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Can the surgical tourniquet be used in patients carrying Hb S ? A Review of the literature

Marco Pignatti, Sara Zanella & Caterina Borgna-Pignatti

Abstract

Introduction

In patients with sickle cell disease, circulatory stasis, acidosis, and hypoxemia induce sickling. Tourniquets are an important adjunct in limb surgery to obtain a bloodless field. Many local and systemic effects, due to the inflation and deflation of the tourniquet, can develop. These effects may have severe consequences if comorbidities are present. The use of a tourniquet in sickle cell patients is controversial because it may provoke vaso-occlusive complications.

Areas covered: We reviewed the literature to detect reports of the use of tourniquet in sickle cell disease or sickle trait. We found only three case reports and five case series, three of which controlled, none randomized, on the complications of tourniquet.

Expert commentary:

From what we could find in the literature and contrary to what is suggested by most guidelines it appears that complications are rare. However,caution must be applied and the risk/benefit ratio carefully considered.

Key words: HbS, orthopedic surgery, sickle cell disease, sickle trait, tourniquet.

Introduction

The use of arterial tourniquets is a device that is commonly used when performing surgery of the extremities in order to obtain a bloodless field. Many local and systemic effects due to the inflation and deflation of the tourniquet can develop. These complications can be particularly worrisome in patients with sickle cell disease, because circulatory stasis, acidosis, and hypoxemia can induce sickling.

1. Sickle Cell Anemia

Sickle cell anemia, so-called because of the sickle shape of the deoxygenated red cells, is due to the inheritance of two abnormal hemoglobin genes and it is the most common

hereditary hematologic disease in the world. The sickle mutation derives from the encoding of a valine instead of glutamic acid in the sixth position of the beta chain. It has been clearly demonstrated that the abnormal shape of the red cells containing hemoglobin S (HbS) is dependent on deoxygenation. Deoxygenated HbS polymers form long bundles of HbS fibers that run parallel to the long axis of the cell, the so called tactoids, that deform the erythrocytes. [1] The equilibrium of HbS between its liquid and solid phases is determined by oxygen tension, HbS concentration, and hemoglobins other than HbS. Even small reductions in blood pH reduce oxygen affinity and promote sickling. Also, high intracellular concentrations of HbS facilitate sickling, while fetal hemoglobin (HbF) and adult hemoglobin (HbA) have an inhibitory effect on polymers formation. Deoxygenation alters the phospholipid structure of the red cell membrane exposing posphatidylserine and initiating the coagulation cascade. [2]

In individuals heterozygous for the defect, the red cells contain both the abnormal hemoglobin S (HbS) and the normal adult hemoglobin (HbA). This is a benign condition that is not usually associated with increased morbidity or mortality. On the contrary, the double heterozygous states resulting from two variant hemoglobins, such as Hb S and C, or from a variant Hb disease and a thalassemia gene (HbS/β-thalassemia) result in sickling syndromes. Sickle cell disease can cause severe pain, cerebral stroke, osteonecrosis, osteomyelitis, significant end-organ damage, pulmonary complications, and premature death.

1.2 Perioperative management of SCD

Numerous studies have been dedicated to the treatment of sickle cell patients in the perioperative period and, in particular, to the role of anesthesia and of the hematocrit level that should be maintained. [3,4] There is common agreement on the importance of correcting the anemia, by simple or exchange transfusion, [5] and of avoiding hypoxia, hypothermia, and acidosis because they facilitate sickling that, in turn, obstructs the microvasculature. In the first randomized study evaluating the best regimen of preoperative transfusion, Vichinsky et al (5) compared the rates of perioperative complications among patients randomly assigned to receive either an aggressive transfusion regimen designed to decrease the HbS level to < 30 % or a conservative regimen designed to increase the hemoglobin level to 10 g per deciliter. They demonstrated that the conservative transfusion regimen (where HbS averaged 59%) was as effective as the aggressive regimen in preventing perioperative complications.

