

含盐酸肾上腺素的局部浸润麻醉对鼻内镜手术影响的研究进展

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摘要

目前鼻内镜手术的开展已经日渐成熟, 但视野狭窄、术中出血是仍此项手术的一个主要缺点。在术前运用不同比例的利多卡因和盐酸肾上腺素混合液渗透到手术区域的鼻黏膜中保持视野清晰、减少手术出血是诸多术者所采取的常用方法, 但鼻腔黏膜血管丰富, 是否会影响术中血流动力学的稳定性、术后的恢复以及是否会产生并发症尚不明确。故本文结合国内外相关文献, 对含盐酸肾上腺素的局部浸润麻醉给鼻内镜手术带来的影响进行综述。

关键词

麻醉, 肾上腺素, 鼻内镜手术, 血流动力学, 并发症

Research Progress on the Effect of General Anesthesia Combined with Local Infiltration Anesthesia Containing Epinephrine on Nasal Surgical Procedures Surgery

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Abstract

Endoscopic sinus surgery is becoming more and more mature, but the main shortcomings of this surgery are narrow field of vision and surgical field bleeding. It is a method adopted by many researchers that they use mixed liquid of different proportion of lidocaine and epinephrine hydrochloride to penetrate into the nasal mucosa of the surgical area before surgery to maintain a clear visual field and reduce surgical bleeding. However, because of rich blood vessels in the nasal mucosa, it remains unclear that whether it will affect the stability of intraoperative hemodynamics, postoperative recovery and have complications. Based on relative domestic and foreign literature, this paper tempts to make a review about the effect of general anesthesia combined with local infiltration anesthesia containing epinephrine on nasal surgical procedures surgery.

Keywords

Anesthesia, Epinephrine, Endoscopic Sinus Surgery, Hemodynamics, Postoperative Complications

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1. 引言

我国开展鼻内镜手术(Endoscopic sinus surgery, ESS)已经有 30 余年，鼻中隔成形术、鼻窦炎、鼻腔鼻窦良恶性肿瘤等手术技术日渐成熟[1]。视野狭窄、术中出血是 ESS 的一个主要缺点，这反过来会增加并发症的风险，术后患者的鼻塞、疼痛问题也不可小觑。故许多专家学者在术前运用不同比例的利多卡因和肾上腺素混合液等药物渗透到手术区域的鼻黏膜中，在术中以达到减少手术出血，减轻粘膜充血，保持视野清晰的目的[2]，术后起到缓解疼痛、瘀斑、水肿等症状的作用[3]，提高康复质量，提高患者满意度[4]。鼻腔和副鼻窦粘膜血管丰富，肾上腺素在此过程中被吸收，会产生肾上腺素相关的副作用，比如血压波动和心率失常，甚至应激性心肌病[5]。如果耳鼻喉和麻醉医师没有重视，会对患者造成伤害。故我们在此讨论鼻内镜围手术期中使用含肾上腺素的局部浸润麻醉是否利大于弊。

2. 血流动力学分析

在血流动力学分析上，医者们各执己见。在血压方面，有研究者发现在术中运用利多卡因注射液和少量的肾上腺素混合液血压平均升高值会下降，且最高峰值在 1.5~2 分钟左右。比如 Yang 等人[6]分别给予 1% 利多卡因 4 ml 和不同剂量肾上腺素(I 组 20 μg、II 组 40 μg 和 III 组 0 μg)，与组内基础值比较，I 组和 II 组在 1.5 分钟时平均动脉压、全身血管阻力指数值下降，心脏指数、心率升高；III 组血流动力学无明显改变；Bhatia 等人[7]的研究中发现最高峰值在 2 分钟，且低浓度组(2% 利多卡因和 1:20 万肾上腺素，高浓度组为 2% 利多卡因和 1:40 万肾上腺素)在鼻粘膜浸润后收缩压从基线值上升>50% 的情况较少。此外低浓度组的收缩压、舒张压和平均动脉压的平均升高也显著降低。还有学者沈锦春发现[8]血压上升幅度和肾上腺素用量有关，肾上腺素用量越大，血压上升出现的越早，上升的幅度越大。Thevasagayam 等人[9]接受肾上腺素治疗的患者的收缩压显著升高，但文献中未明显标明肾上腺素的使用量。

