Cost-effectiveness of two treatments for excessive menstrual bleeding in large uteri

Custo-efetividade de dois tratamentos para o sangramento menstrual excessivo em úteros grandes

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Daniella de Batista Depes
PhD in Health Sciences
Institution: Hospital do Servidor Público Estadual de São Paulo “Francisco Morato de Oliveira”
Address: R. Pedro de Toledo, 1800, Vila Clementino, São Paulo - SP, CEP: 04029-000
E-mail: danidepes@yahoo.com.br

Marcos Vinícius Maia da Mata
Graduate in Medicine
Institution: Hospital do Servidor Público Estadual de São Paulo “Francisco Morato de Oliveira”
Address: R. Pedro de Toledo, 1800, Vila Clementino, São Paulo - SP, CEP: 04029-000
E-mail: drmarcosmaiasp@gmail.com

Ana Maria Gomes Pereira
Master in Health Sciences
Institution: Hospital do Servidor Público Estadual de São Paulo “Francisco Morato de Oliveira”
Address: R. Pedro de Toledo, 1800, Vila Clementino, São Paulo - SP, CEP: 04029-000
E-mail: reparea.namarai@hotmail.com

João Alfredo Martins
Graduate in Medicine
Institution: Hospital do Servidor Público Estadual de São Paulo “Francisco Morato de Oliveira”
Address: R. Pedro de Toledo, 1800, Vila Clementino, São Paulo - SP, CEP: 04029-000
E-mail: jalfredom@uol.com.br

Maita Poli de Araujo
PhD in Health Sciences
Institution: Escola Paulista de Medicina, Universidade Federal de São Paulo
Address: R. Botucatu, 740, Vila Clementino, São Paulo - SP, CEP: 04023-062
E-mail: dramaita@gmail.com
Reginaldo Guedes Coelho Lopes  
PhD of Health Sciences  
Institution: Hospital do Servidor Público Estadual de São Paulo “Francisco Morato de Oliveira”  
Address: R. Pedro de Toledo, 1800, Vila Clementino, São Paulo - SP, CEP: 04029-000  
E-mail: jarelu@uol.com.br

Zsuzsanna Jármy-Di Bella  
PhD in Health Sciences  
Institution: Escola Paulista de Medicina, Universidade Federal de São Paulo  
Address: R. Botucatu, 740, Vila Clementino, São Paulo - SP, CEP: 04023-062  
E-mail: zsuvl@uol.com.br

ABSTRACT
Introduction: Excessive menstrual bleeding is menstrual loss that interferes with the woman's quality of life, regardless of the absolute amount. Drug treatment is preferred to avoid surgical risks and preserve fertility. Anti-inflammatory, antifibrinolytic, oral contraceptive and progestogen are prescribed. These therapies result in 40 to 50% reduction in menstrual loss. The intrauterine levonorgestrel system (SIU-LNG) is the most effective long-term clinical treatment. On the other hand, hysterectomy is the most widely performed gynecological surgical procedure in the world and, although it offers complete control of symptoms, it is the most invasive, morbidly, irreversible and costly method of treatment. Objective: To compare the results and costs of clinical treatment with SIU-LNG and hysterectomy in women with large uteri and excessive menstrual bleeding. Method: It is a retrospective cohort study with 62 patients who performed two treatments: SIU-LNG insertion or videolaparoscopic hysterectomy (HVLP) and followed for four years. Results: The groups were homogeneous regarding age, parity, body mass index, schooling and uterine volume. SIU-LNG failed in 32.3% of patients, while the efficacy of hysterectomy was 100%. Complications occurred 22.6% after UIS insertion and 19.4% in the surgical group, the most serious. The cost of clinical treatment, including its complications, was nearly five times lower than the cost of surgical treatment with its complications. Conclusion: Compared to hysterectomy, treatment with SIU-LNG had lower efficacy, but simpler complications and lower costs.

Keywords: intrauterine devices, hysterectomy, uterine bleeding, efficacy, costs and cost analysis.

