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Role Of Vincristine In Treatment Of Refractory Idiopathic Thrombocytopenic Purpura (Itp)

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Abstract*:** *Chronic immune thrombocytopenia (ITP) is a condition associated with significant morbidity; however the management options for refractory ITP are often unsatisfactory despite various lines of treatment including splenectomy. The comparison of vincristine costs with other lines of treatment as intravenous immunoglobulin revealed many folds lower costs of vincristine.* ***The aims of this study are*: to evaluate the role of vincristine in treating (splenectomized and non splenectomized) refractory ITP patients who are resistant to corticosteroids therapy, to assess the use of vincristine in clinical situations requiring increase in the platelet count as a preoperative management and to evaluate the long term (6 months) follow up effect after stoppage of vincristine treatment in refractory ITP patients.* ***Patients and Methods:*** *Twenty nine refractory ITP patients with maximum dose of corticosteroids (21 of them non-splenectomized "group I" and the remaining 8 splenectomized " group II") were treated with two- hour intravenous infusion of vincristine (1-2 mg) once a week for 6 weeks . In every patient, the platelet count was evaluated just before and just after the infusion of vincristine, follow up of these patients for 6 months after stoppage of vincristine was by evaluating platelet count every 2 months . Patients with hepatitis and chronic liver diseases were excluded from this study.* ***Results****: a significant increased level of the mean platelet count was observed in "group I" after the 2nd week of vincristine treatment ($p < 0.005$) and after the 3rd , 4th , 5th and 6th week of vincristine treatment ($p<0.001$) when compared to before the use of vincristine . Also there was statistically significant increase of the mean platelet count in "group II" after the 3rd, 4th, 5th and 6th weeks of vincristine treatment than before the use of vincristin treatment ($p< 0.05$) for all comparison , the study also revealed that " group II" had a significantly increased mean platelet count than "group I" after the 4th week of vincristine treatment ($p< 0.05$) , while no significant differences could be detected after the 1st , 2nd ,3rd , 5th and 6th weeks of vincristine treatment. A persistent increase of the mean platelet count was observed after 2 , 4 and 6 months follow up after stoppage of vincristine treatment when compared with the mean platelet count before the use of vincristin treatment in "group I" ($p<0.001$, $p< 0.05$ and $p< 0.05$) respectively and in "group II" ($p< 0.05$) for all comparisons. Higher mean value of platelet count was observed after 4 and 6 months of stoppage of vincristine treatment among "group II" than "group I" with no statistically significant difference, while this comparison was statistically significant after 2 months of stoppage of vincristine treatment ($p< 0.05$).* ***Conclusion:*** *Administration of vincristine to chronic corticosteroid refractory (ITP) patients was associated with a significant increased platelet count in both non splenectomized "group I" and splenectomized "group II" and this increase was persistent after stoppage of vincristine treatment for 6 month.*

I. Introduction

Immune thrombocytopenic purpura (ITP) is also known as idiopathic thrombocytopenic purpura **(Cooper and Bussel, 2006)**. It is an autoimmune disorder characterized by immunologic destruction of otherwise normal platelets most commonly occurring in response to an unknown stimulus. ITP may occur as primary or in association with other disorders (secondary) **Cindy et al., 2011**. The clinical course of ITP is usually chronic in adults. In cases of chronic ITP, serious bleeding is not expected even with significant thrombocytopenia. The mortality rate due to bleeding secondary to ITP is less than 1% (**George , 2009),** but it is associated with significant morbidity; however the management options are often unsatisfactory with a portion of patients exhibiting a refractory-relapsing disease path despite various lines of treatment including splenectomy **(Alhossain et al ., 2012).**

Corticosteroids are given as the first line of therapy in ITP cases with serious thrombocytopenia. Splenectomy is the standard care for cases that are non-responsive to corticosteroids. The rate of complete remission is 66% **(British Committee, 2003)**. The treatment of referactory ITP is often difficult **(Ahn et al., 1974).** When a beneficial response is not achieved, the disease is said to be refractory **(Karpatkin et al., 1972).** Various post-splenectomy treatments have been administered to refractory patients as azathioprine, vinka alkaloids, danazol, cyclophosphamide, high dose dexamethasone, rituximab, interferon, and cyclosporine have been used. The treatment of chronic refractory ITP is difficult because response to treatment is variable **(Vesely**

et al., 2004). Vincristine can produce responses in platelet counts after days to weeks of administration with considerable variability in response by individual patients **(Provan et al., 2010).**

