ORIGINAL ARTICLE

# Corticosteroid side-effects and risk for bleeding in immune thrombocytopenic purpura: patient and hematologist perspectives

Jacqueline A. Guidry[1,2,3], James N. George[1,2], Sara K. Vesely[1], Shelia M. Kennison[3], Deirdra R. Terrell[1]

[1]Department of Biostatistics & Epidemiology, College of Public Health University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA; [2]Department of Medicine, College of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA; [3]Department of Psychology, Oklahoma State University, Stillwater, OK, USA

## Abstract

*Objectives:* The purpose of this study was to examine hematologist and patient perspectives about the side-effects of the corticosteroid treatment of immune thrombocytopenic purpura (ITP) and their perspectives about the patient's risk for bleeding. The specific aim was to compare patient and hematologist perspectives and, if a difference was documented, the implications of that difference. We hypothesized that patients with ITP may have more concern about corticosteroid side-effects and less concern about serious bleeding than hematologists. *Methods:* We surveyed 80 patients in the Oklahoma ITP Registry and all 83 hematologists in Oklahoma about the occurrence and severity of 18 corticosteroid side-effects and risks for serious bleeding. *Results:* Response rates were 80% (patients) and 71% (hematologists). Responses of patients and hematologists were significantly different from each other regarding both the frequency of severe corticosteroid side-effects and the risk of serious bleeding. For 13 of the 18 corticosteroid side-effects, patients reported more frequent occurrence of severe symptoms than hematologists ($P < 0.05$); physicians reported more frequent occurrence for one side-effect ($P < 0.05$). Conversely, 69% and 93% of hematologists reported being very worried about serious bleeding when responding to two case scenarios describing patients with platelet counts of 10 000/$\mu$L and 5000/$\mu$L ($P < 0.05$), compared with only 16 (31%) of 51 patients whose lowest platelet count had been <10 000/$\mu$L. *Conclusion:* Awareness of the different opinions about corticosteroid side-effects and risk for bleeding between ITP patients and hematologists may improve management decisions.

**Key words** immune thrombocytopenic purpura; corticosteroids; steroids; bleeding

**Correspondence** Deirdra R. Terrell, PhD, The University of Oklahoma Health Sciences Center, Room CHB 358, PO Box 26901, Oklahoma City, OK 73126-0901, USA. Tel: (405) 271-4222; Fax: (405) 271-6444; e-mail: deirdra-terrell@ouhsc.edu

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Corticosteroids are the standard initial treatment for adults with immune thrombocytopenic purpura (ITP) because of their effectiveness for increasing the platelet count, their low cost and convenience (1–3). For most patients with ITP, the platelet count response only lasts as long as the corticosteroids are continued. The duration of corticosteroid treatment is not standardized; it is often continued for 3–4 wk, or until side-effects become intolerable (3), because subsequent therapies appear to have greater risks.

Patients with ITP are typically healthy except for their low platelet count and resulting risk for excessive bleeding. When they first learn of their diagnosis of ITP patients may be worried about their bleeding symptoms, but with time their experience often provides confidence that the risk for serious bleeding may be minimal (4). As most patients have a benign clinical course (5), their concern for serious bleeding decreases and tolerance for the side-effects of corticosteroid treatment also decreases (4). Patients may begin to question whether the side-effects of corticosteroid treatment are worse than their disease (4, 6).

ITP is uncommon; prevalence has been estimated to be 9.5 (7), 23.6 (8) and 11.2 (9) patients per 100 000 population. Therefore, hematologists' experience may be

limited and patients' low platelet counts may be alarming. From the hematologists' perspective, continued corticosteroid treatment to maintain a higher platelet count may be justified to prevent potentially life-threatening bleeding in an otherwise healthy person. To hematologists, the side-effects of corticosteroid treatment may seem less dangerous than the potential for serious bleeding.

Therefore, patients with ITP may have more concern about corticosteroid side-effects and less concern about serious bleeding than hematologists. These different perspectives may cause conflicting goals for management. To understand this potential conflict, we documented the opinions of ITP patients and hematologists about the side-effects of corticosteroid treatment and the risks of serious bleeding.

