Low-dose aspirin before spinal surgery: results of a survey among neurosurgeons in Germany

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Abstract The main problem faced by the increasing numbers of patients presenting for spinal surgery are receiving concurrent medication with low-dose aspirin, leading to dysfunctional circulating platelets. The contribution of low-dose aspirin to increased peri-operative risk of bleeding and blood loss is a contentious issue with conflicting published results from different surgical groups. Data from neurosurgical spine patients is sparse, but aspirin has been identified as an important risk factor in the development of post-operative hematoma following intracranial surgery. We surveyed the opinions and working practices of the neurosurgical facilities performing spinal operations in Germany regarding patients who present for elective spinal surgery. Identical questionnaires were sent to 210 neurosurgical facilities and proffered five main questions: (1) the adherence of any policy of stopping aspirin pre-operatively, (2) the personal risk assessment for patients with spinal surgery under low-dose aspirin medication, (3) the preferred method of treatment for excessive bleeding in this context, (4) personal knowledge of hemorrhagic complications in this group of patients, and (5) the characteristics of the neurosurgical units concerned. There were 145 (69.1%) responses of which 142 (67.6%) were valid. Of the respondents, 114 (80.3%) had a (written) departmental policy for the discontinuation of pre-operative aspirin treatment, 28 (19.7%) were unaware of such a policy. The mean time suggested for discontinuation of aspirin pre-operatively was 6.9 days (range: 0–21 days), with

seven respondents who perform the operations despite the ongoing aspirin medication. Ninety-four respondents (66.2%) considered that patients taking low-dose aspirin were at increased risk for excessive peri-operative hemorrhage or were indetermined (8.6%), and 73 (51.4%) reported having personal experience of such problems. Ninety-two respondents (65.5%) would use special medical therapy, preferably Desmopressin alone or in combination with other blood products or prohemostatic agents (46.1%), if hemorrhagic complications developed intra- or post-operatively. The average number of spinal operations per year in each service was 607.9 (range: 40–1,500). Despite the existence of distinct departmental policies concerning the discontinuation of low-dose aspirin pre-operatively in the majority of neurosurgical facilities performing spinal operations, there is a wide range of the moment of this interruption with an average of 7 days. Two-thirds of the respondents felt that aspirin was a risk factor for hemorrhagic complications associated with spinal procedures, and more than half of the interviewees reported having personal experience of such problems. Finally, various medicamentous methods of counteracting aspirin-induced platelet dysfunction and excessive bleeding in this context are elicited, discussed and evaluated.

Keywords Aspirin · Spine surgery · Hemorrhage · Survey · Desmopressin

Introduction

Aspirin is increasingly prescribed for its antithrombotic properties [18, 41, 49], and more patients are therefore

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presenting for elective spine surgery with dysfunctional circulating platelets.

Acetylsalicylic acid (ASA) irreversibly blocks the platelet cyclo-oxygenase enzyme system, preventing formation of thromboxane A₂ and inhibiting platelet aggregation for the life of the affected platelet (approximately 10 days) [28, 31, 37]. This block occurs even at the lowest therapeutic/prophylactic ASA dose usually prescribed, 81 mg/day [5, 6, 40]. Based upon the customary rate of platelet production, approximately 5–6 days are required after cessation of ASA to replace approximately 50% of the circulating platelets (10%/24 h). Because the ASA effect on individual platelets is complete, it cannot be reversed [5, 6].

The contribution of low-dose aspirin to increased peri-operative risk of bleeding and blood loss is a contentious issue with conflicting results published from different surgical groups [2, 3, 8, 9, 14, 20, 24, 30, 33, 35, 45, 46, 48–50, 53, 54, 56] and anesthesiologists performing regional or spinal anesthesia [15, 21–23, 43].

Data from neurosurgical spine patients is sparse [26, 27, 52], describing spontaneous hematoma associated with anticoagulant therapy in patients with spinal meningioma [51] or without [4, 7, 12, 19, 29, 55]. However, aspirin has been identified as an important risk factor in the development of post-operative hematoma following intracranial surgery [13, 25, 32, 36], not only in emergencies [40].

A wide range of literature is available focusing on pharmacological strategies to urgently counteract the aspirin-induced platelet dysfunction intra- and post-operatively [10, 11, 40], and to manage aspirin-associated bleeding in patients undergoing surgery [1, 16, 17, 28, 34, 38, 39].