No optimal treatment is currently available for patients with chronic ITP who were resistant to splenectomy (**Murat et al., 2010).** It has been pointed out that vincristine could be more effective in splenectomized patients (**Ries, 1976).** Administration of vinca alkaloids (VA) to chronic corticosteroid refractory immune thrombocytopenia ITP patients results in a temporary increase of platelet count **(Szczepanik et al.,2007)** and considered to be an useful treatment in patients with ITP **(Matsushima et al., 1992)**.Vincristine having the advantage of a faster action **(Ahn et al.,1974)** and could find their application in clinical situations requiring short-term increase of the platelet count in chronically ill patients with ITP, resistant to corticosteroids or with contraindication to their application **(Sikorska et al.,2004),** because of this, its use has been recommended for producing a rise in the platelet count before splenectomy or to control bleeding **(Burton et al.,1976).**

Matching of vincristine costs with treatment efficacy and comparison with the costs of intravenous immunoglobulin treatment revealed many folds lower costs of the vincristive method (**Szczepanik et al., 2007). (Shvidel et al ., 2006)** reported that vincristine-loaded platelet infusion in patients with refractory (ITP)who failed to respond to two to six different treatment modalities, including corticosteroids and splenectomy was prompt and useful approach in patients with ITP refractory to primary therapy.

II. Patients and methods

1-Study Site:

The patients were chosen from those admitted to Clinical Hematology Unit, Internal Medicine Department, Assiut University Hospitals and from Assiut Health Insurance.

2-Study Design:

One arm experimental clinical trail hospital based study

3- Study population sample size:

Twenty nine refractory ITP patients(21 of them non-splenectomized "group I" 14 females and 7 males and the remaining 8 splenectomized " group II" 6 females and 2 males) were previously diagnosed as ITP on the basis of history, Clinical data and examination of peripheral blood and marrow smears.

4-Technical design:

All those patients had been unsuccessfully treated with corticosteroids therapy with its maximum dose and even after high dose of dexamethason IV (24-32 mg/day) for four days. The patients were chosen from those admitted to Clinical Hematology Unit, Internal Medicine Department, Assiut University Hospitals and from Assiut Health Insurance. Full history taking and thorough clinical examination were done for all studied patients. Follow up complete blood counts - on automated cell counter MAX-M coultronics, France- were performed for all patients before and after every dose of vincristine infusion (1-2mg once a week for 6 weeks) and follow up of those patients after stoppage of vincristine treatment for 6 months were evaluated by complete blood counts every 2 months. Patients with secondary ITP or with chronic liver diseases were excluded.

5- Ethical consideration

Patients were invited to participate in the study on their full well and the steps and aim of the research were explained to participants before taking verbal consent.

Statistical analysis:

Data were analyzed and expressed as mean values ± standard deviations (SD). SPSS version 16 program was used for data processing. Differential semen concentration of lead and cadmium was determined by dividing their seminal concentrations on serum concentration in the same subject. Unpaired t-test has been used in comparison of numerical parametric data between patient and control groups. Mann-Whitney test was used in comparison of numerical non parametric data between patient and control groups. Pearson correlation test was applied to analyze correlations between different quantitative variables within each group. Values were considered significant when P values were equal or less than 0.05.

III. Results

Table 1: Age and sex distribution of the studied patients

Variables	Non splenectomized Group I (21)		Splenectomized Group II (8)	
	No	%	No	%
Sex				
• Males	7	24.1%	2	6.8%
• Females	14	48.3%	6	20.6%
Age (years) Mean±SD	30.6± 8.9		31.7±10.8	

This study showed that the total number of patients was 29 patients (21 non splenctomized "group I" , 7 males , 14 females ; mean age ±SD = 30.6 ± 8.9 years, range 16 - 45 years) and (8 splenctomized patients "group 2" , 2 males and 6 females; mean age ±SD = 31.7 ± 10.8 years , range 23 - 44 years.

Table (2): Platelet count before and after vincristine therapy in the studied sample

Variables **Platelet count**	**Mean platelet count x 10^9/L ± S.D (Range)**	
	Non splenectomized Patients Group I (no=21)	**Splenectomized Patients Group II (no=8)**
1. Before vincristine treatment	11.3 ± 6.1 (4:24)	17 ± 4.53 (12:21)
2. After one week of vincristine treatment	11.4±5.1 (4:21)	16± 3.5 (12:21)
3. After two weeks of vincristine treatment	16.7±7.2 (6:30)	22.5±9.1 (10:35)
4. After three weeks of vincristine treatment	37.1±22.47 (7:70)	41.75±25.79 (8:70)
5. After four weeks of vincristine treatment	53.76±34.82 (5:96)	78.87±59.47 (8:140)
6. After five weeks of vincristine treatment	94.86±71.29 (6:200)	103.87±79.11 (8:190)
7. After six weeks of vincristine treatment	80.03±60.73 (4:200)	111.5±84.54 (8:200)

This table revealed that the mean platelet count was (11.3 ± 6 x 10^9/L) in "group I" before the vincristine therapy and increased to reach its maximum level after the fifth and six weeks of vincristine therapy (94.8 ± 71.2 and 80 ± 60.7 x 10^9/L) respectively , and in "group II" was (17 ± 4.53 X 10^9/L) and increased to (78.87±59.47 , 103.87±79.11 and 111.5±84.54) after the fourth, fifth and six weeks of vincristine therapy respectively.