In a prospective randomized multicenter trial, conducted in Europe and Canada in 2013,

(TAPS) patients with HbSS or HbS/β0-thalassemia undergoing low-risk or medium-risk surgery were randomly assigned to preoperative transfusion aimed to increasing Hb to 10.0 g/dL or no transfusion. Preoperative transfusion was associated with significantly less perioperative complications than no transfusion. The unadjusted odds ratio of clinically important complications for medium-risk surgery patients was 3.8. To avoid an increase in blood viscosity, patients whose initial hemoglobin was >9 g/dL underwent partial exchange transfusion. Preoperative transfusion appears to be necessary also for patients with hemoglobin SC (HbSC) disease, for all surgical risk levels. Lynne Neumayr, Am. J. Hematol. 57:101–108, 1998. Koshy Surgery and Anesthesia in Sickle Cell Disease Mabel Koshy 1995 by The American Society of Hematology In adults and children with HbSC or HbS/β-thalassemia a sickle cell expert should be consulted to determine if full or partial exchange transfusion is indicated before a surgical procedure involving general anesthesia
or who require the use of tourniquet. (NIH) Particular care should be dedicated to the prevention of factor that favour sickling, such as hypothermia, dehydration, acidosis, and hypoxia. Preoxygenation using high inspired oxygen fraction (FiO2) of 100% prior to intubation is recommended. Oxygen saturation should be monitored until discharge and supplemental oxygen provided as necessary. (SMJ) Incentive spirometry is of help in preventing the acute chest syndrome that represents a frequent and severe risk during after anesthesia, sometimes resulting in death of the patient. (TAPS)A history of pulmonary disease and a higher risk associated with surgery are significant predictors of the acute chest syndrome. (Vichinsky) Pain control is mandatory.
In a study, complications were higher in both SS and SC patients who received regional compared with those who received general anesthesia.(?)
In addition, the surgeon should select the least possible aggressive or extensive surgical procedures.[6]

2.Use of the tourniquet

Many surgical procedures in the limbs, both on bone or soft tissues, are best performed with the use of a tourniquet, a medical device designed to block the blood flow, in order to maintain a bloodless surgical field, optimizing operating conditions, obtaining better accuracy, precision and speed, reducing blood loss, and improving safety. Sterling Bunnell, the founding father of hand surgery once stated that "operating on a hand without a tourniquet is like trying to fix a watch in a bottle of ink.[7]

The tourniquet can also be used to limit the circulation of drugs infused at high doses in the isolated limb, all the same preventing systemic toxic effects. This is important in intravenous regional anesthesia (Bier block anesthesia), intravenous regional sympathectomy for regional pain syndrome, and isolated limb perfusion with chemotherapeutic agents in patients with advanced melanoma and other malignancies localized to the limb. External tourniquet systems typically include a pneumatic cuff, which is wrapped around a patient's limb proximal to the desired surgical field, a compressed gas source and a mechanism designed to maintain pressure above the systolic pressure of the patient. Prior to tourniquet inflation, the limb should be exsanguinated, most commonly using an Esmarch bandage for emptying the blood vessels from the distal to the proximal end. Exsanguination results in autotransfusion of blood from the peripheral circulation into the central circulation. [8] Pneumatic tourniquets are used in an estimated 15,000 surgical procedures daily in the United States and elsewhere.[9]

2.1 History

The history of tourniquets goes back to ancient Rome when constricting bandages, mainly of bronze and leather, were used to control bleeding in case of limb amputation. The term tourniquet comes from the french "tourner", because, initially, the device was a simple garrot, tightened by twisting a rod. The French surgeon Jean Louis Petit, in 1718, developed a device with a screw mechanism to occlude the blood flow in a limb. Joseph Lister is considered to be the first to have used a tourniquet in the surgical setting in 1864. [7,10]

To prevent local lesions, Harvey Cushing introduced in 1904 the first inflatable tourniquet.

2.2 Safety Complications

Despite the great advantages of the use of tourniquet, the surgical team should not underestimate the risks associated with it. Complications can be local or systemic.

2.2.1 Local complications

In addition to establishing a bloodless surgical field, the tourniquet stops the blood flow to non-surgical regions of the limb, causing ischemic damage to those regions. The risk increases with the duration of ischemia. Further, the tourniquet applies pressure to underlying skin, muscles, blood vessels and nerves proximal to the surgical site, resulting

in a risk of mechanical (rarely chemical) injury that increases with the level and duration of pressure application.[11]
Tissue edema develops if the tourniquet time exceeds 60 min. [12] The post-tourniquet syndrome manifests itself as pain, numbness, weakness without paralysis, stiffness and pallor; skin changes including blistering, and ischemic necrosis.