We surveyed the opinions and working practices of the neurosurgical facilities performing spinal operations in Germany regarding patients taking low-dose aspirin medication who present for elective spinal surgery. With the aim to elicit the departmental policies, we exposed the personal risk assessment of bleeding and any personal experience with bleeding complications in this context. Furthermore, an overview and an evaluation of methods for counteracting the effect of antiplatelet agents are provided.

Materials and methods

Identical questionnaires with stamped addressed return envelopes were sent to 210 neurosurgical facilities in Germany. The current mailing list was provided by the German Society of Neurosurgery (DGNC), and included neurosurgical departments in hospitals as well

as all kinds of private practices performing spinal operations on an ambulant or in-patient basis.

The questionnaires were collected during 6 months, and no second demand was sent if no reply had been received after this period of time. The questionnaire consisted of questions designed to elicit information about: (1) adherence to any policy (either departmental or personal) for discontinuation of aspirin before elective spinal surgery, (2) the personal risk assessment for patients with spinal surgery under low-dose aspirin medication, (3) the preferred method of treatment of any hemorrhagic complications occurring after surgical hemostasis in this context, (4) any personal experience of intra- and post-operative bleeding complications in this group of patients and (5) the characteristics of the neurosurgical units and departments concerned (average number of spinal operations per year).

The data is expressed as percentages of the total number of returned valid questionnaires.

Results

Of the 210 questionnaires dispatched, 145 (69.1%) were returned, of which 142 (67.6%) were valid. Of the respondents, 114 (80.3%) had a (written) departmental policy for the discontinuation of pre-operative aspirin treatment or had a personal policy (Group I), 28 (19.7%) were unaware of such a policy or did not have a personal policy (Group II).

The mean time for discontinuation of aspirin pre-operatively was 6.9 days. In Group I, among those who had a policy, it was 7.3 days (range: 0–21 days), with one respondent who continues the aspirin medication until the time of operation. The mean time for discontinuation of aspirin in Group II was 6.9 days (range: 2–10 days), with six respondents who perform the operations despite the ongoing aspirin medication.

Ninety-four respondents (66.2%) felt that patients taking low-dose aspirin directly before elective spinal surgery were at increased risk of peri-operative hemorrhagic complications or were indetermined (8.6%). Eighty-three respondents in Group I (72.8%), and ten respondents (35.7%) in Group II estimated an increased risk for peri-operative hemorrhage in patients with low-dose aspirin medication and operative spinal procedures.

Seventy-three respondents (51.4%) reported having personal experience of patients with such problems requiring re-operation. Sixty-two interviewees in Group I (54.4%), and seven (25%) in Group II had personal experience with excessive peri-operative

hemorrhage in patients operated on with continued aspirin medication.

A total of 92 respondents (64.8%) would use special medical therapy, preferably Desmopressin alone or in combination with other blood products or prohemostatic agents (70.7%), if hemorrhagic complications developed intra- or post-operatively (Table 1). Fifty-seven respondents (50.1%) in Group I, as well as nine (32%) in Group II would prefer Desmopressin alone or in combination in case of hemorrhagic complications (Table 1).

The mean number of spinal operations per year in each neurosurgical facility was 608 [Group I, 688 (range: 60–1,500) and Group II, 582 (range: 40–1,200)].

Discussion

The question whether the pre-operative low-dose aspirin medication has to be stopped before elective spinal surgery has never been answered in the literature. Even more, because of the proximity of neural structures and an incalculable risk for neurological deficits it is almost impossible to find an answer by means of a prospective, randomized study. This differs from transurethral prostatectomy where Nielsen et al. [35] analyzed the effect of low-dose acetylsalicylic acid on bleeding in a prospective, randomized, double-blind, placebo-controlled study.

A postal survey among a manageable number of specialists familiar with this problem can be a tool to illuminate this controversial issue and to draw the attention to this subject. Needless to say, such a survey would not provide the exhaustive answer to the crucial question.

Comparable surveys

There are a limited number of comparable postal surveys performed in the last 10 years focussing on the