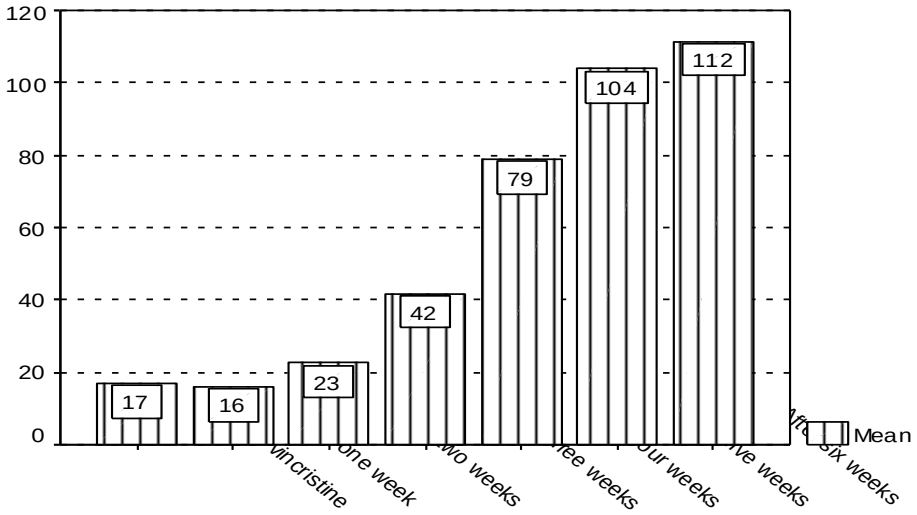

Figure 2 B :Referactory splenectomized ITP patients

Table 3 : Comparison of the mean platelet count before and after vincristine treatment In non splenectomized ITP patients

Variables (No=21 patients)	**After Vincristine treatment**					
	After 1st week	After 2nd week	After 3rd week	After 4th week	After 5th week	After 6th week
Platelet count (Mean ± SD x10 9/L)	11.4±5.1	16.7±7.2	37.1±22.47	53.76±34.82	94.86±71.29	80.03±60.73
	Before Vincristine treatment 11.3 ± 6.1					
P-value	NS	*	**	**	**	**

Wilcoxon test was used NS: not significant, *: significant (p< 0.05), **: highly significant (p<0.001)

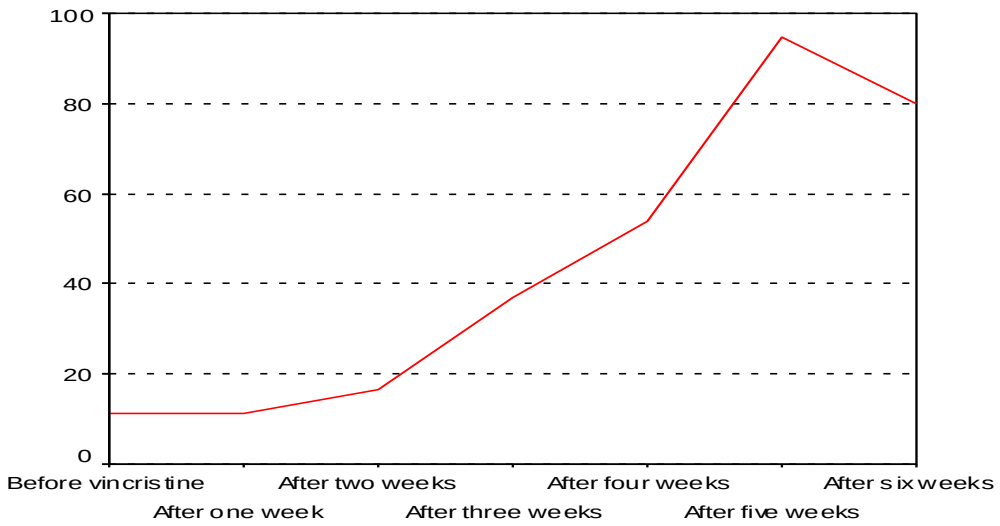

Figure 3 :Mean platelet count in non splenctomized ITP patients

There was statistically significant increase of the mean platelet count in group II after the 3rd,4th ,5th and 6th weeks of vincristine treatment than before the use of vincristin with ($p< 0.05$) for all comparison , while no significant statistical difference was detected after the 1st and 2nd week of vincristine treatment when compared with before the use of vincristine treatment (table 4 & figure 4) .