2.2.2 Systemic complications
The use of a tourniquet can be associated with systemic complications affecting many organs. They have been reviewed in detail by Kam et al. [13] and are summarized below and in Table 1.

2.2.2.1 Hemodynamic effects
The hemodynamic changes associated with tourniquet inflation or deflation may represent a problem for patients with poor cardiac function. Limb exsanguination and tourniquet inflation result in an expansion of central blood volume and in an increase in systemic vascular resistance. In practice there is usually a small increase in central venous and arterial blood pressure. In patients with poor ventricular compliance pulmonary artery blood pressure may increase significantly. Prolonged tourniquet inflation can cause increases in heart rate and blood pressure [14] that are more frequent during general anesthesia and least frequent in patients operated on under spinal anesthesia or brachial plexus block. The overall frequency of hypertension during operation in 500 patients to whom a tourniquet was applied during surgery was 11%, as compared with 1% in patients treated without a tourniquet. After deflation of the tourniquet, both central venous pressure and arterial blood pressure decrease as a result of sudden but temporary reduction in peripheral vascular resistance and return of blood back into the extremity.

2.2.2.2 Respiratory system
After deflation of the tourniquet, end-tidal carbon dioxide (CO2) and PaCO2 increase within one minute. The arterial blood pH decreases significantly, with the maximal fall occurring within four minutes but remaining below baseline for a longer time. These data indicate that in patients whose acid-base status is compromised by preexisting disease, or in whom sickling may develop, PaCO2 and pH should be monitored closely.[15]

2.2.2.3 Brain circulation

A 50% increase in middle cerebral artery blood flow velocity follows the deflation of the tourniquet representing a risk for patients with increased intracranial pressure or in patients predisposed to stroke. (Sparling RJ BJNeurosurgery 1993) After tourniquet deflation, deleterious increases in intracranial pressure can be prevented hyperventilating the patient. (Kadoi 1999 12 di Kam)

2.2.2.4 Hematological effects

The use of the tourniquet can induce several coagulation abnormalities. Tissue compression causes increased platelet aggregation. In addition, tissue ischemia after tourniquet inflation promotes the release of numerous catecholamines that interfere with the coagulation system. Tourniquet inflation and surgical pain may be associated with a hypercoagulable state. Deflation, on the contrary, results in a brief increase in fibrinolytic activity caused by tissue plasminogen activator released in the affected limb. Applying an arterial tourniquet does not seem to increase the risk of deep vein thrombosis. [16] However, the procedure may be contraindicated in patients at risk of deep vein thrombosis and in patients, such as those affected by sickle cell disease (including HbSS, HbSC, and HbS/β-thalassemia), who are prone to develop pulmonary embolism. [17,18]

2.2.2.5 Metabolism and thermoregulation

During prolonged ischemia, anaerobic metabolism and accumulation of lactate decrease the ATP levels and the intracellular pH. After reperfusion, a sudden, large increase in reactive oxygen species occurs and neutrophils infiltrate ischemic tissues exacerbating the ischemic injury. [8,19]
The thermoregulatory system maintains core body temperature in a relatively narrow temperature range. Studies have demonstrated that the use of the tourniquet interferes with core body temperature, increasing it during inflation and decreasing it a mean of 0.7°C within 90 seconds after deflation of a lower limb tourniquet. This phenomenon is due to the redistribution of body heat and to return into the circulation of hypothermic blood from the extremity.[20,21]

2.3 Tourniquet pain

About an hour after the positioning of an arterial tourniquet, up to 66% of patients receiving spinal or epidural anesthesia will develop a dull or burning pain in the extremity, that may be relieved by deflating the tourniquet for 10 to 15 minutes and then reinflating it. [22] Sometimes, however, the pain is so intense that it is necessary to resort to general anesthesia. The neurophysiologic mechanisms of tourniquet related pain have been reviewed by Crews et al. [23] Tourniquet pain is frequently associated with a significant increase in blood pressure during inflation and a significantly larger increase just before deflation. [24]