RESUMO
Introdução: Sangramento menstrual excessivo é a perda menstrual que interfere na qualidade de vida da mulher, independente da quantidade absoluta. O tratamento medicamentoso é o preferencial, para evitar riscos cirúrgicos e preservar a fertilidade. Prescreve-se anti-inflamatórios, antifibrinolíticos, contraceptivos orais e progestagênios. Essas terapêuticas resultam em 40% a 50% de redução na perda menstrual. O sistema intrauterino de levonorgestrel (SIU-LNG) é o tratamento clínico mais efetivo a longo prazo. Por outro lado, a histerectomia é o procedimento cirúrgico ginecológico mais
realizado no mundo e, embora ofereça controle completo dos sintomas, é o método de tratamento mais invasivo, com maior morbidade, irreversível e de maior custo. Objetivo: Comparar os resultados e os custos do tratamento clínico com o SIU-LNG e a histerectomia em mulheres com úteros grandes e sangramento menstrual excessivo. Método: É um estudo de coorte retrospectiva com 62 pacientes que realizaram dois tratamentos: inserção do SIU-LNG ou histerectomia videolaparoscópica (HVLP) e acompanhadas por quatro anos. Resultados: Os grupos foram homogêneos quanto à idade, paridade, índice de massa corpórea, escolaridade e volume uterino. O SIU-LNG falhou em 32,3% das pacientes, enquanto a eficácia da histerectomia foi 100%. Ocorreram 22,6% de complicações após a inserção do SIU e 19,4% de complicações no grupo cirúrgico, estas mais graves. O custo do tratamento clínico, incluindo suas complicações, foi quase cinco vezes inferior ao custo do tratamento cirúrgico com suas complicações. Conclusão: Comparado à histerectomia, o tratamento com o SIU-LNG teve menor eficácia, porém complicações mais simples e menores custos.

Palavras-chave: dispositivos intrauterinos, histerectomia, hemorragia uterina, eficácia, custos e análise de uso.

1 INTRODUCTION

Excessive menstrual bleeding is menstrual loss that interferes with the woman's quality of life, regardless of the absolute amount of bleeding. Affects 33% of them, resulting in significant costs to the Health System. In the United States, more than $1 billion is spent annually on treating women who suffer from such a problem, and it is estimated that more than $12 billion is wasted indirectly through lost productivity.

Treatment is aimed at decreasing menstrual flow, reducing morbidity, and improving quality of life. It may be surgical, by endometrial ablation and hysterectomy or medicated, this is based primarily on hormonal drugs, non-hormonal anti-inflammatory drugs, and antifibrinolytics.

Hysterectomy is traditionally considered the definitive treatment for excessive menstrual bleeding, and is one of the most common surgeries performed on women. They are very effective, however, rather, the laparoscopic pathway, although less invasive and traumatic, is more costly.
The SIU-LNG is the most effective clinical treatment for SUA, being used for this purpose since 2009 in the USA and even earlier in Europe.\textsuperscript{4, 7-11} It acts locally in the endometrium leading to atrophy and consequently to decreased menstrual flow.\textsuperscript{4,12}

In nonstructural bleeding, there is an 86% reduction in excessive bleeding after 3 months and 97% after 12 months.\textsuperscript{13} More recently, several endometrial and myometrial diseases are being controlled with SIU-LNG, such as adenomiosis, endometriosis and endometrial hyperplasias.\textsuperscript{8.10 ,14,15}

Expulsion, malpositioning, uterine perforation, and infection are possible complications.\textsuperscript{16}

Spencer and col.\textsuperscript{2} evaluated the cost and effectiveness of surgical procedures and the use of SIU-LNG in the treatment of excessive uterine bleeding. The SIU-LNG cost about three times less and provided better quality of life when compared to hysterectomy.

Morgan and col. (2019)\textsuperscript{17} observed a 9%-17% decrease in hysterectomies indicated for the treatment of SUA, fibroids and endometriosis after professional associations recommended the use of SIU-LNG before the indication of surgery. They also reported that there is evidence that the cost of hysterectomy and its complications are greater than those found with the SIU-LNG, even if surgery is necessary.