Table 4 : Comparison of the mean platelet count before and after vincristine treatment in splenectomized ITP patients

Variables (No=8 patients)	Vincristine treatment					
	After 1st week	After 2nd week	After 3rd week	After 4th week	After 5th week	After] 6th week
Platelet count (Mean ± SD x10 9/L)	16± 3.5	22.5±9.1	41.75±25.79	78.87±59.47	103.87±79.11	111.5±84.54
	Before vincristine treatment (17 ± 4.53)					
P-value	NS	NS	*	*	*	*

Wilcoxon test was used NS: not significant, *: significant ($p< 0.05$)

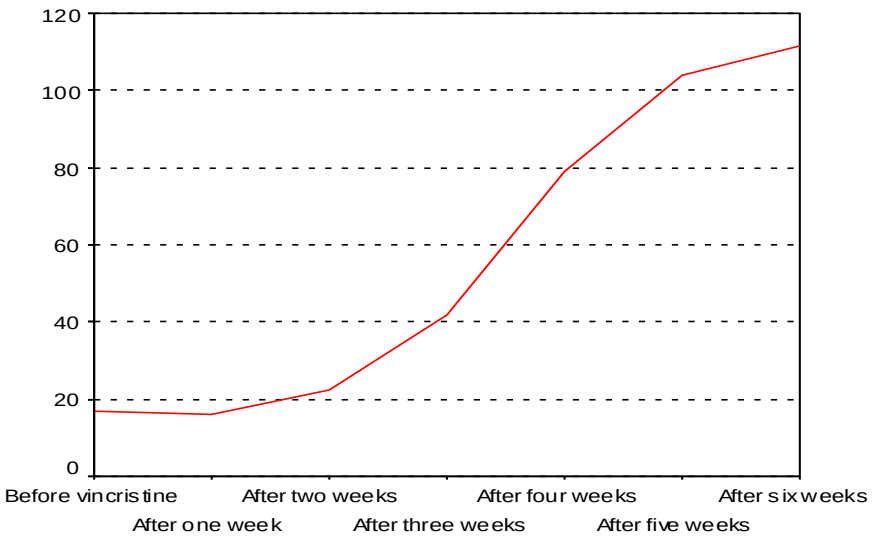

Figure 4 :Mean platelet count in referactory splenectomized ITP patients

Table 4 revealed that when the both groups were compared to each other, group II had a significantly increased mean platelet count than group I after the 4th week of vincristine treatment with ($p< 0.05$) , while no significant differences could be detected after the 1st , 2nd ,3rd , 5th and 6th weeks of vincristine treatment (table 5 & figure 5) .

Table 5: Effect of vincristine treatment on the platelet count between Splenectomized and non splenectomized ITP patients

Variables	Mean platelet + SD X 109 L	P-value
Before vincristine therapy • Non splenectomized (no=21) • Splenectomized (no=8)	11.33 ± 6.1 17 ± 4.53	NS
After one week • Non splenectomized (no=21) • Splenectomized (no=8)	11.38±5.09 16 ±3.51	NS
After two weeks • Non splenectomized (no=21) • Splenectomized (no=8)	16.71±7.2 22.5±9.134	NS
After three weeks • Non splenectomized (no=21) • Splenectomized (no=8)	37.1±22.47 41.75±25.8	NS
After four weeks • Non splenectomized (no=21) • Splenectomized (no=8)	53.77±34.82 78.88±59.47	*
After five weeks • Non splenectomized (no=21) • Splenectomized (no=8)	94.86±71.29 103.88±79.11	NS
After six weeks • Non splenectomized (no=21) • Splenectomized (no=8)	80.1±60.73 111.5±84.59	NS P=0.055

Mann-Whitney U test was used NS: not significant, *: significant ($p< 0.05$)

Table 5 shows that mean platelet count after 2 , 4 and 6 months of stoppage of vincristine treatment in group I were (68.67±62.9 , 62.095±63.63 and 61.86 ±67.32) respectively , and in group II were (118±89.52 , 117.16±89.54 and 104.63±79.18) respectively (table 6 and figure 6 A&B) .