3.0 Tourniquet and Sickle cell anemia

Bone manifestations, including avascular necrosis and osteomyelitis, are among the commonest presentations of sickle cell disease. Aseptic necrosis of the hip occurs in up to 50% of patients. In the multicentered study by the National Sickle Cell Surgery Study Group the overall serious complication rate in patients undergoing orthopedic procedures was 67%. The most common of these were excessive intraoperative blood loss, defined as in excess of 10% of blood volume. (Vichinski 1999) To prevent excessive bleeding and to improve accuracy many of the necessary orthopedic procedures require the use of a tourniquet, but its use in these patients is controversial. The majority of existing guidelines discourages the use of tourniquets in patients with sickle cell disease and recommend great caution in individuals with sickle trait. [6,25–27] In fact, the tissue ischemia induced by the cuff leads to perturbations in oxygen levels, temperature and pH, that may result in the formation of HbS tactoids, precipitating the vaso-occlusive crises that are the hallmark of the disease. Severe postoperative pain, edema, and necrosis can follow. In a study of venous blood drawn distally to a tourniquet in the arm, the oxygen tension decreased from an initial value of 45 mmHg to 24 mmHg after 30 minutes, to 20 mmHg after 60 minutes and to 4 mmHg after 120 minutes [12]. In the 1950's, Harris et al.[28] demonstrated that, in vitro, more than 90% of red cells of patients with HbSS had sickled when the oxygen tension reached 25 mmHg. In contrast, the same study found that in blood of HbAS patients no sickling developed until the oxygen tension declined to 15 mmHg. Molecular polymerization occurs in stages and acute deoxygenation may not necessarily lead to sickling. Nonetheless, when sickle cells are continuously deoxygenated, the classic sickle shape may result impairing their passage through the microcirculation.[29] The individual with sickle trait, having 20-40% HbS in the blood, is less prone to sickling, that develops only in conditions of severe hypoxemia. Sunshine et al. [30] demonstrated that when

compared with pure HbS solutions, mixtures with 60% HbA, as seen in sickle cell trait, show significantly longer delay times between the initiation of polymerization and the exponential rise in polymer formation. In addition to deoxygenation, all the systemic effects reviewed above, in particular the output of CO_2 and lactic acid from the ischemic limb and the consequent decrease in arterial pH, represent severe risk factors in patients who are particularly sensitive to acid-base status or who are at risk for cardiovascular and cerebral events. There is a general agreement that inflation time should not exceed 60 minutes for an upper extremity and 90 minutes for a lower extremity. [26] Searching for the evidence on which the recommendations are based, we reviewed the literature using MEDLINE®, PubMed, ScienceDirect, EMBASE, Cochrane databases, and Google Scholar. The search terms were HbS, orthopedic surgery, sickle cell anemia, sickle trait, tourniquet, tourniquet AND sickle cell. All searches are current to August 24, 2016. We considered reports of any surgical procedure where a tourniquet was used on patients with sickle cell disease or trait, in addition to reviews and editorials discussing the problem.

3.1 Results

The outcomes of different studies and case reports are not uniform. We were able to find 8 articles on the use of tourniquet for limb surgery in 116 patients with a form of sickle cell disease. (Table 2) The interventions differed in tourniquet type, perioperative care, and operative procedure. A previous review article had identified 12 complications in 96 patients (12.5%) in four studies, all of which are included in the present review.[31] Nineteen patients with sickle-cell anemia 14 of whom with HbSS and 5 with HbSC aged between 5 and 23 years underwent twenty orthopedic operations performed in Nigeria with the use of a tourniquet. Seven of them suffered some complications as compared with 3 hematologically normal patients ($P < 0.01$). However, only three of the complications were significant and all resolved within two weeks. These were bone pains, severe post-operative pain and jaundice, and tissue edema. The patient who developed bone pains was not known to have sickle cell anemia prior to surgery and was later diagnosed with a malarial infection. No patient died.[32] One article reported, [33] in a heterozygous woman with a HbS of 40%, taut edema and pain lasting 48 hours in both feet after tourniquet-assisted surgery, that the authors interpreted as a sickle cell crisis. Stein and Urbaniak [34] reported on 26 patients (4 HbSS, 1 HbSC and 21 HbSA) who underwent 29 operative tourniquet-assisted procedures, compared retrospectively with a control group made of 50 patients of the same ethnic background who did not carry the sickle gene and who had undergone 57 similar operative procedures. Among patients with sickle cell trait, one

