDA a therapeutic trial of oral iron supplement therapy is one of the recommended initial approaches<sup>16</sup>.

The symptoms of anemia, especially fatigue, weakness, impaired cognitive function, and even depression, can lead to a substantial reduction in functional ability and diminished QOL in affected patients, even in cases of mild and moderate anemia (Hb levels of 10–12 g/dl and 8–10 g/dl, respectively)<sup>4,6,17</sup>. The problem is more significant if the symptoms persist for a long period of time. Following the education project the average duration of anemia as well as the number of other specialist's consultations was significantly reduced. The final diagnosis and therapy initiation were achieved in significantly shorter time period resulting in faster improvement in patient's general health, functional ability and QOL.

Although, initiation of iron supplementation therapy is important in order to reduce symptoms of anemia in patients with IDA, we cannot forget that IDA should never be considered an end diagnosis. It has physiologic and pathophysiologic causes, so the work-up is not com-

plete until the underlining reason is known or serious disease might be overlooked. As in our study, previous studies have labeled diseases of gastrointestinal system as the most common underlining cause of IDA<sup>16,18–21</sup>. The diagnostic strategy and generally suggested evaluation for underlying cause of IDA that should be indicated according to patient's age<sup>7,16,19,21,22</sup> has not been completed in general practice. Generally, patients suspected to have IDA, other type of anemia or symptoms resulting from anemia, were directed to different specialist depending on the symptoms present, an average number of specialist consultation being significantly higher (three different specialist) before the education project (one specialist consultation). We presume, that following the education of general practitioners their knowledge about managing the patients with anemia and generally suggested evaluation for underlying cause of IDA was improved resulting in better management of these patients through directed work-up according to patients age and symptoms leading to decrease in the number of different specialist consultations and shorter diagnostic period.

In conclusion, continuing medical education of general practitioners as well as clinicians of other specialties has significant role in establishing an early diagnosis and treatment of patients with IDA. Education programs result in benefits for the patients and physicians. Most significantly the continuing medical education could improve QOL in patients with IDA due to more commonly applied diagnostic algorithm of IDA in a general practice, shorter diagnostic period, less specialist consultations and less hospitalization days. Also, we presume that these programs could reduce government expenses for medical care in these patients.

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## ULOGA KONTINUIRANE MEDICINSKE EDUKACIJE LIJEČNIKA PRIMARNE ZDRAVSTVENE ZAŠTITE O UČESTALIM BOLESTIMA – SIDEROPENIČNA ANEMIJA

### SAŽETAK

Prospektivna, trogodišnja studija provedena je s ciljem utvrđivanja utjecaja kontinuirane medicinske edukacije liječnika primarne zdravstvene zaštite na kvalitetu liječenja bolesnika s učestalim bolestima kao što je sideropenična anemija. Ukupno 1586 bolesnika upućenih u ambulantu za hematologiju, KBC Rijeka, s uputnom dijagnozom sideropenične anemije pregledao je hematolog tijekom prvog pregleda i perioda praćenja. Svi su bolesnici ispitani pomoću upitnika, te je učinjena kompletna laboratorijska analiza kako bi se: evaluirao fizikalni status bolesnika i laboratorijski nalazi, utvrdilo trajanje anemije, broj pregleda drugih specijalista radi simptoma anemije, primjena terapije preparatima željeza i odredio tip anemije. U inicijalnoj skupini ispitano je 983 bolesnika upućenih u hematološku ambulantu tijekom godine dana. Nakon provedene edukacijske kampanje isti parametri analizirani su tijekom naredne godine u 603 bolesnika završne skupine. Nakon provedene edukacije broj bolesnika upućenih u ambulantu za hematologiju pod uputnom dijagnozom sideropenične anemije bio je značajno snižen, sa 983 (61,97%) na 603 (38,02%) bolesnika ( $p < 0,05$ ), kao i broj bolesnika u kojih je utvrđen drugi oblik anemije, sa 661 (97,24%) na 149 (24,71%) ( $p < 0,001$ ). Broj bolesnika u kojih je primijenjena terapija preparatima željeza prije utvrđivanja oblika anemije bio je značajno snižen nakon provedene edukacije sa 543 (55,24%) na 76 (12,60%) bolesnika ( $p < 0,001$ ), kao i trajanje terapije preparatima željeza u ovih bolesnika ( $21 \pm 9,8$  vs.  $6 \pm 8,7$  tjedana) ( $p < 0,001$ ). Utvrdili smo značajno sniženje: vremena potrebnog za utvrđivanje konačne dijagnoze ( $49 \pm 19,2$  vs.  $28 \pm 9,1$  tjedana) ( $p < 0,001$ ), broja specijalističkih pregleda ( $2,9 \pm 1,35$  vs.  $1,1 \pm 0,94$ ) ( $p < 0,05$ ), trajanja anemije prije uvođenja terapije ( $41 \pm 29,8$  vs.  $26 \pm 18,7$  tjedana) ( $p < 0,01$ ). Vrijednost hemoglobina (Hg) u bolesnika upućenih hematologu bila je značajno niža nakon edukacije ( $98,9 \pm 15,5$  vs.  $82,6 \pm 14,2$ ) ( $p < 0,05$ ). Kontinuirana medicinska edukacija liječnika primarne zdravstvene zaštite ima važnu ulogu u dijagnostici i liječenju bolesnika sa sideropeničnom anemijom. Edukacijski su programi od koristi i bolesnicima i liječnicima.