Table 6: Follow up of platelet count after stoppage of vincristine therapy

Variables	Mean platelet count ± SD X 10^9 L	P-value
Before vincristine therapy • Non splenectomized (no=21) • Splenectomized (no=8)	11.33 ±6.05 17 ± 4.54	
After six weeks of vincristine treatment • Non splenectomized (no=21) • Splenectomized (no=8)	80.1± 60.73 111.5±84.59	**
Platelet count after 2 months of stoppage of vincristine therapy • Non splenectomized (no=21) • Splenectomized (no=8)	68.67±62.9 118±89.52	*
Platelet count after 4 months of stoppage of vincristine therapy • Non splenectomized (no=21) • Splenectomized (no=8)	62.095±63.63 117.13±89.54	*
Platelet count after 6 months of stoppage of vincristine therapy • Non splenectomized (no=21) • Splenectomized (no=8)	61.86 ±67.32 104.63±79.18	*

Mann-Whitney U test was used NS: not significant, *: significant ($p< 0.05$)

Table 6 shows that there was statistically significant persistent increase of the mean platelet count after 2 , 4 and 6 months of stoppage of vincristine treatment when compared with the mean platelet count before the use of vincristin treatment in group I with ($p<0.001$, $p< 0.05$ and $p< 0.05$) respectively and in group II with ($p< 0.05$) for all comparisons (table 6& figure 6 A and B) .

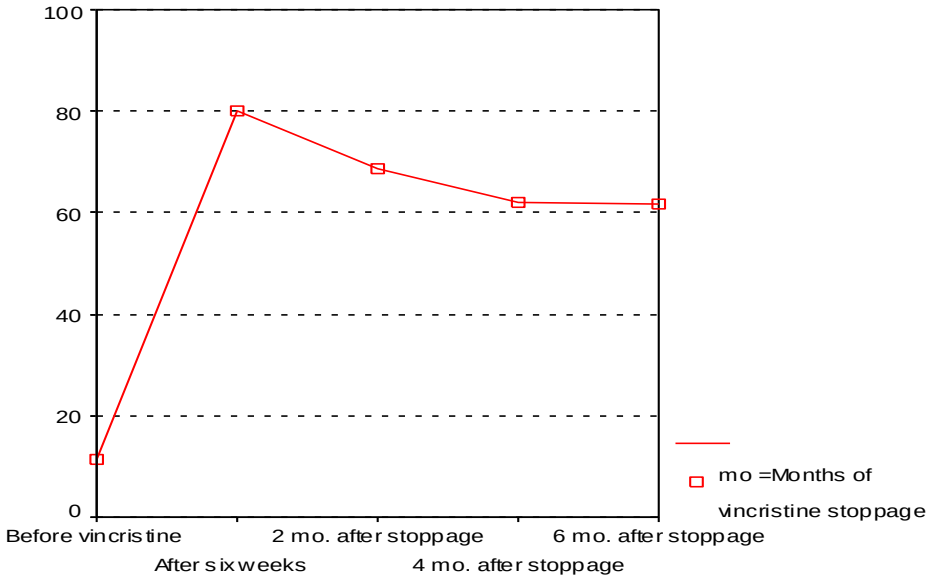

Figure 6A: Mean platelet count before and after stoppage of vincristine therapy in non splenectomized ITP patients

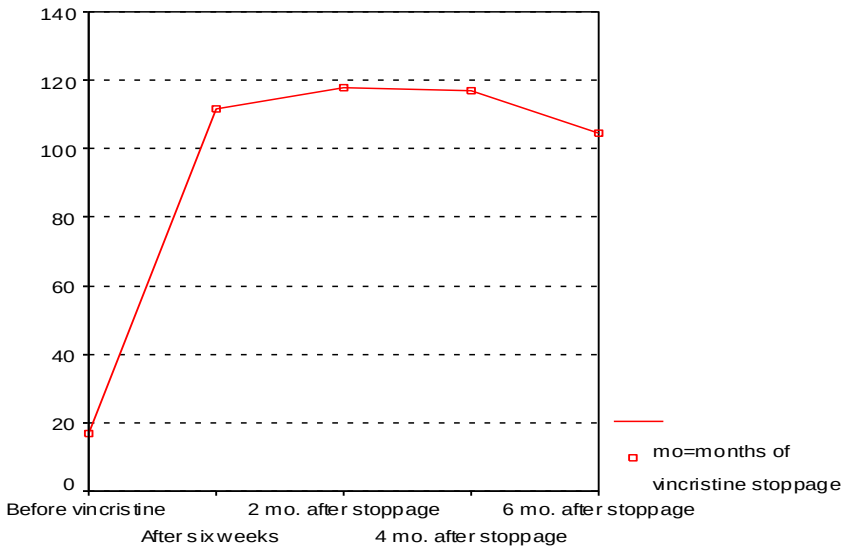

Figure 6B: Mean platelet count before and after stoppage of vincristine therapy in splenectomized ITP patients

Table 7: Comparison of mean platelet count before and after Stoppage of vincristine treatment in all studied patients

