Advances in Medical Sciences 59 (2014) 132–135

Contents lists available at ScienceDirect

Advances in Medical Sciences

journal homepage: www.elsevier.com/locate/advms

Original Research Article

Intraoperative bleeding during endoscopic sinus surgery and microvascular density of the nasal mucosa

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ARTICLE INFO

Article history:
Received 15 February 2013
Accepted 24 October 2013
Available online 16 March 2014

Keywords:
FESS
Intraoperative bleeding
CD34 antigen
Nasal mucosa
Microvascular density

ABSTRACT

Purpose: To evaluate the correlation between quality of the surgical field, intraoperative bleeding during endoscopic sinus surgery (ESS) and the density of microvasculature of the nasal mucosa.
Material/methods: Nasal mucosa of 30 patients, operated for chronic rhinosinusitis, was biopsied to assess expression of CD34 antigen on vascular endothelium. Quality of surgical field was evaluated with Fromm-Boezaart scale at mean arterial pressure (MAP) of 70–80 mmHg. If at this MAP surgical field quality was not satisfactory further reduction of hemodynamic parameters was performed until 'bloodless surgical field' (grade 2 or lower) was achieved. The rate of intraoperative bleeding was calculated from the ratio of total blood loss and the operative time. The extent of the disease was assessed according to computed tomography findings using Lund-Mackay staging system.
Results: Significant positive correlation (Spearman correlation test; $p < 0.05$) was found between CD34 antigen expression and quality of surgical field at MAP between 70 and 80 mmHg as well as the rate of intraoperative bleeding. More intense reduction of MAP was necessary to achieve 'bloodless surgical field' in patients with high CD34 expression than in those with moderate and low expression. Lund-Mackay score correlated with quality of surgical field but not with the rate of intraoperative bleeding.
Conclusion: During ESS, it is microvascular density of the nasal mucosa rather than the extent of the disease that contributes to the intensity of intraoperative bleeding, although both factors negatively influence the quality of surgical field.

1. Introduction

Precision of transnasal endoscopic procedures is highly dependent on the good visualization of surgical field obtained with modern optical systems. Intraoperative bleeding negatively influences the quality of surgical field and consequently diminishes the precision, extends the time of procedure, and increases the risk of complications and the possibility of recurrence of the disease.

Locally administered vasoconstrictors, reverse Trendelenburg position and decreased hemodynamic parameters in order to obtain 'bloodless surgical field' during ESS are sometimes ineffective. More intensive intraoperative bleeding and larger blood loss may be anticipated in patients with the severe mucosal inflammation and extensive nasal polyposis [1–3]. It may either result from extensive surgical trauma due to eradication of advanced inflammatory lesions, or from the increased microvascular density of the nasal mucosa, remodeled upon inflammation. Such remodeling with the increased angiogenesis was confirmed in numerous studies concerning lower respiratory tract in patients with allergy, asthma and chronic obstructive pulmonary disease [4–6]. Data concerning remodeling and angiogenesis within nasal mucosa are not that numerous and the results are ambiguous [7–9].

One of the methods assessing angiogenesis and density of vascular network is immunohistochemical evaluation of CD34 antigen expression in endothelial epithelium of blood vessels [10]. To the best of our knowledge no studies on correlation between intraoperative bleeding and the microvascular density of nasal mucosa have been published so far.

The aim of the study was to assess whether microvascular density influences the intensity of bleeding and surgical field quality during ESS.

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1896-1126/$ – see front matter
http://dx.doi.org/10.1016/j.advms.2013.10.001

2. Materials and methods

The study protocol was approved by the local Bioethical Committee and the patients signed the informed consent.

Thirty patients aged 23–51 years (mean age 42) who underwent endoscopic surgery due to chronic sinusitis constituted the study group. Patients with hypertension, coronary heart disease and diabetes or those with American Society of Anaesthesiology (ASA) physical status classification system III or above were excluded from the study. Patients receiving antithrombotic, antiplatelet or steroid therapies (30 days prior the surgery), and subjects with the history of surgery were also excluded from the study.

The extension of inflammatory lesions was assessed on the basis of the computed tomography findings with Lund-Mackay staging system [11].

General anesthesia was performed according to the same standard protocol in all patients. Propofol at a dose of 2 mg/kg i.v. was used for induction followed by cis-atracurium at the intubation dose of 0.1 mg/kg i.v., sevoflurane at minimal alveolar concentration (MAC) 0.8 occasionally to 1.5 and remifentanil in continuous intravenous infusion at a rate of 0.1–0.5 μg/kg/min were administered for the maintenance of the anesthesia.

The initial target mean blood pressure (MAP) was set at 70–80 mmHg. After this level of MAP was achieved by gradual increment of anaesthetics' doses, the intensity of bleeding was assessed by the surgeon, blinded to the current hemodynamic parameters, in 10 minutes intervals, with the use of Fromm-Boezaart scale [12]. Grades 0–2 of this scale stand for optimal bloodless surgical field. If at MAP between 70 and 80 mmHg operative conditions were not satisfactory (grade 3 and higher) HR and MAP were further smoothly decreased until bleeding in the operative area was reduced (grade 2 and lower). The final hemodynamic parameters (MAP and HR) at the moment of reduced bleeding and improvement of the surgical field quality were recorded.