但也有研究者有不同的结论，全身麻醉下鼻内镜手术中局部浸润注射含肾上腺素的利多卡因可引起

以血压先下降后上升的双相变化为主的血流动力学改变[8] [10]。不同浓度(I组 1:20万；II组 1:40万)相同剂量的肾上腺素(10 μg)引起的血流动力学变化无明显差别[10]；不同剂量的肾上腺素(I组、II组 10 μg；III组 20 μg)引起的血流动力学变化虽有差别，但不具统计学意义($P > 0.05$)。

少数研究发现血压会下降，比如 Cohen-Kerem 等人[11]的临床试验中把 1%利多卡因联合注射肾上腺素 1:10 万和注射生理盐水相比，肾上腺素组的患者心率显著降低，血压相对较低。Schechtman 等人通过建立了一个混合效应 Logistic 回归模型，得出结论术前使用 β -受体阻滞剂(肾上腺素)是手术后 1 小时内高血压反应过度的独立预测因素，除此外还发现了性别(女性)、年龄的增长等因素[12]。也有医者提出血流动力学改变不明显[13] [14]，比如 Ahmed [13]等人比较 1:10 万和 1:20 万浓度，血流动力学参数没有显著差异，但两种溶液与基线相比都会增加血压和心率。

3. 术中比较

有文献指出术前腭大孔注射局部麻醉剂对鼻内镜手术可以有效地减少术中出血，并且发现肾上腺素浓度为 1:8 万是恰当的[15]。Shenoy 等人[16]在功能性鼻内镜手术(Functional endoscopic sinus surgery, FESS)中采用 2%利多卡因和 1:8 万肾上腺素进行渗透翼腭窝，浸润侧手术野改善 25%~30%，影响持续时间为 2.5 h，超过平均功能性鼻内镜手术持续时间，并且发现真菌性鼻窦炎患者的出血程度高于鼻息肉病或慢性鼻窦炎患者。Wormald 等人[17]在翼腭窝注射 2 mL 2%利多卡因和 1:8 万肾上腺素记录到内窥镜鼻窦手术期间手术视野有所改善。Al-Qudah 等人[14]术中用 1:10 万的生理盐水混合肾上腺素溶液冲洗减少了患者的出血量，但没有明显可能改善术中视野，且没有改变心率和血压。

但也有学者提出相反看法，比如 Tangbumrungtham 等人[18]在慢性鼻窦炎手术中用 1%利多卡因和 1:10 万肾上腺素浸泡鼻腔侧与用生理盐水浸泡相比，除手术时间缩短外，术野、术中以及术后出血量在统计学上没有显著差异。Gungor 等人[19]在鼻中隔成形术中，使用利多卡因和肾上腺素联合使用和生理盐水相比，在出血量、手术时间以及术中粘膜损伤率等客观参数没有优势。Thevasagayam 等人[9]在鼻中隔成形术中，一组接受利多卡因(2%)和肾上腺素(1:8 万)渗透，另一组接受利多卡因(2%)渗透。两组在出血量、手术视野等方面差异无统计学意义。

4. 术后比较

术后疼痛会影响手术后的恢复质量，一些研究调查了周围神经阻滞对患者康复质量的影响。Gümüş [3]等人在鼻中隔成形术后加用 2%利多卡因 5 ml 加 1:10 万肾上腺素灌洗，发现此操作对患者术后的早期疼痛缓解、肿胀和瘀斑消退有效。Kim 等人[20]在全身麻醉下的鼻骨骨折整复术中采用筛前神经阻滞加鼻骨背侧骨膜注射注入 2%含肾上腺素(1:10 万)的利多卡因，可有效减轻术后疼痛。Gencer 等人[21]拔除鼻腔填塞时，利多卡因组(1:10 万肾上腺素和 1%利多卡因)术后疼痛评分和出血评分均明显好于生理盐水组。Ibrahim 等人[4]把 2%利多卡因加肾上腺素 1:20 万用于外鼻神经阻滞，发现能在不增加并发症发生率的情况下，充分缓解疼痛，减少麻醉用药量，提高恢复质量，减少鼻腔手术后苏醒激动的发生率。以上的对照组均为肾上腺素合利多卡因的联合与生理盐水的对照，无法评估肾上腺素或利多卡因的单一效应。