developed massive pulmonary embolism after open reduction and internal fixation of a bimalleolar fracture, while another developed chronic osteomyelitis. A third patient developed a small skin slough and an infected hematoma and a fourth had a loss of internal fixation for a calcaneal fracture. A patient homozygous for HbSS suffered from deep vein thrombophlebitis of the calf. In the control group there were two complications. The authors concluded that there was no significantly increased incidence of complications in sickle cell anemia or trait. Other articles [35–38] report on the uneventful use of tourniquet and do not confirm the risk of sickling, especially when careful preventive measures are set in place. Gilbertson[35] reported no complications in 12 operative procedures in patients with sickle cell trait or HbSC considered together. Tourniquets were not, however, applied to any patient with sickle cell anemia. Martin and coworkers [36] reported on 41 patients, diagnosed as heterozygous on the basis of a positive sickle cell test, in the absence of anemia or a history of crises, who underwent foot surgery under tourniquet. No complications were observed. However, the same authors had previously seen a case of vascular occlusion 24-48 hours following surgery under tourniquet for less than 40 minutes in a patient with sickle trait. The exact cause of the occlusion was undetermined. In a study carried out in Saudi Arabia,[37] 15 patients, (12 HbSS and 3 HbAS) were operated on for orthopedic problems after preoperative oxygenation and hyperventilation during surgery. The tourniquet time was 61.7± 27.5 min, all patients made an uneventful recovery and none developed a sickle cell crisis. No clinically important changes were observed in blood gases or in the irreversibly sickled-cell count. Similarly, an Arabian 27-year-old male patient, with homozygous sickle cell disease, after preoperative exchange transfusion, received bilateral total knee replacement under tourniquet and tolerated the procedure well. [38] Commenting on this case, Sarjant and Callum [39] challenged the use of the tourniquet for sickle cell patients of African origin, attributing the good results obtained in Saudi Arabia to the relative mildness of Arabian sickle cell disease. In a more recent case report from Nigeria,[40] however, a 25 years old man with hemoglobin SS underwent a sequestrectomy and saucerisation with the use of the tourniquet without perioperative problems.

Conclusions

Overall we were able to find data on 32 patients with HbSS and 66 HbAS (sickle trait) and 6 HbSC who have been operated upon under tourniquet. Twelve patients with either

HbSC or HbAS reported by Gilbertson et al. were not included in the account. The reported results are not uniform, but the available evidence suggests that, when strictly necessary, tourniquets can be used without complications in most patients with sickle cell disease, provided that proper perioperative measures are put in place and extra caution is dedicated to maintaining the correct temperature, acid-base status and oxygenation during surgery. In particular the risk appears to be lower, as expected, in individuals heterozygous for the gene mutation.

Expert Commentary

Tourniquet is routinely used in limb surgery, because of the advantages that it provides in terms of accuracy, speed, blood loss and overall safety for the patient.
The few commonly accepted exceptions to the use of this device include sickle cell disease or sickle trait. Ischemia and acidosis are well known triggering factors of sickle crises. Therefore it has always been assumed that the use of an inflatable tourniquet to purposefully avoid blood perfusion of a limb in these patients might have severe clinical consequences. Several management guidelines and recommendations, [26] anesthesia textbooks [24] and protocols from some local institutions [25,27] regard sickle cell disease as an absolute contraindication and sickle trait as a relative contraindication to the use of tourniquet and recommend that at presentation all patients ethnically at risk of being carriers of a sickle mutation and requiring limb surgery should be screened preoperatively. Due to the lack of proper evidence-based guidelines many local protocols leave the decision to the surgeon. In clinical practice, the experience of the surgical and anesthesiological team, the complexity of the operation, and the general condition of the patient dictate whether or not to use a tourniquet. Despite the theoretical risk of perioperative complications, from our review of the literature it appears that there are not strong data on which to base recommendations against the use of a tourniquet in patients carrying the HbS gene. Several reports suggest that this risk, although real, is quite rare. Only one case report out of three described pain and edema and of the five published case series only two reported some postoperative complications for a total of 12 events. (Table 2)
A possible explanation is that chronic hypoxemia and acidosis are more likely to cause erythrocyte sickling than the acute and short lasting tourniquet-induced deoxygenation.