## Methods

### Patients

Our goal was to assess the opinions of all patients in the Oklahoma ITP Registry; therefore patients were included who had experienced ITP either as children or adults. The Registry was initiated in 2004 by contacting all hematologists for both adults and children in the State of Oklahoma, asking them to provide consent forms and enrollment questionnaires to their patients with ITP. The Registry has enrolled 92 patients. Complete data concerning their experience with ITP are recorded initially and patients are contacted annually to document current health and treatments. This study was limited to 82 (89%) of the 92 registered patients who were at the age of 16 yr or older at the time of the survey and who had reported taking corticosteroids for at least 1 wk. One patient who had died was excluded. Questionnaires were sent to 81 patients.

### Hematologists

Our goal was to assess the opinions of all hematologists in the State of Oklahoma; therefore hematologists for both children and adults were included. Hematologists in the State of Oklahoma were identified by searching the websites of the Oklahoma Board of Medical Licensure and Supervision as well as the American Osteopathic Association for physicians who listed hematology, oncology, hematology/oncology or pediatric hematology/oncology as their specialty (all are described as hematologists in this study). In March 2008, 97 hematologists were identified who had active licenses to practice in Oklahoma; 14 were excluded because they did not care for patients with ITP (surgical oncologists, pathologists, researchers, administrators). Questionnaires were sent to 83 hematologists.

Based on the selection criteria for patient and hematologist participants, it is probable, although not required, that the patients surveyed for this study were treated by the hematologists who were surveyed for this study.

### Corticosteroid side-effects

The list of side-effects included in the questionnaires sent to patients and hematologists was compiled from (i) data previously collected from Registry patients, who are asked as part of their enrollment and follow-up to list the corticosteroid side-effects they had experienced, (ii) the experience of the authors and (iii) a systematic literature search. Ovid software was used to search the MEDLINE database using (i) corticosteroid side-effects as keywords, combined with (ii) keywords and MeSH terms for ITP (*purpura*, *thrombocytopenic*; *purpura, thrombocytopenic*, *idiopathic*; *immune thrombocytopenic purpura*; *autoimmune thrombocytopenic purpura*) and (iii) keywords and MeSH terms for corticosteroids (*glucocorticoids*, *prednisone*, *prelone*, *solumedrol*, *corticosteroids*, *methylprednisolone hemisuccinate*, *methylprednisolone*, *dexamethasone*, *prednisolone*, *prednisolone syrup*). Each individual corticosteroid side-effect term was searched in combination with the terms for both ITP and corticosteroids. Each article identified by a combination of a side-effect term, an ITP term and a corticosteroid term, was reviewed for additional corticosteroid side-effects and also their bibliographies were searched for additional articles. Additional identified corticosteroid side-effects were then added to the search process. The search was limited to humans and English language.

Sixty-five corticosteroid side-effects were identified: wounds, injuries, hematoma, contusions, bruising, petechiae, purpura, Cushing syndrome, moon face, red face, facial swelling, swelling, ballooning, puffiness, bloating, stretch marks, fluid retention, water retention, hunger, weight gain, increased appetite, acne, hair loss, depression, vertigo, dizziness, fainting, syncope, headache, shaky, light-headed, anxiety, nervousness, stress, irritability, restlessness, sleep disorders, insomnia, trouble sleeping, anger, hostility, hot flushes, sweating, visual problems, light sensitivity, decreased visual acuity, bodily pain, osteoporosis, joint stiffness, generalized weakness, fatigue, muscle weakness, muscular diseases, muscular atrophy, muscle cramps, upset stomach, nausea, vomiting, diarrhea, hypertension, high blood pressure, diabetes, blood glucose, immunosuppression, lowered immune system. Of these 65 terms, 38 were included in 18 symptom groups listed on the questionnaires. For our analysis, these 18 symptom groups were referred to as individual corticosteroid side-effects. Twenty-seven side-effect terms were omitted for three reasons: (i) they were redundant with the selected terms (for example, Cushing

 

syndrome, facial swelling, red face, ballooning and puffiness were redundant with the symptom group that included moon face, bloating and swelling); (ii) they overlapped with the side-effects of ITP itself (such as purpura, petechiae, bruising, contusions, hematoma); or (iii) they may not be apparent to a patient (such as immunosuppression).