In the light of so much evidence in the use of SIU-LNG for the treatment of excessive menstrual bleeding, mainly from a non-structural cause, we chose to study its use specifically in enlarged uteri, comparing the results and costs with hysterectomy.

\section*{2 GOALS}

Compare the efficacy, complications, and costs of clinical treatment with SIU-LNG and HVLP in women with enlarged uteri and excessive menstrual bleeding.

\section*{3 METHODS}

A retrospective cohort study with a comparison between intervention groups, carried out at the Hospital do Servo Estadual de São Paulo, of the patients treated for excessive menstrual bleeding in enlarged uteruses, between May 2012 and May 2015, through the insertion of SIU-LNG or HVLP. The paper was approved by the Research
Ethics Committee under number 80024117.5.0000.5463.

Consecutive patients attended to in the gynecology clinic were included, refractory to clinical treatment (anti-inflammatory, antifibrinolytic, combined oral contraceptive or progestagen).

The inclusion criteria were:
- menacal patients with FSH dosage <20 mIU/ml
- excessive menstrual bleeding (> than 3)
- enlarged uterus measured by endovaginal pelvic ultrasonography.

The intensity of bleeding was classified as:
0 = absent (no bleeding)
1 = menstrual stain or escapes (presence of discreet bleeding/use of sanitary pad only)
2 = mild bleeding (less than the patient’s usual menstrual period)
3 = moderate bleeding (same as the patient's usual menstruation)
4 = heavy bleeding (greater than the patient's usual menstrual period)

The uterus was considered to be enlarged, with a volume greater than expected for the Brazilian woman, and the average volume for this population was 90.48cc and 105cc in multiparous women. 18

Patients with submucosal fibroids or endometrial polyps were excluded from the group treated with SIU-LNG.

The two treatment options were then offered, allowing the patient’s choice: insertion of the SIU-LNG in an outpatient regimen (group 1) or surgery (group 2), being standard in the Service the total hysterectomy, performed by VLP.

After an average of four years of the intervention (between 31 and 74 months), the patients were summoned for an interview and signed the Informed Consent Form. The main factor evaluated was the effectiveness of the treatment, using the score in the bleeding intensity questionnaire, comparing the results obtained before and after the procedures. For the analysis of complications, all information recorded in the medical record related to the immediate and late pre and post-operative period was noted and the patient was verbally questioned about other possible events until the evaluation visit in
the fourth year after treatment.

The collected data was recorded in Excel spreadsheet for Windows® and analyzed by the statistical program Epi Info version 7. Continuous variables were presented in means and standard deviations or in medians and quartiles, depending on the normality in the distribution. The categorical variables were presented in percentages. Student's t-test was used for mean comparison and Fisher's Chi-Square and Exact tests for frequency comparison between groups, considering a 95% confidence interval.

For the analysis of the costs, the costs recorded in the patient's records were inserted. Indirect expenses, such as laboratory tests, radiological tests, home medication and work separation, were not considered.

The expenses were also inserted into a decision tree, providing a graphical representation of the possible consequences and expected results from a decision made.

4 RESULTS

Sixty-two patients were evaluated, the majority of them being black (53.2%), followed by white (45.2%) and yellow (1.6%). As for schooling, 54.8% had higher education. The age of the patients ranged between 30 and 54 years, being the mean of 44.8 (±4.3) years in the SIU-LNG group and 44.9 (±4.8) years in the surgical group (p=0.90). The body mass index (BMI) was 27 (±4.2) kg/m² in the SIU-LNG group and 28 (±5.5) kg/m² in the surgical group (p=0.38) (Table 1).

<table>
<thead>
<tr>
<th>Table 1 Group 1 (SIU-LNG) and 2 (HVLP) demographic and clinical data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic and clinical data</td>
</tr>
<tr>
<td>Age: Mean (SD)</td>
</tr>
<tr>
<td>BMI: Mean and (SD)</td>
</tr>
<tr>
<td>Myoma: n and (%)</td>
</tr>
<tr>
<td>Adenomyosis: n and (%)</td>
</tr>
<tr>
<td>Uterine volume: mean (SD)</td>
</tr>
</tbody>
</table>

SD: standard deviation; CI: confidence interval; *: significant
Source: Authors.
The majority had up to 2 deliveries, 71% in the LNG-IUS group and 67.7% in the surgical group.