[41] In fact it is now recognized that, due to the rheology of sickle cells, acute deoxygenation can be tolerated without consequences, but sickling occurs when these cells are slowly and persistently deoxygenated. [42] Hyperoxygenation, hyperventilation, proper hydration, and accurate exsanguination are all important measures to prevent adverse events during and after surgery. The key weaknesses in clinical management derive from the lack of studies on a large population of patients. A prospective randomized controlled study would help to assess the real risks for sickle cell patients to undergo a procedure under limb ischemia. However such a study would probably be ethically unacceptable. A retrospective review of large series of patients operated on with and without tourniquet might help clarify potential predictors of surgical outcomes. The genetic asset of the patient may be of importance. Data from the Cooperative Study of Sickle Cell Disease indicated that sickle-cell-related surgical complication rates are similar in patients with HbSC and HbSS. Patients with HbSS and HbSC are probably at higher risk of complications, when operated upon under tourniquet, than HbAS carriers who might be protected by their lower level of HbS. However, the level of HbS in carriers goes from 20 to 40%, a large range that can make the difference in the risk of developing a crisis. It has been suggested [39] that Saudi Arabian patients carrying the Arab-Indian HbSS haplotype, are characterized by less severe disease, because of a higher percentage of HbF in their circulation. Therefore patients of African descent might be more at risk than the Arabian ones reported by Al-Ghamdi.[38] However two series and one case report from West Africa do not seem to support this hypothesis. [32,35,40] Keeping the operative field warm, the patient well hydrated, well oxygenated, and without systemic acidosis is of utmost importance. Also preoperative blood transfusion is associated with decreased perioperative complications. [4] No consensus exists, however, on whether simple transfusion or exchange transfusion should be preferred in this setting. A randomized controlled trial showed that preoperative simple transfusion to achieve a Hb of 10 g/dL is equally effective in preventing postoperative complications as erythrocytapheresis aimed to decrease the HbS level to less than 30%.[5,43] Whether the tourniquet-induced ischemia might benefit from lower levels of HbS is unkown, but the improved oxygen saturation obtained by erythrocytopheresis, independent of any change in the total hematocrit, could decrease postoperative complications.[44] In any case, it is important that anesthesiologist and surgeon be aware of the presence of a sickle hemoglobinopathy.Therefore at presentation all patients ethnically at risk of being carriers of a sickle mutation scheduled to undergo orthopedic surgery should be screened

preoperatively and a pre-operative plan discussed with the hematologist consultant.
In conclusion, the available evidence suggests that with the appropriate perioperative precautions, tourniquets can be used with relative safety in most patients with sickle cell disease. Patients with sickle cell trait are not likely to develop an adverse outcome from the use of tourniquet.

Next five years

The existing literature on the use of tourniquet-assisted surgery in patients with a sickle mutation is quite old. Hopefully, in the absence of controlled randomized trials that are unlikely to be performed for ethical constraints, registries and carefully reviewed retrospective studies will offer reliable guidance. Genomic analysis might, in the future, reveal which patients are more at risk for vascular occlusive crisis, infection, acute chest syndrome, and other complications that occur postoperatively in this large population of fragile patients.

Key issues

- Tourniquet use in limb surgery allows careful dissection of tissues and significant advantages in accuracy, speed, and blood loss.
- Patients with sickle cell anemia, Hb SC and HbS/β-thalassemia and, in a lesser measure, with sickle cell trait are exposed to the theoretical risk of developing a crisis when a tourniquet is applied and most guidelines and recommendations discourage its use.
- Reviewing the literature we found reports on 111 sickle cell patients operated upon with the use of a tourniquet. Only three papers reported significant postoperative complications.
- The dogma that tourniquet use is contraindicated in patients with sickle cell disease should therefore be reexamined and the balance between risks and benefits carefully evaluated.
- Meticulous perioperative care in terms of patient's oxygenation, avoidance of acidosis and cooling and appropriate transfusion is mandatory.

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