### Questionnaires

Questionnaires were sent by mail to the patients; if they did not respond after 1 month, they were contacted by phone to ask for their participation. If they agreed, they were given the option to complete the survey over the phone or to receive another mailed questionnaire. If there was no response to the second mailing, the process of contacting participants by phone was repeated two more times. The hematologist questionnaires were initially sent by fax, usually to a nurse or office manager. If hematologists did not respond after 1 month, they were reminded by email from one of the authors (J.N.G.), with the questionnaire attached. If there was still no response, the email process was repeated two more times.

Questionnaires sent to patients and hematologists contained the same list of corticosteroid side-effects and the same scale to estimate severity (Tables 1 and 2). For each of the 18 side-effects, the patient or hematologist could respond that side-effect had not been experienced, for a score of 0; if the side-effect had been experienced, the severity was scored with a range from 1 ('did not bother') to 4 ('bothered a lot') (Tables 1 and 2). For each responder, the number of side-effects that had been experienced was recorded; also an overall severity score was calculated as the sum of the responses for each side-effect, with a maximum score of 18 times 4, or 72. For both the number of side-effects and the overall severity score, missing data were recorded as a zero, which was 'did not experience'; missing values were minimal. Coding the data as zero resulted in a conservative estimate of both of these values. Additional survey questions for the patients and hematologists are shown in Tables 1 and 2.

**Table 1** The survey for patients (in addition to the questions shown here, the questionnaire also asked for the current age and age at diagnosis)

1. What was your lowest platelet count?
   [__] Less than 10 000
   [__] 10 000–30 000
   [__] 30 000–50 000
   [__] More than 50 000
2. How long was your longest duration of prednisone or other steroid treatment for ITP?
   [__] Less than 1 month
   [__] 1–3 months
   [__] 4–6 months
   [__] 7–12 months
   [__] More than 12 months
3. Side-effect assessment: Fill-in the following table based on your longest duration of steroid treatment described in the question above. For each side-effect, indicate the severity with which you feel the side-effect impacted your life by rating it on a scale from 0 to 4 using the following scale. Choose one answer per side-effect.
   0 – I did not experience these side-effects
   1 – These side-effects did not bother me
   2 – These side-effects bothered me a little
   3 – These side-effects bothered me sometimes
   4 – These side-effects bothered me a lot
4. Do you feel your doctor paid an appropriate amount of attention to the side-effects you experienced?
   [__] Never
   [__] Rarely
   [__] Sometimes
   [__] Often
5. Bleeding risks. How concerned were you about serious bleeding? By serious bleeding, we mean severe or life-threatening bleeding.
   [__] I was not at all worried
   [__] I was rarely worried
   [__] I was sometimes worried
   [__] I was very worried

### Statistical methods

Calculations were performed in MICROSOFT EXCEL or SAS v9.1 (Cary, NC, USA). Significance was determined by an alpha of 0.05. For the patients, the relationship between the duration of corticosteroid treatment and the mean number and mean severity of side-effects was determined by analysis of variance. Analysis of variance was also used to compare the mean number and mean severity score of corticosteroid side-effects across the categories of the hematologists' length of practice and separately across the categories of the number of ITP patients seen. The patients' and hematologists' responses about the severity of corticosteroid side-effects and the risk for severe bleeding were compared with chi-squared tests.

### Ethics approval

This study and the Oklahoma ITP Registry were approved by the Institutional Review Board of the University of Oklahoma Health Sciences Center.