5. 并发症

在内窥镜鼻窦手术中使用肾上腺素偶有并发症的发生。大部分研究者在手术过程中没有记录到对患者构成风险的事件[7] [11] [19]。在没有已知心脏病的患者中，局部使用浓缩肾上腺素的不良事件的风险非常低(0.05%) [22]。Shenoy [16]的研究中出现 3 例患者发生并发症，均为心动过速，且未经干预，在 5~6

分钟内自行消退。考虑到可能是由于腭大管血管损伤或不慎注入上颌动脉或其分支，并吸收了一定量的肾上腺素溶液而引起的。Schechtman [12]的研究中记录了1例患者发生缺血性中风，1例患者发生血栓栓塞性中风，均发生在手术后1天内，但这两名患者在手术的第一个小时内都没有发生高血压事件。通过文献检索，还找到FESS手术中采取利多卡因+肾上腺素后发生并发症的些许个案共参考，比如出现心律失常[23]、应激性心脏病[5]、冠状动脉痉挛[22]、心肌病[24][25]、出血性脑梗塞[26]、癫痫[27]、急性视网膜中央动脉闭塞[28]，甚至心脏骤停[29]，在积极治疗下，患者均未出现后遗症和相关疾病的体征。

6. 动物实验

动物试验研究较少，Zehra Çınar 等人[2]在兔子试验鼻中隔成形术中，总结出肾上腺素+利多卡因组(总量0.5 ml；利多卡因剂量20 mg/ml，肾上腺素剂量0.0125 mg/ml)的术中各项指标(包括术中出血量、手术时间、手术平面可达性、视野质量和软骨膜粘液损伤程度)均优于生理盐水组。

7. 讨论

由于鼻粘膜血供丰富，在鼻内镜手术中，外科医生为保证术野清晰，都会对术中出血进行控制，常采用压迫、电凝、控制性降压、局部应用血管收缩药等方法加强止血[15][30]。止血对于优化手术野，安全有效地进行手术至关重要。诸多学者，目前仍采用利多卡因和肾上腺素混合液进行收缩血管、改善术野。Dow 等人[31]除在鼻中隔手术中先经鼻道(下鼻甲及鼻中隔)注入1:10万肾上腺素和1%罗比卡因外，再将1:1000或1:1万的含肾上腺素棉片放在鼻道10分钟，两者相比术中血流动力学稳定性相似，但相比于1:1万及1:1000手术可视化程度更加高。

利多卡因通过调节异位神经元放电，阻断钠通道，调节G蛋白偶联受体、N-甲基-D-天冬氨酸受体以及钙和钾通道，减少炎症反应和痛觉过敏，被广泛用作小手术或大手术后的全身和局部麻醉剂[32]。在全身麻醉鼻腔整形术中，利多卡因和肾上腺素联合对比肾上腺素组渗透不仅减少了吸入麻醉药的用量和费用，而且维持了血流动力学的稳定[33]。利多卡因加肾上腺素组术中出血量及术区外观清晰度虽无明显差异，但术后恢复质量提高，提高了外科医生的满意度。

肾上腺素可以直接兴奋肾上腺素 α 和 β 受体，在血浆浓度较高时，它作为一种非选择性的 α 激动剂，导致小动脉和静脉收缩。这些作用机制可能会导致有害的心肺效应，包括心律失常和高血压。然而，在较低浓度下，肾上腺素可以起到 β 激动剂的作用，并导致血管扩张状态。临床有研究表明，无论在鼻腔内放置多个浸泡的棉球，局部应用1:1000肾上腺素是安全的[34]。但对于已知有心脏病史的患者，必须权衡其益处与心肌缺血和梗塞、肺水肿、心源性休克、心律失常和心脏骤停的风险，要谨慎使用。对于这些患者，发现术中第一个小时内经历高血压事件的可能性是健康患者的3倍[31]。并且有研究已经强调过在任何情况下都应避免在裸露的面神经上局部应用肾上腺素[35]。

