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Analysis of Relative Cost Variations and Relative Effectiveness Of Anemia Treatment Via Alternate Methods of Iron Administration

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Abstract

We compare the cost of different routes of iron administration for severe iron deficiency anemia. The strength is based on in the analysis that included all type of costs, including direct-indirect costs related to the institution, staff members and patients.

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INTRODUCTION

Anemia is a frequent and serious problem of health defined by the World Health Organization (WHO) as the decrease in hemoglobin levels below 13.5 g/L for males and 12.0 g / L for women (WHO, 1968; Huch & Breymann, 2006). WHO estimates that about 2,000 million people is affected by anemia, and since a disease influenced by the socio-economic conditions, the major causes are related to nutritional deficiencies, specially iron deficiency (Ailinger et al., 2009; WHO, 2003)**.**

In non-industrialized countries, the prevalence of this type of anemia is 44% in pregnant women (WHO/UNICEF/ONU, 2004; Moy et al, 2006); 42% of preschool children and 51% in elderly (Hercherg et al, 2001; Mozaffarian et al, 2003; De la Pietra et al., 2002).

In Argentina, anemia due to iron deficit goes from 13% to 29% according by patient's place of residence (Buys et al, 2005; Meier et al., 2003). In the province of Buenos Aires, anemia's prevalence in adult population is 26.3% (Marin et al, 2008).

It is important to determine the level of severity of anemia. Adult patients in whom a hemoglobin level is less than 8.0 g/dl have low duty performance at their jobs, increase the absenteeism, and decrease their daily activities. Iron deficiency anemia becomes then a heavy burden on the health system economy.

The objective of this research is to evaluate the economic impact of treatment in adult patients with moderate to severe iron deficiency anemia according to the route of iron administration.

MATERIALS AND METHODS

Type of study: It is a prospective randomized clinical trial.

Characteristics of local population: The universe of study is the population of individuals born in Bahia Blanca city, Argentina. This metropolis is geographically located in the southwest of the province of Buenos Aires. According to the last census the population is 301.531 inhabitants, 48% of them were male and 52% female. In the beginning of XXI siècle the inhabitants suffered a deterioration of their employment conditions, and a decrease in their quality of life. 35% of the population had no specific health coverage (Prieto, 2010). The incidence of poverty was 47.8%. (Prieto, 2010).

Table I: Distribution of patients by sex and age.

Age range (yrs)	Male	Female	Total
<30 years	9	73	82
31 to 50 years	101	232	333
> 50 years	36	56	92
Total	146	361	507

Patients: All patients aged with more than 18 years old, which attended to the Hematology Service of Dr. Leonidas Lucero Public Hospital that showed less than 8 gr/dl in the initial blood test with iron deficit and that accepted to sign the informed consent form; were included in randomization process.

Groups of Study: After an initial survey and blood test analysis patients were randomized in two arms**.** Stratification was performed according to patient's age, gender, and socio-economical conditions (Rubio Terres, 1996)**.** Randomization was assigned using "SAS Proc Plan" randomizer software (2x1). After randomization, patients were admitted into one of the two intervention groups: *Group I*: treated with oral iron therapy in doses of 180 mg ferrous sulfate daily, over a period of 90 days, and *Group II* submitted to intravenous treatment, weekly doses of 200 mg in a 1-hour infusion for five weeks long.

Sample size: For sample size estimation, it was taken into account the frequency of consultation by patients with hemoglobin levels below 8.0 g/dl; the efficacy of oral and intravenous treatment, considering a 95% (α 0.05) of interval confidence, a power of 80% (β 0.20). According to these aspects, the theoretical number of patients to be included in oral treatment was 349, while the sample for intravenous treatment was 158.

Exclusion Criteria: Patients under age 18, patients with hemodynamic unbalanced blood pressure secondary to anemia; those individuals requiring an emergency blood transfusions; those patients presenting iron allergy; or with diagnostic of malabsorptive syndrome, were excluded from the study.

Variables: *Age* (determined by date of birth), *sex* (defined by the legal record in the official ID document), *socioeconomic condition* (determined with a self-administered survey shown in Appendix I) including unmet basic needs variables extracted from the National Official Statistical Bureau -INDEC- formula[15]. Other variables considered were: *Hb normal level recovery*; *tolerance to treatment*; treatment *dropout*; treatment-related *complications*; *days of hospitalization*; rate of *re-consultation*; *type of treatment received*. These parameters were evaluated before the assignment to the group of study (basal levels); and also at 4^{th} and 12^{th} weeks. *Total cost* variable was a composite index that included the amount of all resources mobilized for patient care. Each resource was identified by its *unit cost*. Estimation of the costs related to external consultations and hospitalization practices was focused on two types of