## Results

### Patients' responses

One patient responded that he could not remember his corticosteroid treatment. Sixty-four (80%) of the

 

**Table 2** The survey for hematologists (in addition to the questions shown here, the questionnaire also asked how long the hematologist had been in practice and how many patients with ITP he/she saw each year)

1. How long have you been practicing medicine?
   [__] Less than or equal to 5 yr
   [__] 6–10 yr
   [__] 11–15 yr
   [__] 16–20 yr
   [__] More than 20 yr
2. How many ITP patients do you see each year?
   [__] None
   [__]<5 patients
   [__] 5–20 patients
   [__] >20 patients
3. Side-effect assessment: Indicate the severity with which you feel the following side-effects impact the quality of life of ITP patients by rating it on a scale from 0 to 4 using the following scale.
   Only rank the side-effect if it is a result of the corticosteroid treatment of ITP. If you feel the side-effect is caused by something other than corticosteroid treatment, please circle a zero for that side-effect. Choose one answer per side-effect.
   0 – ITP patients do not experience this side-effect
   1 – This side-effect does not bother ITP patients
   2 – This side-effect bothers ITP patients a little
   3 – This side-effect bothers ITP patients sometimes
   4 – This side-effect bothers ITP patients a lot
4. Bleeding risks: For the following scenarios, please rank how much you are worried about the patient's risk for serious bleeding. By serious bleeding, we mean severe or life-threatening bleeding. Choose only *one* answer for each question.

A. A 35-yr old woman has had minor bruising and prolonged menstrual periods. On physical examination, she has mild petechiae on her ankles and legs. She is not taking any medications.
   Her platelet count is 10 000/$\mu$L.
   [__] Not at all worried
   [__] Rarely worried
   [__] Sometimes worried
   [__] Very worried

B. A 35-yr-old woman. On physical examination, she has blood blisters in her mouth and gum bleeding. She is not taking any medications. Her platelet count is 5000/$\mu$L.
   [__] Not at all worried
   [__] Rarely worried
   [__] Sometimes worried
   [__] Very worried

remaining 80 patients completed the questionnaires; 46 (72%) of the responding patients currently live in Oklahoma. The total number of ITP patients in Oklahoma is 408 (9), estimated from the Oklahoma prevalence of ITP (9) and the 2008 population of Oklahoma [3 642 361 (10)]. Therefore, the 46 responding patients living in Oklahoma represent 11% of all ITP patients in the State. Fifty (78%) of the 64 patients were women. The mean interval from their diagnosis to the completion of the questionnaire was 11 yr (range 2–34 yr). The patients' mean age at the time they completed the survey was 51 yr (range 19–83 yr). The patients' mean age at the time of their diagnosis with ITP was 39 yr (range 5–75 yr); nine (14%) of the 64 patients who responded were diagnosed with ITP when they were children less than 18 yr old. We combined the results of all patient responses because children were represented across all durations of corticosteroid treatment. The longest duration of corticosteroid treatment was less than 1 month for one (2%) patient, 1–3 months for 14 (22%) patients (including 2 children), 4–6 months for 14 (22%) patients (three children), 7–12 months for 16 (25%) patients (three children) and more than 12 months for 19 (30%) patients (one child). The lowest platelet count that patients had experienced during the course of their ITP was less than 10 000/$\mu$L for 51 (80%) patients, 10 000–30 000/$\mu$L for 10 (15%) patients and greater than 30 000/$\mu$L for three (5%) patients.

The patients' perceptions about the side-effects of corticosteroid treatment are presented in Table 3. There was a significant association between the duration of corticosteroid treatment and the mean number of side-effects experienced ($P = 0.005$). Patients who received corticosteroid treatment for 3 months or less reported experiencing a mean of 8.5 side-effects; 4–6 months, 11.3 side-effects; 7–12 months, 12.4 side-effects; and greater than 12 months, 13.8 side-effects. There was also a significant association between the duration of corticosteroid treatment and the mean severity score of the side-effects ($P = 0.0003$). The average severity score for patients treated for 3 months or less was 25; 4–6 months, 37; 7–12 months, 41; and greater than 12 months, 49.

Thirty-six (59%) of 61 patients responded that their doctor often paid an appropriate amount of attention to their corticosteroid side-effects; the responses of the remaining 41% of patients were divided evenly among the three other answer choices on the questionnaire (sometimes, rarely and never) (Table 1).