Of the total, 25.8% of the patients had a definitive contraceptive method and all reported excessive bleeding (class 4). As for the causes of bleeding, 88.6% of the patients were diagnosed with uterine myoma, 32.2% with adenomyosis, 14.4% with endometrial hyperplasia without atypias and 1.6% as a non-structural cause. Uterine volume ranged from 141 cc to 423 cc, averaging 237.3 (±45.7) cc in group 1 and 244.9 (±78.4) cc in group 2 (p=0.64) (Table 1). Hysterometry was obtained in group 1, ranging from 7 to 11 cm, with a mean of 9.2 (±0.9) cm.

In group 2, 18 total hysterectomies were performed per VLP and 13 subtotals were performed due to intraoperative technical difficulties. One patient (3.2%) had bleeding comparable to the usual menstrual volume after the procedure.

Table 2 compares treatment results. SIU-LNG was observed to have failed to reduce bleeding in 32.3% of patients, while the effectiveness of hysterectomy was 100% (p=0.00*).

Regarding the response to treatment with SIU-LNG, 67.7% of the patients had a lower bleeding pattern than the initial one, 35.5% were in amenorrhea, 12.9% reported escapes, 9.7% bled less than normal menstruation and 9.7% bled in a similar way to normal menstrual flow.

Thirteen patients had complications, 6 (19.4%) after hysterectomy and 7 (22.6%) after SIU-LNG insertion (p=0.76). Postsurgical complications were: a conversion to laparotomy, an operative wound dehiscence, a vaginal cupola granuloma, a vaginal cupola dehiscent infection, a residual colon bleeding, and a bladder lesion with a vesicovaginal fistula formation. In the SIU-LNG group, there were seven expulsions (Table 2).

Table 2 Comparison of results obtained with SIU-LNG and HVLP in the treatment of excessive menstrual bleeding

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SIU-LNG (n=31)</th>
<th>HVLP (n=31)</th>
<th>OR (CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe bleeding (&gt;3)</td>
<td>10(32.3%)</td>
<td>0(0.0%)</td>
<td>Undefined</td>
<td>0.00*</td>
</tr>
<tr>
<td>Complications</td>
<td>7(22.6%)</td>
<td>6(19.4%)</td>
<td>1.21 (0.36-4.14)</td>
<td>0.76</td>
</tr>
</tbody>
</table>

OR: odds ratio; CI: 95% confidence interval; *: significant
Source: Authors.
In seven patients (22.6%) there was expulsion of the device, between 2 and 16 months after insertion, and in two of them, the bleeding returned to the normal menstrual period and five returned to the pattern of excessive flow.

Table 3 shows the values spent with each treatment. The total expenditure was R$396,126.21, of which R$68,748.79 was spent on SIU-LNG (17.35%) and R$327,377.42 on HVLP (82.64%).

The calculation of the costs was done as follows:

SIU-LNG (R$) + \{query (R$) \times 3\} = 728.67 + 387.84 = 1,116.51
HVLP (R$) + \{query (R$) \times 5\} + \{hospitalization (R$) \times 3\} = 6,464.68 + 646.40 + 2,528.64 = 9,639.72

| Table 3 Unit values of treatments at the São Paulo State Public Server Hospital |
|-------------------------------|------------------|
| Cost                          | Unit value (r$)  |
| Day of hospitalization        | 842.88           |
| Outpatient visit              | 129.28           |
| Surgical time                 | 1,370.94         |
| HVLP                          | 6,464.68         |
| GnRH analog (10.8mg)          | 904.86           |
| GnRH analog (3.6mg)           | 649.06           |
| SIU-LNG                       | 728.67           |

Source: Authors.

Figure 1: Total spending with the two treatments performed for excessive menstrual bleeding

Source: Authors.
Figure 2 Analysis of the costs of inserting the SIU-LNG and its complications

Key: HTA - Total abdominal hysterectomy; CC - Surgical Center; HSC - Surgical Hysteroscopy

Source: Authors.
Figure 3 Analysis of HVLP costs and their complications

Source: Authors.