costs: a) recurrent *directly costs* associated with the health care diagnoses procedures, patient attention during consultation or hospitalization, blood tests, or drug for anemia's treatment. b) *indirect costs* was calculated for both: the costs from health system and from the patient itself. The *direct costs* included the cost of time of professional and non-professional involved in the query, the average number of inquiries from patients enrolled in each treatment group, the cost of hospital placements in each group, the average cost per day of hospitalization and the procedures used in the care of patients, according to the criteria established by official guidelines (Themes et al, 1994; National Ministry of Health 2011). Laspeyres equation was used in order to calculate the costs of providing the services necessary for patients' care or attention (electricity, water and gas). All single cost was calculated and added to the total costs variable. Costs related to patient's transport from home to the hospital, either for programmed visits, emergencies, spontaneous consultation, were also took in consideration for individual and total cost. Finally we considered the loss of profits due to job's absenteeism associated with both the consequences of the disease and the health care of it; as well as the economical impact caused by the lost of working hours as a result hospital consultations or hospitalizations, by the following formula:

$$\text{Value of job's hour} = \frac{\text{basic salary x 28 days /}}{30} 180$$

An average of the results obtained was estimate for each group of study.

Tools for data collection: Complete patient data were collected from: survey, daily care sheets, registration data, laboratory database results, pharmacy records, through a program developed in Microsoft Visual Basic 6. Data related to cost of outpatient services, inpatients care at hospital, laboratory practices, drugs used, were captured through software developed by Microsoft Excel XP. Sources for each cost item (cost of general services cost tables, administrative databases local health system, prices of outsourced services) were also identified. Data was stored in Microsoft program Access 2000.

Statistics analysis: results obtained from the two types of iron administration were compared by two Chi Square formulas (Pearson Chi Square and Chi Square MV-G2) and ANOVAs tests using Info-Stat 7 software.

Ethical Considerations: This study was conducted in compliance with the regulatory requirements of good clinical practice and the Declaration of Helsinki. Patients signed a written consent and received a booklet with information about the trial and their rights. The trial's protocol was approved by the Ethics Committee of the Municipal Leonidas Lucero Hospital, Bahia Blanca, Argentina.

RESULTS

11,000 surveys and blood tests were performed among patients admitted in consultation during the period of time in which this work was developed. Of them 507 patients (361 females and 146 males) filled out all the inclusion criteria of this work and had severe iron deficiency anemia (Hb <8.0 g / dL).

After randomization (according to 2x1 procedure described in “Materials and Methods”) 349 patients were assigned to group I (oral treatment) and 158 to group II (intravenous therapy). More than 65% of the patients were aged between 31 and 50 years old (table I).

Table II: Tolerance analysis for both treatments.

TOLERANCE 00000000000000000000x< <							
TREATMENT	Good	%	Fair	%	Poor	%	Total
VO	287	82,23	33	9,45	29	8,30	349
IV	143	90,50	7	4,43	8	5,06	158
TOTAL	430		40		37		507

Tolerance to treatment received was appropriated for both groups (82.23% for oral treatment and 90,50% for intravenous group - p value < 0.04) (table II and III). This statistical difference between both groups of study in relation to treatment tolerance was obtained with a 95% confidence interval (95%CI) and a margin of error less than 6%.

Table III: Statistical study of frequencies for both treatments’ tolerance

Statistical	Value	gl	P
Pearson Chi Square	5,93	2	0,0516
Chi Square MV-G2	6,42	2	0,0404

Chi-square was used to compare the observed with the endovenous data with data expected to obtain according to oral treatment

Drop-out cases had differences between both administration schemas since 21.9% of the patients receiving oral iron discontinue their treatments, whereas those patients assigned to intravenous iron’s group had only 4.6% of drop outs, with a statistically significant difference between groups (p <0.0001).

In 32.7 % of the patients enrolled in group I, and in 8.9% of group II, it was required to give a second course of treatment because their clinical conditions (table IV and V). Hence, based on the results obtained, we can assure with a high statistical significance (p <0.0001) that the number of patients that needed a second treatment was lower for iron intravenous administration.

Table IV: Analysis from the second treatment.

Second Treatment			
	NO	YES	Total
VO	263	86	349
IV	145	13	158
Total	408	99	507

Table V: Statistical comparative analysis from the second treatment depending on route of administration.

Statistical analysis	Value	gl	P
Pearson Chi Square	18,65	1	<0,0001
Chi Square MV-G2	21,1	1	<0,0001

Chi-square was used to compare the observed with the endovenous data with data expected to obtain according to oral treatment

For oral iron administration it existed on average, 9.6 ± 3.9 consultations per patient while for the intravenous treatment group (including day hospital visit for drug administration) consultations were 6.4 ± 3.2 (statistically significant difference p 0.02).

Hospital admissions were 6.9 ± 2.5 in the oral treatment group, versus 5.3 ± 4.0 in the group IV (p = 0.06). The duration of hospitalization was 11.4 ± 9.2 days of stay for group I and 7.7 ± 3.9 days for the group II (p = 0.02).