影响术中出血的原因，除医师操作外，不同疾病的出血程度也有不同，在真菌性鼻窦炎患者中，出血量高于其他鼻部病变，这可能是因为在感染性病理中，粘膜发炎，粘膜血管增多，毛细血管壁脆弱，毛细血管通透性增加[16]；不同部位进行注射可能也会影响血管收缩的程度，比如经腭大孔局部麻醉和血管收缩药对翼腭窝的渗透。当上颌动脉进入翼腭窝时，渗入该间隙的血管收缩药将作用于上颌动脉的第三部分。这反过来会导致上颌动脉的血管痉挛，从而减少进入蝶腭动脉的血流量，从而导致进入鼻腔粘膜的血流量减少[16]。

既往研究中，也提出了不同的血管收缩药物，除肾上腺素外，羟甲唑啉已被证明是一种有效的血管收缩药物[30][36]。硝酸萘甲唑啉的药理学特征与羟甲唑啉非常相似，两者都是具有相似性质的减充血剂，

因此也是可行的替代品[36]。还有局部使用氨甲环酸也可以减少术中和术后出血[37]。有少量证据表明，术前口服或鼻腔使用皮质类固醇可以通过对周围炎症的影响显著减少了术中出血和手术时间[38][39]，并提出有利于恢复正常鼻窦生理和粘液纤毛清除[38]。此外，类固醇可以缩小鼻息肉的大小，改善症状。还有学者提出左旋布比卡因局部渗透用于鼻腔手术后的镇痛效果明显好于利多卡因加肾上腺素，且持续时间更长[40]。

希望将来在寻找安全的肾上腺素使用配比上有更多的研究，通过严格控制变量，比如注射的解剖位置、减少全身麻醉对血流动力学的影响[41]；是否要混合其他局部麻醉药物等，能够在不引起全身血液动力学影响的情况下找到理想的止血药物，在鼻腔局部血管收缩上发挥更有效、安全的作用。