opinion and current practice of different surgical groups in view of the pre-operative use of antiplatelet agents [25, 47, 56]. James et al. [25] conducted a survey among 140 consultant neuroanesthetists in the UK asking for their policies, experience, risk-assessment and treatment of bleeding complication in the setting of low-dose aspirin and intracranial surgery. Two-thirds of the respondents (67.2%) were unaware of a policy for the discontinuation of pre-operative aspirin treatment and had no personal policy. The mean time suggested for discontinuation of aspirin before intracranial surgery was 11.3 days, with a wide range of 1–42 days. Almost half of the respondents (44.0%) considered that patients taking low-dose aspirin were at increased risk of excessive peri-operative cranial hemorrhage, and 12.9% neuroanesthetists reported having personal experience of such problems. The discrepancy between his results among neuroanesthetists and our findings among neurosurgeons is surprising even when considering the different surgical fields. Far more of his respondents had no policy concerning the low-dose aspirin discontinuation pre-operatively than ours (67.2 vs. 19.7%), but the mean time for the cessation was 4 days longer (11.3 vs. 6.9 days). Furthermore, the risk-assessment of the neuroanesthetists, not operating themselves, was lower than in the group of neurosurgeons performing spinal operations themselves (44.0 vs. 66.2%), and personal experience with bleeding complications in patients taking low-dose aspirin pre-operatively was stated much more often in the group of physicians, performing the operations by their own hands (51.4 vs. 12.9%), even when performed in the spinal, extracranial region.

There are two other surveys, one among vascular surgeons in the UK and one among transplantation centers in Germany in connection with pre-operative use of antiplatelet agents available [47, 56]. Smout and Stansby [47] sent questionnaires to vascular surgeons in the UK and found out that 77% to over 90% continue antiplatelet agents (clopidogrel and aspirin) peri-

Table 1 Practice of neurosurgeons in Germany with regard to correction of aspirin-induced platelet dysfunction during spine surgery

	Treatment method	Group I (%)	Group II (%)	Neurosurgeons surveyed (%)
Group I (<i>n</i> = 114) special aspirin-policy, Group II (<i>n</i> = 28) no aspirin-policy	Desmopressin (DDAVP)	50 (43.9)	8 (28.6)	58 (40.9)
	Nothing	37 (32.5)	13 (46.4)	50 (35.2)
	Fresh frozen plasma (FFP)	10 (8.8)	4 (14.3)	14 (9.9)
	DDAVP + FFP	5 (4.4)	1 (3.6)	6 (4.2)
	DDAVP + Aprotinin	2 (1.8)	0	2 (1.4)
	Aprotinin	1 (0.8)	0	1 (0.7)
	Platelets	1 (0.8)	0	1 (0.7)
	Other, unstated	8 (7.0)	2 (7.1)	10 (7.0)
		114 (100)	28 (100)	142 (100)

operatively, depending on the type of vascular surgery. Among the 38 transplantation centers in Germany surveyed by Werner et al. [56], only 7.9% refused to operate on aspirin-treated patients. The majority performs the transplantation of a kidney even though the patient has been treated with aspirin (daily dosage up to 100 mg), but at the same time an increased bleeding tendency is observed and tolerated in 34.2% of the centers. However, the authors recommend a pre-operative change in medication (e.g., heparin instead of aspirin) in elective surgery.

Assessment of bleeding-risk in various non-spinal surgical fields

The intra- and post-operative bleeding risk of various surgical procedures in patients taking low-dose aspirin medication has been evaluated by a broad range of investigators in their area of expertise. The majority of the results is controversial and rarely leads to clear recommendations and guidelines. Assia et al. [2] studied the association between chronic intake of aspirin and intra-operative bleeding during cataract surgery and the effect of discontinuing the medication before surgery. They stated that discontinuation of aspirin before cataract surgery is usually not indicated, because aspirin intake was not associated with significant intra-operative bleeding during these type of operations. A similar low risk of bleeding in patients with low-dose aspirin medication was observed by Shiffmann et al. [46] after endoscopic biopsy or polypectomy, and by Madan et al. [30] who conducted a prospective study and performed minor oral surgery in 51 patients without stopping daily low-dose aspirin therapy. When focusing on more invasive operative procedures, like in the topic of prostatectomy [35, 50, 54] and cardiac surgery [3, 8, 9, 14, 20, 33, 44, 45, 53], aspirin is a recognized risk factor contributing to excessive peri-operative bleeding and the need for re-operation. Watson et al. [54] identified aspirin ingestion, already in 1990, to be a significant etiological factor in post-prostatectomy hemorrhage, and Nielsen et al. [35] approved the same statement in a prospective, randomized, double-blind, placebo-controlled study 10 years later. They stated that although there was no significant difference in the median operative blood loss between patients receiving a transurethral prostatectomy either with or without pre-operative aspirin medication, the long-term low-dose ASA therapy is associated with a significant increase in the post-operative blood loss. Accordingly, they recommended a discontinuation of the ASA therapy 10 days before such an operation.