Fifty-one (80%) of the patients reported that their lowest platelet count was less than 10 000/$\mu$L; however, only 16 (31%) of these 51 patients responded that they had been very worried about serious bleeding. Seventeen (33%) responded that they were sometimes worried, 13 (26%) rarely worried and five (10%) not at all worried (Fig. 2).

### Hematologists' responses

Fifty-nine (71%) of the 83 hematologists completed the questionnaires; nine (15%) of 59 responding hematologists were pediatricians. As we did not anticipate a difference between the responses of hematologists for children and adults and because the responses of these two

**Table 3** Patient and hematologist responses regarding experience with side-effects of corticosteroids (side-effect descriptions are listed as they were in the questionnaires; for each side-effect, patients and hematologists selected one response, as directed by the question 3 in Tables 1 and 2)

| Side-effect (no. patients and physicians responding) | Did not experience | Did experience (amount of bother) | | | |
|---|---|---|---|---|---|
| | | None | Little | Sometimes | A lot |
| *Appearance* | | | | | |
| 1. Moon face, bloating, swelling | | | | | |
| Patients (63) | 4 | 3 | 6 | 7 | 43 |
| Hematologists (58) | 0 | 2 | 11 | 18 | 27 |
| 2. Weight gain/increased appetite | | | | | |
| Patients (64) | 6 | 6 | 6 | 5 | 41 |
| Hematologists (59) | 0 | 0 | 10 | 18 | 31 |
| 3. Hair loss | | | | | |
| Patients (63) | 26 | 5 | 10 | 9 | 13 |
| Hematologists (58) | 23 | 13 | 13 | 6 | 3 |
| 4. Acne | | | | | |
| Patients (64) | 35 | 4 | 7 | 7 | 11 |
| Hematologists (58) | 8 | 10 | 21 | 17 | 2 |
| 5. Stretch marks | | | | | |
| Patients (61) | 31 | 7 | 6 | 7 | 10 |
| Hematologists (58) | 5 | 12 | 19 | 14 | 8 |
| *Emotional symptoms* | | | | | |
| 6. Insomnia, restlessness and/or trouble sleeping | | | | | |
| Patients (61) | 11 | 4 | 9 | 9 | 28 |
| Hematologists (59) | 1 | 2 | 9 | 30 | 17 |
| 7. Anxiety and/or nervousness | | | | | |
| Patients (62) | 9 | 2 | 11 | 16 | 24 |
| Hematologists (59) | 0 | 6 | 15 | 29 | 9 |
| 8. Depression and/or stress | | | | | |
| Patients (63) | 8 | 3 | 10 | 19 | 23 |
| Hematologists (59) | 2 | 11 | 19 | 23 | 4 |
| 9. Anger and/or irritability | | | | | |
| Patients (63) | 13 | 4 | 9 | 16 | 21 |
| Hematologists (58) | 1 | 5 | 15 | 28 | 9 |
| *Physical symptoms* | | | | | |
| 10. Generalized weakness, fatigue | | | | | |
| Patients (63) | 16 | 2 | 7 | 16 | 22 |
| Hematologists (59) | 1 | 11 | 18 | 22 | 7 |
| 11. Muscle weakness | | | | | |
| Patients (63) | 22 | 3 | 7 | 15 | 16 |
| Hematologists (59) | 1 | 11 | 15 | 25 | 7 |
| 12. Body pain (joint stiffness, muscle cramps, osteoporosis) | | | | | |
| Patients (63) | 15 | 4 | 10 | 11 | 21 |
| Hematologists (59) | 8 | 11 | 21 | 18 | 0 |
| 13. Hot flushes and/or sweating | | | | | |
| Patients (63) | 19 | 3 | 15 | 9 | 17 |
| Hematologists (57) | 8 | 10 | 20 | 18 | 2 |
| 14. Visual problems (light sensitivity/decreased visual acuity) | | | | | |
| Patients (63) | 23 | 6 | 9 | 14 | 11 |
| Hematologists (58) | 13 | 17 | 21 | 5 | 2 |
| 15. Nausea, upset stomach, vomiting, diarrhea | | | | | |
| Patients (62) | 31 | 5 | 9 | 10 | 7 |
| Hematologists (57) | 8 | 10 | 23 | 14 | 2 |
| 16. Dizziness, headaches | | | | | |
| Patients (61) | 22 | 4 | 13 | 16 | 6 |
| Hematologists (58) | 14 | 17 | 21 | 6 | 0 |
| *Other side-effects* | | | | | |
| 17. Trouble with blood glucose levels, diabetes | | | | | |
| Patients (61) | 45 | 5 | 2 | 3 | 6 |
| Hematologists (58) | 2 | 0 | 13 | 21 | 22 |
| 18. High blood pressure | | | | | |
| Patients (62) | 41 | 6 | 6 | 5 | 4 |
| Hematologists (55) | 4 | 10 | 17 | 23 | 1 |