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参考文献

- [1] 王振晓, 张二朋, 时光刚. 内镜技术在鼻颅底外科手术中的应用和展望[J]. 中华耳鼻咽喉头颈外科杂志, 2022, 57(8): 1005-1011.
- [2] Çınar, Z., Yiğit, Ö., Savran, T.F. and Koca, S.B. (2021) A Clinical and Histopathological Comparison of Saline, Adrenaline and 2-Mercaptoethanesulfonate (MESNA) in Mucoperichondrial Elevation: Which Is Superior? *ACTA Otorhinolaryngologica Italica*, **41**, 51-58. <https://doi.org/10.14639/0392-100X-N0920>
- [3] Gümüş, N. (2020) Lavage with Lidocaine and Adrenaline Mixture Reduces the Early Side Effects of Septorhinoplasty. *Annals of Plastic Surgery*, **84**, e29-e32. <https://doi.org/10.1097/SAP.0000000000002219>
- [4] Ibrahi, M., Elnabitiy, A.M. and Keera, A. (2018) Efficacy of External Nasal Nerve Block Following Nasal Surgery : A Randomized, Controlled Trial. *Der Anaesthetist*, **67**, 188-197. <https://doi.org/10.1007/s00101-018-0410-0>
- [5] Yamamoto, W., Nishihara, T., Nakanishi, K., et al. (2021) Takotsubo Cardiomyopathy Induced by Very Low-Dose Epinephrine Contained in Local Anesthetics: A Case Report. *American Journal of Case Reports*, **22**, e932028. <https://doi.org/10.12659/AJCR.932028>
- [6] Yang, J.J., Zheng, J., Liu, H.J., et al. (2006) Epinephrine Infiltration on Nasal Field Causes Significant Hemodynamic Changes: Hypotension Episode Monitored by Impedance-Cardiography under General Anesthesia. *Journal of Pharmaceutical Sciences*, **9**, 190-197.
- [7] Bhatia, N., Ghai, B., Mangal, K., et al. (2014) Effect of Intramucosal Infiltration of Different Concentrations of Adrenaline on Hemodynamics during Transsphenoidal Surgery. *Journal of Anaesthesiology Clinical Pharmacology*, **30**, 520-525. <https://doi.org/10.4103/0970-9185.142848>
- [8] 沈锦春, 杨建军, 胡益民, 等. 鼻内镜手术中局部浸润注射含肾上腺素的利多卡因引起血压双相性变化[J]. 临床麻醉学杂志, 2007(2): 107-109.
- [9] Thevasagayam, M., Jindal, M., Allsop, P. and Oates, J. (2007) Does Epinephrine Infiltration in Septoplasty Make Any Difference? A Double Blind Randomised Controlled Trial. *European Archives of Oto-Rhino-Laryngology*, **264**, 1175-1178. <https://doi.org/10.1007/s00405-007-0339-4>
- [10] 王秋萍, 李泽卿, 王天友, 等. 局部麻醉剂中小剂量肾上腺素引起血压下降的原因探讨[J]. 中国耳鼻咽喉颅底外科杂志, 2006(1): 30-35.
- [11] Cohen-Kerem, R., Brown, S., Villaseñor, L.V. and Witterick, I. (2008) Epinephrine/Lidocaine Injection vs. Saline during Endoscopic Sinus Surgery. *Laryngoscope*, **118**, 1275-1281. <https://doi.org/10.1097/MLG.0b013e31816dd2d9>
- [12] Schechtman, S.A., Wertz, A.P., Shanks, A., et al. (2017) Preoperative β -Blockade and Hypertension in the First Hour of Functional Endoscopic Sinus Surgery. *Laryngoscope*, **127**, 1496-1505. <https://doi.org/10.1002/lary.26492>
- [13] Ahmed, O.G., Yu, J., Choi, J.S., et al. (2020) Real-Time Hemodynamic Effects of 1:100,000 and 1:200,000 Injectable Epinephrine and Placement of Topical 1:1000 Epinephrine Pledgets in Patients Undergoing Endoscopic Sinus and Skull-Base Surgery: A Randomized, Prospective Study. *International Forum of Allergy & Rhinology*, **10**, 141-146. <https://doi.org/10.1002/alr.22493>
- [14] Al-Qudah, M.A. (2022) The Effect of Intranasal Irrigation with Epinephrine Solution on Intraoperative Visualization and Bleeding during FESS. *European Archives of Oto-Rhino-Laryngology*, **279**, 1911-1917. <https://doi.org/10.1007/s00405-021-06952-w>