The statements become more controversial in the operative cardiovascular domain, where numerous publications exist regarding this topic [3, 8, 9, 14, 20, 33, 45, 53]. The majority of cardiovascular surgeons underline the negative effect of aspirin induced platelet dysfunction during their operations, measurable in higher re-operation rates for bleeding [3], higher intraoperative blood loss [8], increases in transfusion requirements [3, 8, 9, 45], prolonged chest tube drainage time [33] and prolonged time for completion of wound closure [45]. However, the benefit of aspirin therapy, especially the improvement of graft patency as one main indication for this medication, has to be weighed up [41, 49].

The role of pre-operative low-dose aspirin as a risk factor for increased peri-operative blood loss and transfusion requirements in patients undergoing coronary artery bypass graft surgery is less clear. While Jakics et al. [24] saw no correlation in this context, Taggart et al. [48] demonstrated a significant increase in post-operative blood loss, resulting in a substantial increase in blood transfusion and hemostatic pack (fresh frozen plasma, platelets) requirements.

Different surgical interventions, notably prostate, cardiac and possibly intracranial surgery [32, 36], have well-known and adverse effects on hemostatic and fibrinolytic mechanisms, such that the additional effect of aspirin induced platelet dysfunction may lead to complex bleeding problems [25].

Assessment of bleeding risk in spinal surgery and spinal regional anesthesia/neuraxial anesthesia

The impact of aspirin as a risk factor for increased intra- and post-operative bleeding in spinal surgery and spinal regional anesthesia is less clear. In this context, even spontaneous spinal epidural hematomas without [12, 29, 55] and with [51] concomitant pathologies like a spinal meningioma have been described. However, apart from reviews focusing on a large number of spinal hematomas in general, addressing the issue of aspirin as an etiological risk factor only marginally [4, 27], or seeking risk factors for delayed spinal hematoma after spinal surgery including the role of ASA peripherally [26, 52], a postal survey of the opinions and working practices among neurosurgeons performing a large number of spinal surgeries concerning pre-operative low-dose aspirin medication is new and unique.

The German Society of Anesthesiology and Intensive Care Medicine (DGAI) released guidelines for para-spinal regional anesthesia and prevention of thromboembolism/anticoagulation in 1997 [15] and adapted them in 2003. Although the general risk of

spinal hematomas after para-spinal regional anesthesia was judged as small, but the dimension of such a hematoma in case it occurs was estimated as high, concise recommendations for the discontinuation of various antihemostatic medicaments were published. Among these a discontinuation of low-dose aspirin was recommended more than 2 days before a para-spinal puncture/regional anesthesia and catheter removal, especially when aspirin was given in combination with other antithrombotic medicaments [15].

Horlocker et al. [21, 22] represented an adverse opinion and stated that pre-operative antiplatelet therapy does not increase the risk of spinal hematoma associated with regional anesthesia, analyzing a subgroup of 39% of 924 matching their criteria. The same opinion was represented in the second ASRA consensus conference on neuraxial anesthesia [23] in 2003, where the problem and risk of regional anesthesia in the anticoagulated patient by a broad spectrum of different medicaments was reevaluated. However, regional anesthesia technically comprises a spinal puncture and at most a catheter insertion/removal, which is, beyond question, much less invasive than neurosurgical or orthopedic spinal surgical procedures.

Similar statements were discussed and determined by the French society of anesthesiology and intensive care medicine (SFAR) in 2002 [43], and at the seventh conference on antithrombotic and thrombolytic therapy by the American college of chest physicians in 2004 [37]. Furthermore, it was underlined that the cardiovascular risk should be kept clearly in mind when ASA is discontinued before any kind of elective surgery and that there is an increasing number of reports suggesting a substantial interindividual variability in the response to antiplatelet agents, and that different effects on platelet function in case of combining antithrombotic medicaments with aspirin has to be considered.

Counteracting aspirin-effects

Among our respondents 65.5% quoted to give specific drugs and to apply particular measures in case of disturbed hemostasis due to aspirin induced altered normal coagulation during or after spinal surgery. Only one-third (35.2%) would not respond to this situation by initiating prohemostatic therapy. Focussing on the method of counteracting the antiplatelet effect of aspirin there is a great variability visible in Table 1. However, of those neurosurgeons performing spinal surgery adopting measures to “normalize” the coagulation, almost half (50.1%) would use Desmopressin alone or in combination (Table 1). In his survey among

neuroanesthetists in the UK, James et al. [25] found out that during intracranial surgery only 16.4% would not do anything to correct aspirin-induced platelet dysfunction. The vast majority among his respondents would use a wide variety of different agents, but half of them (49.1%) would use platelet infusion alone or in combination with other blood products or hemostatic agents if hemorrhagic complications developed.