groups of hematologists were similar for both the number and severity of the corticosteroid side-effects and for the risk of bleeding, we combined the results for all hematologists' responses for our analyses. Ten (17%) hematologists responded that they had been in practice for 5 or fewer years; 13 (22%), 6–10 yr; 5 (9%), 11–15 yr; 12 (20%), 16–20 yr and 19 (32%), more than 20 yr. No hematologists responded that they did not see any ITP patients; 25 (42%) reported they saw less than five ITP patients each year; 29 (49%), 5–20 ITP patients each year; and five (9%), more than 20 ITP patients each year. There was no significant association of the hematologists' duration of practice or the number of ITP patients they saw each year and their report of either the mean number or mean severity of corticosteroid side-effects ($P > 0.05$).

In response to case scenarios (Table 2), 40 (69%) of 58 hematologists reported that they would be very worried about serious bleeding in a patient with mild petechiae and a platelet count of 10 000/$\mu$L and 54 (93%) of 58 would be very worried about serious bleeding in a patient with blood blisters in her mouth and gum bleeding and a platelet count of 5000/$\mu$L (Fig. 2).

### Comparison of patients' and hematologists' responses

Compared with hematologists, the patients more frequently responded that the corticosteroid side-effects caused a lot of bother, which was the greatest level of severity on the questionnaire (Table 3). These data are illustrated in Fig. 1, demonstrating that patients reported the occurrence of severe bother more often than hematologists for 17 of the 18 corticosteroid side-effects included in the questionnaire (Fig. 1); the difference between the patients' and hematologists' perceptions was significant ($P < 0.05$) for 13 side-effects. The only corticosteroid side-effect for which hematologists' more frequently ($P < 0.05$) reported the occurrence of the greatest severity was trouble with blood glucose levels and diabetes.

Patients and hematologists also had significantly different responses about the risk of serious bleeding (Fig. 2) ($P < 0.05$). Among the 51 patients whose lowest platelet count had been less than 10 000/$\mu$L, responses were about evenly divided among the choices of rarely, sometimes or very worried. In contrast, most hematologists were very worried about the risk of serious bleeding in patients in both case scenarios, describing patients with platelet counts of 10 000/$\mu$L and 5000/$\mu$L.

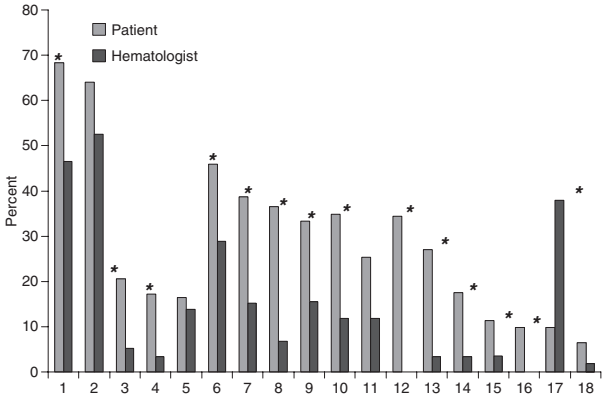


**Figure 1** Comparison of patients' and hematologists' responses to questions about the occurrence of the most severe problems of corticosteroid side-effects. The data illustrate the per cent of patients and hematologists who responded that the corticosteroid side-effect caused a lot of bother, the most severe category in the questionnaire (question 3, Tables 1 and 2). *Significant difference ($P < 0.05$) between the patients' and hematologists' responses. These data are also presented in Table 3. The numbers identifying each side-effect correspond to the numbers of the side-effects in Table 3.