- [15] Hwang, S.H., Kim, S.W., Kim, S.W., et al. (2019) Greater Palatine Canal Injections Reduce Operative Bleeding during Endoscopic Sinus Surgery: A Systematic Review and Meta-Analysis. *European Archives of Oto-Rhino-Laryngology*, **276**, 3-10. <https://doi.org/10.1007/s00405-018-5138-6>
- [16] Shenoy, V.S., Prakash, N., Kamath, P.M., et al. (2017) Is Pterygopalatine Fossa Injection with Adrenaline an Effective Technique for Better Surgical Field in FESS? *Indian Journal of Otolaryngology and Head & Neck Surgery*, **69**, 464-473. <https://doi.org/10.1007/s12070-017-1225-z>
- [17] Wormald, P.J., Athanasiadis, T., Rees, G., et al. (2005) An Evaluation of Effect of Pterygopalatine Fossa Injection with Local Anesthetic and Adrenalin in the Control of Nasal Bleeding during Endoscopic Sinus Surgery. *American Journal of Rhinology & Allergy*, **19**, 288-292. <https://doi.org/10.1177/194589240501900313>
- [18] Tangbumrungtham, N., Hwang, P.H., Maul, X., Borchard, N.A., et al. (2020) The Effect of Topical Epinephrine 1:1000 with and without Infiltration of 1% Lidocaine with Epinephrine 1:100,000 on Endoscopic Surgical Field Visualization: A Double-Blind Randomized Controlled Study. *International Forum of Allergy & Rhinology*, **10**, 147-152. <https://doi.org/10.1002/alr.22468>
- [19] Gungor, V., Baklaci, D., Kum, R.O., Yilmaz, Y.F., et al. (2016) Infiltration with Lidocaine and Adrenaline Instead of Normal Saline Does Not Improve the Septoplasty Procedure. *European Archives of Oto-Rhino-Laryngology*, **273**, 2073-2077. <https://doi.org/10.1007/s00405-015-3870-8>
- [20] Kim, H.S., Lee, H.K., Jeong, H.S., et al. (2013) Decreased Postoperative Pain after Reduction of Fractured Nasal Bones Using a Nerve Block of the Anterior Ethmoidal Nerve. *International Journal of Oral & Maxillofacial Surgery*, **42**, 727-731. <https://doi.org/10.1016/j.ijom.2013.01.017>
- [21] Gencer, Z.K., Ozkiriş, M., Gencer, M., et al. (2013) Comparison of Ropivacaine, Bupivacaine, Prilocaine and Lidocaine in the Management of Pain and Hemorrhage during Nasal Pack Removal. *American Journal of Rhinology & Allergy*, **27**, 423-425. <https://doi.org/10.2500/ajra.2013.27.3945>
- [22] Orlandi, R.R., Warrier, S., Sato, S., et al. (2010) Concentrated Topical Epinephrine Is Safe in Endoscopic Sinus Surgery. *American Journal of Rhinology & Allergy*, **24**, 140-142. <https://doi.org/10.2500/ajra.2010.24.3454>
- [23] Usami, N., Tooyama, M., Oda, W., et al. (2022) A Case of Wide QRS Tachycardia after the Local Administration of Epinephrine to Reduce Bleeding During General Anesthesia. *Anesthesia Progress*, **69**, 38-40. <https://doi.org/10.2344/anpr-68-03-05>
- [24] Kim, C.J., Kim, J.M., Jang, Y.H., et al. (2009) Cardiomyopathy after Local Infiltration or Application of Epinephrine for Plastic Surgery under General Anesthesia : Two cases report. *Korean Journal of Anesthesiology*, **56**, 725-728. <https://doi.org/10.4097/kjae.2009.56.6.725>
- [25] Naddaf, S., Ehrenberg, S., Hakim, R., Mahamid, M., Turgeman, Y. and Koren, O. (2020) Epinephrine Soaked Tampons Induced Transient Acute Dilated Cardiomyopathy during FESS Procedure. *BMC Cardiovascular Disorders*, **20**, Article No. 452. <https://doi.org/10.1186/s12872-020-01706-8>
- [26] Koçyiğit, M., Giran Örtekin, S., Yaslikaya, S. and Akpinar, A. (2015) Intracranial Hemorrhagic Infarct after Local Anesthesia on Nasal Mucosa: A Case Report. *International Journal of Surgery Case Reports*, **17**, 45-47. <https://doi.org/10.1016/j.ijscr.2015.10.011>
- [27] Tsai, C.J., Wang, H.M., Lu, I.C., et al. (2007) Seizure after Local Anesthesia for Nasopharyngeal Angiofibroma. *The Kaohsiung Journal of Medical Sciences*, **23**, 97-100. [https://doi.org/10.1016/S1607-551X\(09\)70383-3](https://doi.org/10.1016/S1607-551X(09)70383-3)
- [28] Maaranen, T.H. and Mäntyläjärvi, M.I. (2000) Central Retinal Artery Occlusion after a Local Anesthetic with Adrenaline on Nasal Mucosa. *Journal of Neuro-ophthalmology*, **20**, 234-235. <https://doi.org/10.1097/00041327-200020040-00003>
- [29] Weber, F., Guha, R., Weinberg, G., et al. (2019) Prolonged Pulseless Electrical Activity Cardiac Arrest after Intranasal Injection of Lidocaine With Epinephrine: A Case Report. *A & A Practice*, **12**, 438-440. <https://doi.org/10.1213/XAA.0000000000000962>
- [30] Feng, M., Lao, V.F., Choby, G., et al. (2022) Survey of Anesthesiologists on Topical Vasoconstrictors and Intravenous Tranexamic Acid for Endoscopic Sinus Surgery. *Annals of Otology, Rhinology & Laryngology*, **131**, 59-70. <https://doi.org/10.1177/00034894211005940>
- [31] Dow, C.L., Sideris, A.W., Singh, R., et al. (2021) A Non-Inferiority Trial: Safety and Efficacy of Topical 1:1000 versus 1:10,000 Epinephrine in Sino-nasal Surgeries. *Annals of Otology, Rhinology & Laryngology*, **130**, 563-570. <https://doi.org/10.1177/0003489420962825>
- [32] Zhu, J., Liu, J., Shen, G., Zhong, T., et al. (2018) Comparison of Efficacy Outcomes of Lidocaine Spray, Topical Lidocaine Injection, and Lidocaine General Anesthesia in Nasal Bone Fractures Surgeries: A Randomized, Controlled Trial. *Medical Science Monitor*, **24**, 4386-4394. <https://doi.org/10.12659/MSM.908468>
- [33] Goktas, U., Isik, D., Kati, I., et al. (2011) Effects of Lidocaine Infiltration on Cost of Rhinoplasty Made Under General Anesthesia. *Journal of Craniofacial Surgery*, **22**, 2176-2178. <https://doi.org/10.1097/SCS.0b013e318232414c>