The cost analysis of visits, hospitalizations or practices conducted by each patient, was calculated considering the direct and indirect costs as described in the Materials and Methods section.

At the time when the study was performed basic monthly salaries for hospital human resources were: administrative staff group: $ 3513 (30 hours/week); physician and biochemist: $ 5208 (36 hours / week); pharmacist: $ 5690 (40 hours / week) and nurses: $ 4340 (30 hours / week). Among medical services costs it could be said that an hematological study cost $ 22.0 and ferritin and serum iron level determination cost was $ 17.2 in average. The number of blood samples extractions for hematological controls and laboratory studies (including outpatient and hospitalization procedures) was 15.6 ± 5.2 in group I while for group II it was 8.8 ± 3.2 (p = 0.02).

Subsequently, average costs required to treat each patient according to the assigned treatment group was calculated considering the total, direct (Cd) and indirect (Ci) costs (including fixed and variable costs).

In Group I, direct costs were $ 1,535.7, representing 66.4% of the total cost while for Group II, these types of costs were $ 1,100.5 (67.3% of total

cost). Indirect costs for the oral iron group was $ 774.8 (33.5% of total costs) and $ 532.9 (32 6% of total costs) for the intravenous treatment group. When lost profits for patients (productive capacity and jobs absentees for being at hospital) were included to total costs (Table VI) a highly significant difference was found in favor of Group II (p <0.0001).The percentage of total costs corresponding to medicines administrated was 14% for group I and 7.9% for Group II, with a highly significant difference in favor of intravenous treatment (p <0.0001). Table VI resumes the results of total cost for I and II groups.

Table VI: Total costs of treatment in each group.

Resource Description	Group I	Group II	p
Direct Costs final care -in pesos- (per patient treated)			
Salaries doctor	344,1	205,1	0.0006
Nursing salaries	195,7	217,2	0.07
Salaries staff biochemist.	42,9	24,8	0.08
Salaries pharmacy	22,8	20,2	0.7
Administrative salaries	65,5	49,5	0.09
Several non-medical supplies	10,7	38,1	0.04
Drugs	325,3	130,3	<0.0001
Disposable	82,9	101,2	0.07
Biochemical practices	323,3	256,0	0.06
Medical practices (endoscopies, images)	98,1	31,5	0.03
Food (day hospital and inpatient)	24,4	26,6	0.8
Indirect costs of care (transfers from other services) *			
Utilities	102,0	85,2	0.09
General services.	78,5	58,1	0.06
General Inputs.	31,1	25,7	0.6
Overhead staff sectors.	152,3	114,4	0.08
Intermediate and final expenses	88,7	76,0	0.3
Indirect costs of patient			
Transportation	55,4	38,4	0.0007
TOTAL COST (per patients without loss of earnings)	2043,7	1498,3	<0.0001
Loss of profits	266,8	135,1	0.002
TOTAL COST (complete by patients)	2310,5	1633,4	<0.0001

DISCUSSION AND CONCLUSIONS

Quality of life and vulnerability are two important items in any health policy. Iron anemia is one of the major causes of reduction of labor capacity, declination of quality of life and drop of incomes among the patients affected by the diseases (WHO, 2009).

On the other hand, iron anemia is consider a low cost disease to be attended by the public health services, since the patients usually are treated ambulatory and receives oral treatment (United Nations,2009).

However this analysis of health's attention considers only consultations and practices (WHO, 2009). When indirect costs are added to the analysis, then the economical burden of iron anemia changes.

This work analyzed all costs related to iron deficit anemia treated with two different iron deliveries (oral and intravenous). The analysis considered not only the direct costs but also aspects like the cost of opportunity of being at the hospital (and absent at work), cost of transportation to attend the consultation, fix cost (capital expenditures, facility's expenses, equipment's maintenance, utilities, or employee salaries and benefits that are not directly related to consultation). Considering all these aspects, this work found that for severe anemia treatment with IV iron delivery schema was cheaper in the overall total cost for a public health service.

The costs in human resources involved to patient's attention and in lab chemical practices were similar for each group. However, the number weeks need for treatment (12 versus 4 weeks), made the costs related to human resources and practices higher for oral administration compared to intravenous iron delivery.

It is well known that patients treated with IV iron may require more attention at the time of consultation, but the lower frequency of visits, the less number of controls and the lowest rate of hospital readmission / admissions reduced the workload of staff unit in the entire treatment period during the performance of this research. The full cost of treatment provided in the IV way was 29.30% lower than oral drug delivery.

There is no doubt that less severe iron deficit should be treated with oral iron formulations. However, this work alerts about a small group of patients with severe anemia that has not only a harmful impact in their own life but also in the health system.

For patients with severe iron deficiency anemia in whom initial hemoglobin values was less than 8.0 g / dL, the results of this research allow considering the IV as an effective, safe and overall less expensive iron delivery; reinforcing the idea of adopting this way of drug administration for these patients in the Public Health service.

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