| Appearance, symptoms | Emotional symptoms | Physical symptoms | Other side-effects |
|---|---|---|---|
| 1. Moon face, bloating, swelling | 6. Insomnia, restlessness and/or trouble sleeping | 10. Generalized weakness, fatigue | 17. Trouble with blood glucose levels, diabetes |
| 2. Weight gain/ increased appetite | 7. Anxiety and/or nervousness | 11. Muscle weakness | 18. High blood pressure |
| 3. Hair loss | 8. Depression and/or stress | 12. Body pain (joint stiffness, muscle cramps, osteoporosis) | |
| 4. Acne | 9. Anger and/or irritability | 13. Hot flushes and/or sweating | |
| 5. Stretch marks | | 14. Visual problems (light sensitivity/ decreased visual acuity) | |
| | | 15. Nausea, upset stomach, vomiting, diarrhea | |
| | | 16. Dizziness, headaches | |

## Discussion

This study was based on two hypotheses: (i) patients with ITP are more affected by the side-effects of corticosteroids than their hematologists recognize; (ii) physicians are more concerned about the risk for serious bleeding than their patients. These conflicting experiences and opinions may create a conflict for management of patients with ITP. Most patients with ITP have no serious bleeding in spite of severe thrombocytopenia (1–3, 5, 11). However, corticosteroid side-effects may be a major cause of morbidity (4). Because common corticosteroid side-effects, such as weight gain, fatigue and emotional

 

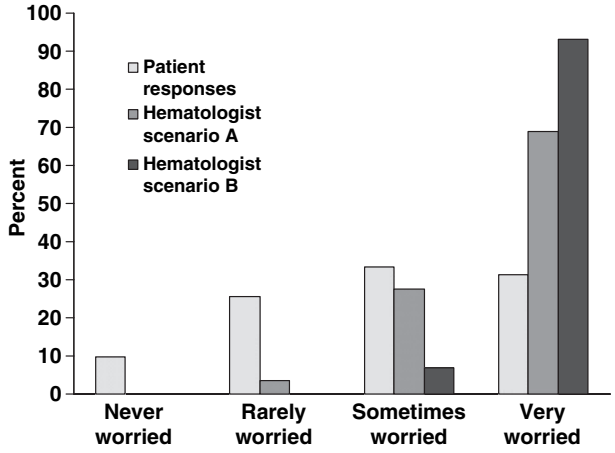


**Figure 2** Comparison of patients' and hematologists' responses to questions about the risk for serious bleeding. The data illustrate the responses of the 51 patients who reported that their lowest platelet count was less than 10 000/$\mu$L (Table 1, question 4) about their level of worry for the risk of serious bleeding. The data for hematologists are their responses about their level of worry for the risk of serious bleeding in two patient scenarios in the questionnaire (Table 2, question 4), that described (A) a patient with a platelet count of 10 000/$\mu$L with mild petechiae and (B) a patient with a platelet count of 5000/$\mu$L with blood blisters in her mouth and gum bleeding.

symptoms, are not specific, they may not be appreciated or attributed to corticosteroids by hematologists. Because most corticosteroid side-effects are reversible, hematologists may not consider them to be serious. And because corticosteroids are inexpensive and are typically effective for increasing the platelet count and therefore decreasing the risk for serious bleeding, they are often prescribed for prolonged periods.