The cost with SIU-LNG, including the amount spent on complications, was R $ 68,748.79, which represents a value of R $ 2,217.70 per patient treated.

At HVLP, R$86,384.42 was spent on complications and R$240,933.00 on uncomplicated procedures. Therefore, its cost per patient was R$ 10,560.56.

Therefore, it is necessary to treat 4.76 patients with SIU-LNG in order to have the cost of a surgical treatment.

5 DISCUSSION

The impact of benign gynecological diseases on women's lives and their costs to society are high. 20

There is already evidence that in patients with a normal-sized uterus, SIU-LNG has high efficacy, low cost, and lower complications than surgical treatment. 13,21
However, other authors evaluated patients with excessive bleeding due to fibroids and enlarged uteri and were unable to replicate this same favorable result. 22,23

In this study, all the patients had enlarged uteri and treatment with the SIU-LNG was effective in reducing bleeding in 67.7% of them, leaving 35.5% of them in amenorrhea.

In turn, corroborating our results, Park and col. (2015) 24 evaluated 48 patients with adenomyosis and enlarged uterine volumes, comparable to 12 weeks of gestation or longer, and observed 68.8% success replacing surgery with

Cochrane Library review with 20 studies and 2052 participants showed that SIU-LNG significantly reduces menstrual blood loss in patients with excessive bleeding, including women with fibroids. However, reinforcing the one found in our study, when compared to hysterectomy, which being a definitive method presents 100% of efficacy, the device was less effective. 4.

Park and col. (2015) 24 observed 37.5% expulsion when using SIU-LNG in bulky uteri with adenomyosis, all in the first year of use, although the expulsion rate was not higher in bulky uteri. In the present research, the larger uterine cavities were a factor of protection.

In this study, the device expulsion rate was 22.6%. In turn, Zapata and col. (2010) 25 reviewed 202 articles and found expulsion rate of 0% to 20% in patients with uterine fibroids treated with SIU-LNG.

As for the major complications of hysterectomy, Davies and col. (2017) 7 report 3% rate intra-operative and 9% post-operative. However, these rates have been reduced with the advent of new less invasive techniques, with reduced risks, lower complication rates, and shorter recovery times.

In the present study, all surgeries were initially laparoscopic, with 19.4% of complications. The only complication encountered with clinical treatment was the expulsion of the device, while in surgical treatment there was a bladder lesion with evolution to vesicovaginal fistula, considered serious.

A Brazilian study compared the complications of two treatment options for bulky menstrual bleeding. Of the 138 patients who used the SIU-LNG, two expelled the device
and two returned with signs of pelvic inflammatory disease, being treated with antibiotics. In the 129 patients submitted to hysterectomy, there were six cases of hemorrhage during surgery, four perforations of the bladder or intestine, one ureteral reimplant, one complication with anesthesia, and two cases of acute abdominal pain. 26

The cost-effectiveness analysis of the SIU-LNG as an alternative to hysterectomy in the treatment of SUA in Latin American countries concluded that the expenditure is reduced to one third of the surgical treatment. 27 In the current study, spending using the SIU-LNG was almost five times lower than that of surgical treatment.

A lower cost in patients who used SIU-LNG, when compared to that observed in patients undergoing hysterectomy, was also previously reported in the Heliövaara-Peippo e col study, conducted from a Finnish health perspective. 28

Laughton and col. compared laparoscopic supracervical hysterectomy with SIU-LNG in treating excessive menstrual bleeding and concluded that surgery is not cost effective. 29

In this study, the SIU-LNG cost R$ 2,217.70 per patient treated and the HVLP R$ 10,560.56. Therefore, it is necessary to treat 4.76 patients with SIU-LNG in order to have the cost of a surgical treatment.

6 CONCLUSION

Compared to hysterectomy, treatment with SIU-LNG had lower efficacy, but simpler complications and lower costs in the 4-year period evaluated.
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