In no patient heart rate and arterial pressure were forced to drop below the values commonly regarded as safe for healthy subjects i.e. HR 60 min^{-1} and MAP 60 mmHg.

Total blood loss was estimated by measuring the volume of blood suctioned from the surgical field during the operation. To prevent passive ingestion of blood by the patients, each time nasopharynx was packed with gauze dripped in Vaseline ointment. Bleeding intensity during the surgery was calculated from the ratio of the total blood loss volume to the total operative time, and expressed in ml per minute.

Nasal mucosa sections were obtained from the anterior part of the medial nasal concha.

2.1. Immunohistochemistry

Thirty specimens were processed through the immunohistochemical technique described earlier [13]. In short, 5 μm-thick paraffin-embedded, formalin-fixed tissue samples were used. Following the deparaffinization and rehydration, epitope retrieval was carried out in the EnVision Flex Target Retrieval Solution (DAKO) in high pH. Endogenous peroxidases were blocked by incubating the sections in methanol and 3% hydrogen peroxidase for 20 min. To evaluate angiogenesis mouse antibody against CD34 protein (DAKO, IR632) in 1:100 dilution was used. After overnight incubation in 4 °C visualization reagent (LSAB plus DAKO) was applied for 30 min followed by DAB solution for 5 min. The slides were than counterstained with hematoxylin and examined under the light microscope Olympus BX45. The evaluation of angiogenesis was performed by two independent pathologists counting the CD34 positive areas (brown stained endothelial cells or endothelial cell clusters) in randomly chosen 10 fields under 10× magnification. Both pathologists had to agree on what constituted endothelial cells of the microvessel before it was included in the count. The CD34 expression in the sample was graded negative (grade 0) if there was no CD34 positive cells in all of the examined areas; low (grade 1) if less than 10% of the examined fields were CD34 positive; medium (grade 2) if ranged between 11 and 50%; and high (grade 3) if more than 50% of the examined fields were CD34 positive.

2.2. Statistical analysis

The Spearman test was applied to assess the correlation between groups of clinicopathological factors. p values of less than 0.05 were accepted as statistically significant.

3. Results

The results of assessment of the CD34 antigen expression intensity, advancement of inflammatory process, quality of surgical field, reduced hemodynamic parameters necessary to achieve bloodless surgical field and bleeding intensity are presented in Table 1.

Spearman test revealed correlation between the expression intensity of CD34 antigen and the quality of surgical field assessed in Fromm-Boezaart scale at MAP 70–80 mmHg and the intensity of intraoperative bleeding evaluated in ml per minute (Table 2).

At MAP between 70 and 80 mmHg 8 patients (26.6%) had satisfactory quality of surgical field (grade 1 or 2 at Fromm-Boezaart scale). All those patients had low or medium CD34 antigen expression in histochemical examination (Fig. 1).

It was necessary to lower hemodynamic parameters systematically in the remaining 22 patients (11 with high and 11 with medium grade of expression) in order to improve the quality of surgical field (grade 1 or 2 in Fromm-Boezaart scale). Patients with high CD34 antigen expression (Fig. 2) required more profound reduction of hemodynamic parameters.

Mean MAP at which the quality of surgical field was satisfactory was 61.8 in the group of patients with high CD34 antigen expression and 66.6 mmHg in patients with medium antigen expression. Both groups had similar heart rate accounting for 62 min^{-1}. The bleeding in the group with high CD34 antigen

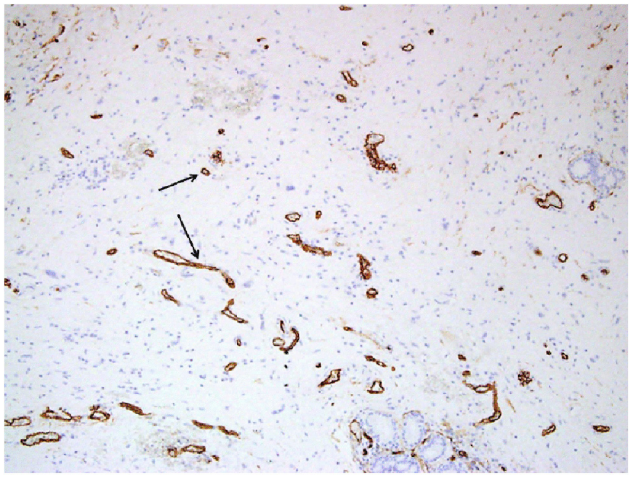

Fig. 1. Immunohistochemical CD34 expression estimated as low. Arrows show small blood vessels with positive CD34 staining within the endothelial cells. Magnification: 200×.