Variables		**Stoppage of vincristine**		
		After 2 months	**After 4 months**	**After 6 months**
Non splenectomized ITP patients (group I) (no= 21 patients)	Platelet count (Mean ± SD x10 ^{9}/L)	68.67±62.9	62.095±63.63	61.86 ±67.32
		Before vincristine treatment (11.33 ±6.05)		
	P value	**	*	*
Splenectomized ITP patients (groupII) (no= 8 patients)	Platelet count (Mean ± SD x10 ^{9}/L)	118±89.52	117.13±89.54	104.63±79.18
		Before vincristine treatment (17 ± 4.54)		
	P value	*	*	*

Wilcoxon test was used NS: *: significant (p< 0.05), **: highly significant (p<0.001)

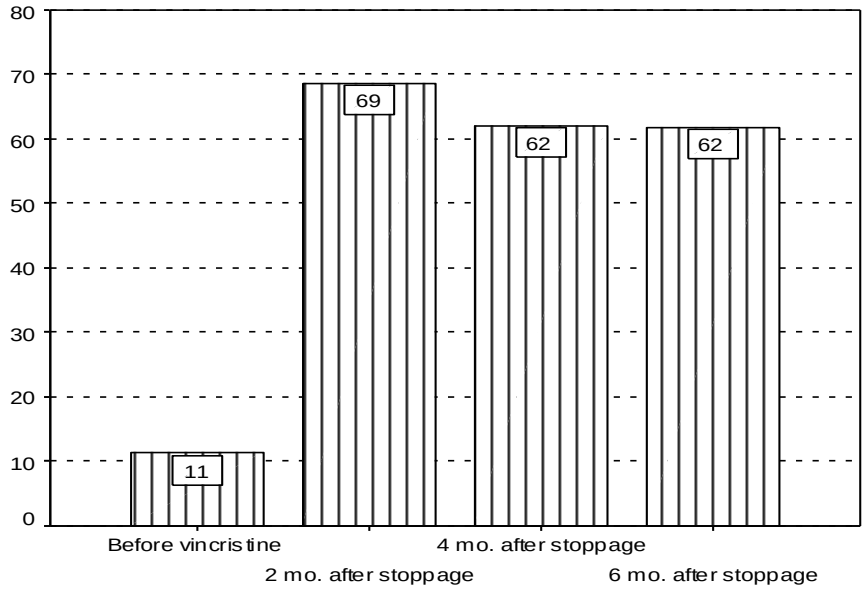

Figure 7A: **Mean platelet count before and after stoppage of vincristine treatment in non splenectomized ITP patients**

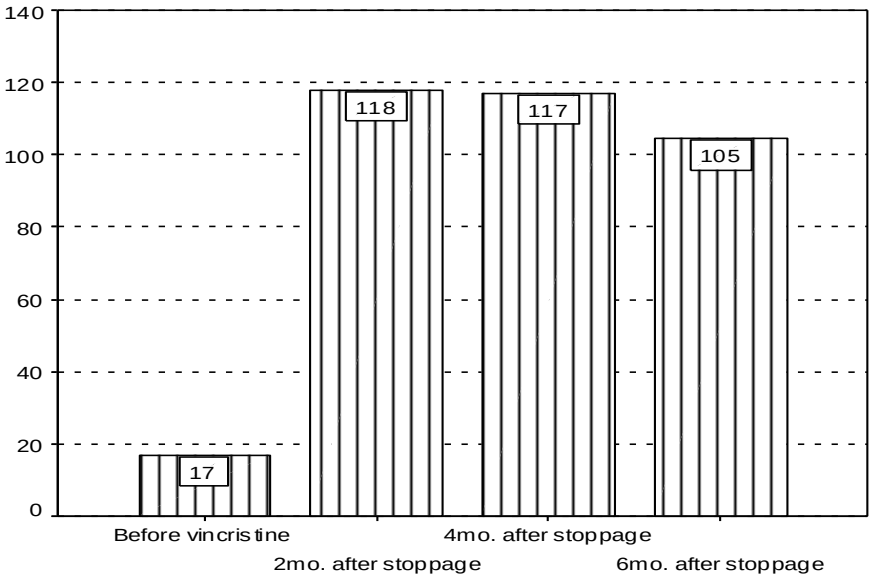

Figure 7B: **Mean platelet count before and after stoppage of vincristine treatment in splenectomized ITP patients**

Table 8: Comparison of the mean platelet count between splenectomized and non splenectomized ITP patients after stoppage of vincristine treatment

Variables	Mean platelet ± SD X 10^9 L	P value
Before vincristine therapy • Non splenectomized (no=21) • Splenectomized (no=8)	 11.33 ± 6.1 17 ± 4.53	 NS
After 2 months of stoppage of vincristine • Non splenectomized (no=21) • Splenectomized (no=8)	 68.67±62.9 118±89.52	 *
After 4 months of stoppage of vincristine • Non splenectomized (no=21) • Splenectomized (no=8)	 62.095±63.63 117.13±89.54	NS P=0.069
After 6 months of stoppage of vincristine • Non splenectomized (no=21) • Splenectomized (no=8)	 61.86 ±67.32 104.63±79.18	 NS

Mann-Whitney U test was used NS: not significant, *: significant ($p< 0.05$)

Table 8 shows that there was higher mean value of platelet count was observed after 4 and 6 months of stoppage of vincristine treatment among group II than group I with no statistically significant difference, while there was statistically significant differences when they compared after 2 months of stoppage of vincristine with ($p< 0.05$) table 8).