Recommendations for the management of bleeding disorders by prohemostatic therapy, including patients with aspirin-associated bleeding [28], and pharmacological strategies to decrease transfusion requirements in patients undergoing surgery [39] are not new. Besides the transfusion of platelets in case of thrombocytopenia or severe platelet disorders [28, 43], a pharmacological improvement of primary hemostasis may be achieved by the administration of desmopressin (DDAVP) [10, 16, 28, 31, 42]. The administration of DDAVP results in a marked increase in the plasma concentration of von Willebrand factor (and associated coagulation factor VIII) and (also by yet unexplained additional mechanisms) a remarkable potentiation of primary hemostasis as a consequence. DDAVP is used for the prevention and treatment of bleeding in patients with von Willebrand disease or mild hemophilia A, and further in patients with an impaired function of primary hemostasis, such as in patients with uremia, liver cirrhosis or in patients with aspirin-associated bleeding [28].

Agents that exert anti-fibrinolytic activity are aprotinin and a subgroup of lysine analogues [28]. The prohemostatic effect of these agents proceeds not only by the inhibition of fibrinolysis (thereby shifting the procoagulant/anticoagulant balance toward a more procoagulant state), but also due to a protective effect on platelets, as has been demonstrated at least for aprotinin [28]. However, the literature search performed by Flordal [11] demonstrated that the only two drugs, which were used in randomized studies for the prevention of bleeding in surgical patients pretreated with aspirin, were aprotinin and desmopressin. Furthermore, all studies, except one, were undertaken in cardiac surgery [1, 10, 16, 17, 34, 38], where both drugs were effective in counteracting the aspirin-induced increase of blood loss and transfusion requirements. Aprotinin is tenfold more expensive than desmopressin, may cause anaphylaxis and may lead to an increased risk of graft occlusion after cardiac surgery. Very little is known about aspirin, aprotinin and desmopressin in other types of surgery [11].

Recently, Powner et al. [40] performed a directed literature review on counteracting the effect of anticoagulants and antiplatelet agents during neurosurgical

emergencies. They reviewed specific interventions for each drug, including ASA, as well as recommended dosages. Finding out that evidence-based data specific to neurosurgery are limited, Powner et al. [40] demanded further controlled studies that incorporate satisfactory dose-finding designs in this context.

Discontinuation of low-dose aspirin before spinal surgery?

Aware of the results of our survey among neurosurgeons performing spinal surgery, and with the majority of these being concerned that low-dose aspirin may increase the risk of excessive bleeding during and after spinal procedures, there still are two fundamental questions to be answered: Must low-dose aspirin be discontinued before elective spinal surgery? And if so, how many days before the scheduled operation? Taking the opinions and working practices of two-thirds of a representative group of specialists of one country, performing a mean of more than 600 spinal operations per year into account, the answer would be that low-dose aspirin should be discontinued 7 days before the operation.

As the whole population becomes older, the proportion of elderly patients requiring spinal surgery for degenerative diseases rises, and additionally the portion of the whole population taking low-dose aspirin regularly for primary and secondary prevention of cardiovascular and cerebrovascular disease increases [18], every surgeon performing spinal operations will be confronted with this question. However, every surgeon answers the questions for himself and his patient, the risk of the discontinuation has to be measured in each patient individually because the low-dose aspirin medication has been initiated for some particular reason. Furthermore, a demand for a controlled, randomized study in order to answer the question is futile and even dangerous. The revaluations and suggestions of other medical specializations, brought together and evaluated in this article, might act as a support for the answer of the question, the pharmacological strategies and recommendations can refresh the already known treatment options or point out alternative measures for the emergency situation.

Conclusion

Despite the existence of distinct departmental policies concerning the discontinuation of low-dose

aspirin pre-operatively in the majority of neurosurgical facilities performing spinal operations, there is a wide range of the moment of this interruption with an average of 7 days. Two-thirds of the respondents felt that aspirin was a risk factor for hemorrhagic complications associated with spinal procedures, and more than half of the interviewed neurosurgeons reported having personal experience of such problems during spinal operations. Finally, various medicamentous methods of counteracting aspirin-induced platelet dysfunction and excessive bleeding in this context are reevaluated. In this context, platelet infusion and the administration of Desmopressin seems to be an effective and accepted as well as frequently adopted measure to antagonize the aspirin effect on platelet function during various major surgical procedures.

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