-
- [34] Gunaratne, D.A., Barham, H.P., Christensen, J.M., *et al.* (2016) Topical Concentrated Epinephrine (1:1000) Does Not Cause Acute Cardiovascular Changes during Endoscopic Sinus Surgery: Topical Epinephrine in Endoscopic Sinus Surgery. *International Forum of Allergy & Rhinology*, **6**, 135-139. <https://doi.org/10.1002/alr.21642>
 - [35] Alicandri-Ciufelli, M., Molinari, G., Beckmann, S., *et al.* (2020) Epinephrine Use in Endoscopic Ear Surgery: Quantitative Safety Assessment. *ORL*, **82**, 1-7. <https://doi.org/10.1159/000503725>
 - [36] Saif, A.M., Farboud, A., Delfosse, E., Pope, L. and Adke, M. (2016) Assessing the Safety and Efficacy of Drugs Used in Preparing the Nose for Diagnostic and Therapeutic Procedures: A Systematic Review. *Clinical Otolaryngology*, **41**, 546-563. <https://doi.org/10.1111/coa.12563>
 - [37] Husain, S., Ramos, J.A., Karaf, J.H.A., *et al.* (2023) Efficacy of Topical Tranexamic Acid to Reduce Bleeding in Endoscopic Sinus Surgery for Chronic Rhinosinusitis with Polypsis. *European Archives of Oto-Rhino-Laryngology*, **280**, 737-741. <https://doi.org/10.1007/s00405-022-07563-9>
 - [38] Wright, E.D. and Agrawal, S. (2007) Impact of Perioperative Systemic Steroids on Surgical Outcomes in Patients with Chronic Rhinosinusitis with Polypsis: Evaluation with the Novel Perioperative Sinus Endoscopy (POSE) Scoring System. *Laryngoscope*, **117**, 1-28. <https://doi.org/10.1097/MLG.0b013e31814842f8>
 - [39] Sieskiewicz, A., Olszewska, E., Rogowski, M., *et al.* (2006) Preoperative Corticosteroid Oral Therapy and Intraoperative Bleeding during Functional Endoscopic Sinus Surgery in Patients with Severe Nasal Polypsis: A Preliminary Investigation. *Annals of Otology, Rhinology & Laryngology*, **115**, 490-494. <https://doi.org/10.1177/000348940611500702>
 - [40] Demiraran, Y., Ozturk, O., Guclu, E., *et al.* (2008) Vasoconstriction and Analgesic Efficacy of Locally Infiltrated Levobupivacaine for Nasal Surgery. *Anesthesia & Analgesia*, **106**, 1008-1011. <https://doi.org/10.1213/ane.0b013e31816174c3>
 - [41] Huh, H., Park, J.J., Seong, H.Y., *et al.* (2020) Effectiveness Comparison of Dexmedetomidine and Remifentanil for Perioperative Management in Patients Undergoing Endoscopic Sinus Surgery. *American Journal of Rhinology & Allergy*, **34**, 751-758. <https://doi.org/10.1177/1945892420927291>