IV. Discussion:

Idiopathic thrombocytopenic purpura (ITP) is an autoimmune disorder mediated by the production of autoantibodies directed against platelets **(Provan et al., 2010)** with a variable clinical course **(Stiakaki et al.,2012**) as suggested by the demonstration of IgG-type anti-platelet antibodies **(Karpatkin et al., 1972**) . Based on the fact that ITP is generally caused by antibodies, immunosuppresive agents may be useful in refractory ITP with serious disease, as well as in patients unsuitable for surgery and for corticosteroids **(Finch et al., 1974**). Cyclophosphamide and azathioprine have been for many years the first choice agents **(Rosse, 1978).** However, they have the disadvantage of the long duration of treatment required, and their myelo-toxicity **(Ahn et al.,1978).** Other agents such as metho-trexate, chlorambucil, 6 mercaptopurine, actino-mycin C, L-asparaginase and thioguanine, have been used generally with disappointing results and In the last years, the Vinca alkaloids have been increasingly used in refractory ITP **(Ahn et al., 1978 and Sikorska et al.,2004)**. Among the Vinca alkaloids, vincristine appears to offer the best results with fewer side effects **(Robertson and McCarthy, 1969).**

Patients with primary immune thrombocytopenia (ITP) may require treatment to reduce the risk of serious bleeding if platelets remain consistently low. While approximately 70-80% of patients respond to an initial course of corticosteroids, relapse is common. For steroid-refractory patients, there is a choice between surgical splenectomy and further medical treatments, based on many factors including the patient's bleeding history, fitness for surgery, comorbidities, tolerance of adverse events, lifestyle and preferences **(Stasi et al ., 2010)**. Splenectomy is currently employed as a second line therapy; however it is ineffective in about 30–40% of the cases. Also these therapies present an increasing risk for opportunistic infection and post surgical complications during their treatment courses and adversely affect the overall outcomes**(Stasi et al ., 2010).**

The decision whether to proceed to splenectomy or try other medical therapies in corticosteroid-refractory ITP patients remains patient-specific. Splenectomy has its risks (including perioperative and long-term risks), and relapse/non response are relatively common, but it offers the possibility of cure in the majority of patients. However, newer treatments may potentially allow splenectomy to be deferred for prolonged periods, as well as providing alternative treatment options for patients who fail splenectomy**(Stasi et al ., 2010).**

Currently, there is a trend towards a decreased rate of splenectomy in ITP **(George, 2006).** Although a safe procedure in the vast majority of patients, complications include surgical mortality, thromboembolic events, and overwhelming sepsis, and the long-term effects remain poorly understood **(Dolan et al, 2007).** With the emergence of alternative therapies, clinicians increasingly consider delaying splenectomy until later in the course of the disease to allow more time for spontaneous resolution **(Cooper *et al* ., 2002 , George et al., 2003 and Kuter et al, 2008).** Thus, it is essential to evaluate the role of vincristine in treating (splenectomized and non splenectomized) refractory ITP patients who are resistant to corticosteroids therapy or who have contraindications to their use with no available other lines of treatment especially with higher costs of other lines

of treatment as immunoglobulin and also to assess the long term (6 months) follow up platelet count after stoppage of vincristine treatment.

This study included twenty nine refractory ITP patients with maximum dose of corticosteroids and even after high dose of dexamethason (21 of them non-splenectomized "group I" and the remaining 8 splenectomized " group II") were treated with two- hour intravenous infusion of vincristine (1-2 mg) once a week for 6 weeks . In every patient, the platelet count was evaluated just before and after the infusion of vincristine , follow up of those patients for 6 months after stoppage of vincristine were evaluated by platelet count every 2 months . Patients with hepatitis and chronic liver diseases were excluded from this study.