Our hypotheses were supported by the data from the surveys of patients with ITP and hematologists who treat ITP. The patients more frequently reported severe corticosteroid side-effects than the hematologists and the hematologists expressed greater concern for serious bleeding than the patients. There are likely multiple reasons for the discrepancy between patients and hematologists regarding risk for bleeding. (i) Patients only know their own experience, while hematologists have experiences with ITP in multiple patients. Therefore, it may be possible that the hematologist has treated an ITP patient who had a severe or life-threatening bleeding event. Perhaps when deciding the course of treatment for the ITP patients, hematologists may be influenced by these rare, yet severe, cases. (ii) If a hematologist stops corticosteroid treatment and then the patient has a serious bleeding event, the hematologist would feel responsible and could be liable for malpractice. A fear of litigation could motivate the hematologists to be more concerned about the risk for bleeding than the patients.

These explanations could account for the potential conflict between ITP patients and their hematologists regarding the appropriate duration of corticosteroid treatment. Patients may want to stop corticosteroid treatment because the side-effects are not tolerable and they perceive that their risk for serious bleeding is small. Hematologists may want to continue corticosteroid treatment because the side-effects are reversible and they perceive that the risk for serious bleeding is substantial.

Previous studies have documented a high frequency of corticosteroid side-effects in patients with ITP (12, 13), which may contribute to the poor health-related quality of life reported by many patients with ITP (14, 15). Although responses of ITP patients and hematologists who treat ITP have not been previously compared, it has been established that physician assessments may underestimate patients' experiences with symptoms caused by immunosuppressive treatments (16). As patient-reported outcomes are increasingly used as study endpoints, including studies of ITP (15), documentation of data obtained from both patients and physicians is essential.

Although the interpretation of our data seems clear, it has important limitations. (i) The ITP patients in this study may not be representative of all ITP patients and therefore their responses may not be generalizable. Their responses, including the data that 80% had platelet counts less than 10 000/$\mu$L at some time during their course and that 77% had been treated with corticosteroids for more than three months, suggest that they may have been more severely affected and more intensively treated than many patients with ITP. (ii) The accuracy of the patients' responses may have been biased by their recall of past experience, because the average interval from their diagnosis with ITP to the completion of the questionnaire was 11 yr, and most treatment with corticosteroids may have been early in the course of their ITP. (iii) The patient group was heterogeneous, including some patients whose ITP had resolved, some whose ITP remained symptomatic and some who had persistent thrombocytopenia without symptoms. For some patients, the status of their ITP was not known. (iv) The patients' and hematologists' responses may not be comparable. The patients' responses reflected their individual experience while the hematologists' responses reflected their total experience with all of their patients and perhaps also didactic material. (v) For the questions about concern for serious bleeding, hematologists responded to scenarios that described actual bleeding; patients may have had no or only minimal bleeding symptoms. (vi) Also patients may report less worry about the risk for serious bleeding if they are responding to the survey some years after they have recovered from ITP. (vii) Hematologists who treat children were combined with hematologists who treat adults and the clinical course of ITP in children is distinct from ITP in adults (1, 2).

 

Hematologists for both children and adults were included in our survey to provide a comprehensive assessment, and also because 14% of patients in this study were diagnosed with ITP as children.

This study also had important strengths: (i) the response rate for the surveys was high for both patients and hematologists; (ii) the data for hematologists represented 71% of all practicing hematologists within a defined geographic region at this time; (iii) the survey questions regarding corticosteroid side-effects were identical for both patients and hematologists.

These surveys document the importance of effective communication between ITP patients and their hematologists. Even though most patients responded that they felt their physician often paid an appropriate amount of attention to their steroid side-effects, the differences between patients and hematologists in their perception of the number and severity of corticosteroid side-effects experienced by ITP patients suggests that communication may be improved. A measure to enhance effective communication would be a routine questionnaire, similar to the questionnaire in this study. This could be completed by ITP patients at each visit to their hematologist, to document the occurrence and severity of corticosteroid side-effects. Hematologists could provide information to their patients to help them to anticipate and understand corticosteroid side-effects (17). Management of the ITP may then be more effectively based on shared decision-making (6, 18).

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## Conflict of interest

The authors have no conflicts of interest for the material in this manuscript.

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