The results of this study were in agreement with the majority of studies, which mostly showed a rise in the platelet count in refractory ITP patients treated with vincristine. This result found that the mean platelet count increased significantly among non splenectomzed patients after the use of vincristin , this in agreement with **Sikorska et al.,2004** study, who reported , a rise in the platelet count of at least 100×10^9/L with statistically significant improvement ($P < 0.01$) in refractory ITP patients treated with vincristine, also with **Cervantes et al., 1980 and Linares et al., 1988** who reported that vincristine may be the therapy of choice in the management of refractory ITP and with **Matsushima et al.(1992)** who reported that vincristine therapy was considered to be an useful treatment in elderly patients with ITP. The same results were observed in **Szczepanik et al. (2007**) study in their evaluation of the efficacy of vinca alkaloids in preparing adult corticosteroid refractory chronic ITP patients for splenectomy and they reported that 75% of their treated patients the platelet count increased to $\geq 80 \times 10^9$/l, which allowed safe splenectomy and they added that , matching of vincristine costs with treatment efficacy and comparison with similar costs for intravenous immunoglobulin treatment revealed many folds lower costs of the vincristine method.

This results were to some extent in agreement with **Fenaux et al. (1990)** who concluded that slow infusions of vincristine may be a useful approach in ITP of recent onset, but they added that in their experience, this treatment has limited benefit in chronic ITP , in contrary to our results in which our patients were chronic ITP and showed good response .Also our result partially in agreement with **Simon et al.(1987)** who reported a complete remission in all ITP patients after vincristine therapy but in our study not all patient get in complete remission.Treatment of patients' refractory to splenectomy (with absence of response or relapse after initial response) is difficult, and their long-term outcome is not well known **(Bourgeois et al., 2003).**

So it was important to study the effect of vincristine in splenectomized refractory ITP patients.Our results showed a significant increase of the mean platelet count in splenectomized refractory ITP patients after the 3^{rd},4^{th} ,5^{th} and 6^{th} weeks of vincristine treatment , this results were in agreement with **Bethan and James.(2008)** who stated that A proportion of patients will be truly refractory to splenectomy, and require further treatment with immunosuppressive second-line therapies as vincristine **.**This results also were to some extent in agreement with **Shvidel et al.(2006)** who used vincristine-loaded platelet infusion in patients with refractory (ITP)who failed to respond to two to six different treatment modalities, including corticosteroids and splenectomy**,** their results suggested that this inexpensive and well-tolerated treatment may be a useful approach in patients with ITP and with **Simon et al.(1987)** who reported a good response with vincristine treatmnt In 12 cases of refractory chronic ITP (of whom 10 had been splenectomized) **.**

This study revealed that vincristine may be effective line of treatment in referactory splenectomized patients than non splenectomized patients and this differences was noted significantly after the 4^{th} week of vincristine treatment ($p< 0.05$) , more studies needed to confirm this result as no available studies compared those groups of patient . But it has been pointed out in **Ries. (1976)** that vincristine could be more effective in splenectomized patients**.**

In this study a persistent increase of the mean platelet count was observed in both groups of patients after stoppage of vincristine treatment for 6 months when compared with the mean platelet count before the use of vincristin treatment , these results were in agreement with **Linares et al.(1988)** who reported that referactory ITP patients showed a return to normal platelet counts maintained for 3 months or longer after vincristine treatment.Also these results were partially in agreement with **Manoharan. (1986)** study who reported that Vincristine therapy appears to be therapeutically beneficial and can achieve sustained recovery of platelet count in patients with ITP of less than six months duration , in contrary to this result in which good response maintained up to 6 months after stoppage of vincristine therapy .This may be explained by that their patients were 10 patients only and they received vincristine at weekly intervals for 4 weeks only in contrary of our patients who received vincristine for 6 weeks . The duration of vincristine treatment may play a role in sustained recovery of platelet count and this point need more studies?

These results disagree with that of **Kueh. (1982)** who reported the duration of platelet response to vincristine without concomitant azathioprine therapy was less than 10 weeks in contrary to this result in which sustained recovery of platelet count maintained up to 6 months after stoppage of vincristine therapy .This may be explained by that their patients were 12 patients and they received weekly (1 mg) vincristine injections to a cumulative dose not greater than 3 mg, but in this study we use vincristine (1-2 mg) up to 6 weeks. The duration

of vincristine treatment in addition of the cumulative dose of vincristine may play a role in sustained recovery of platelet count.

Higher mean value of platelet count was observed after 4 and 6 months of stoppage of vincristine treatment among splenectomized more than non splenectomized patients, this comparison was statistically significant after 2 months of stoppage of vincristine treatment ($p< 0.05$). It seems to be that splenectomized ITP patients may has sustained recovery of platelet after vincristine stoppage more than non splenectomized patients, more studies needed to confirm this result as no available studies compared those groups of patient

V. Conclusion:

Administration of vincristine to chronic corticosteroid refractory immune thrombocytopenia (ITP) patients result in increase platelet count to a significant level and could be used in situations requiring increase of the platelet count in patients who failed to response to maximum dose of corticosteroid-therapy and or splenectomy, especially with limited resources with no available other lines of treatment and also in patients who in need to do surgical intervention.

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