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Hans汉斯

利多卡因在预防全身麻醉拔管呛咳中的应用进展

郭晓帮[1]，张海亮[2*]

[1]延安大学医学院，陕西 延安
[2]延安大学附属医院，陕西 延安

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摘　要

在全身麻醉后气管拔管过程中，吸痰拔管的机械刺激不仅会引起咳嗽、支气管痉挛等气道反应，还会引起血流动力学波动，如高血压、心动过速、心律失常等，导致心脑血管事故甚至危及生命的事件。目前，利多卡因为临床常用的表面麻醉剂来预防呛咳反应的发生。本文综述了利多卡因在预防全身麻醉拔管呛咳中的不同 方式的研究进展。

关键词

利多卡因，全身麻醉，拔管，呛咳反应，预防

Application Progress of Lidocaine in Preventing Cough after Extubation of General Anesthesia

Xiaobang Guo[1], Hailiang Zhang[2*]

[1]Medical School, Yan'an University, Yan'an Shaanxi
[2]Affiliated Hospital of Yan'an University, Yan'an Shaanxi

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Abstract

During extubation after general anesthesia, mechanical stimulation of sputum aspiration and ex-

*通讯作者。

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tubation not only causes airway reactions such as coughing and Bronchospasm, but also causes Hemodynamics fluctuations, such as hypertension, tachycardia, arrhythmia, etc., leading to cardiovascular and cerebrovascular accidents and even life-threatening events. At present, lidocaine is commonly used as a surface anesthetic to prevent the occurrence of choking reaction. This article reviews the research progress of different application methods of lidocaine in preventing cough during extubation of general anesthesia.

Keywords

Lidocaine, General Anesthesia, Extubation, Choking Reaction, Prevention

1. 引言

大约 40%~76%的患者在全麻苏醒后拔管时会发生呛咳[1] [2] [3]。在全麻苏醒期，严重呛咳会导致高血压、心动过速、颅内高压和眼内压增高等各种不良并发症。如在神经外科手术和甲状腺手术等苏醒期，严重的呛咳及血流动力学变化会造成手术部位出血、再次手术等严重后果[4]。甲状腺切除术或颈动脉内膜切除术后的颈部血肿，剖腹手术后的伤口愈合受损，或颅内手术后的脑出血。因此，建议使用顺利拔管技术，以尽量减少咳嗽，避免手术后可能出现的并发症[5]。

多种药物已被证明可以减少单独出现的咳嗽，如利多卡因(静脉注射、皮下注射、局部注射和气管途径)、右美托咪定、芬太尼和瑞芬太尼[6]-[13]。然而，这些研究受到样本量小和药物剂量不一的限制[9] [10]。因此，这些药物在减少围手术期咳嗽方面的比较效果尚不清楚。

利多卡因为临床常用的表面麻醉剂，已知利多卡因能够阻断呼吸道黏膜的应激感受器，降低机械刺激，从而预防呛咳反应的发生[14]。本文就现阶段利多卡因在预防全身麻醉拔管呛咳反应中的应用方式和效果综述如下，以确定利多卡因在降低中度和重度拔管期咳嗽风险方面的比较效果。

2. 呛咳的定义及其发生机制

呛咳是指咽、喉、气管等因异物刺激产生的保护性咳嗽反射，咳嗽感受器广泛分布于喉、气管、支气管等处的黏膜。机械刺激主要作用于喉及气管等大支气管部位的感受器，而二级支气管以下的部位则对化学刺激较敏感。外来的机械刺激和化学刺激通过刺激气管黏膜上皮的外周神经末梢，然后经迷走神经上传至脑干的特定区域[15]，由此构成咳嗽反射的传导通路。全麻苏醒期各种反射逐渐恢复，而气管导管属于异物，很容易因机械性刺激激活咳嗽受体，诱发患者出现呛咳甚至血流动力学剧烈波动，这就是全身麻醉苏醒期拔管呛咳发生率高的主要原因[16]。咽喉和气管有丰富的神经分布，在呼吸系统中主要分布于肺泡壁与支气管壁上的 C 型无髓鞘神经，其约占外周感觉神经的 75%~80%和神经节前纤维的 95%。主要功能为感受疼痛与反射，是脊髓后根中的痛觉传入纤维。而在全麻手术期间，患者的气道保护反射减弱，故对疼痛的感受较为轻微，而当手术结束时，麻醉药物也逐渐代谢，吸痰、气管导管本身以及拔出的不良刺激可激活体内交感肾上腺系统，缩血管物质释放增加，患者血压增高，心率加快[17] [18] [19]。与此同时麻醉药物代谢后，患者的气道保护反射也随之恢复，可感知到较为强烈的疼痛，也可引起患者血流动力学不稳，这种血流动力学的短暂波动也许对心功能正常的患者影响不是很大，但若是针对心脑

血管功能退化的患者却非常危险[20] [21] [22]。

3. 呛咳发生的影响因素及其不良影响

3.1. 呛咳的影响因素

与呛咳有关的因素有性别、吸烟、麻醉方式等。Soh 等[4]发现瑞芬太尼 TCI 用于麻醉苏醒期预防咳嗽时，女性需要的瑞芬太尼浓度低于男性，可能是女性体内存在的 μ 型阿片受体有较高的可用性，阿片类药物能够更好地与其结合发挥抑制呛咳反射的作用。Hans 等[23]研究显示，吸烟者全麻拔管期间呛咳的发生率为 50%，而非吸烟者为 17%，说明吸烟能增加全身麻醉拔管呛咳的发生率。有研究表明，与七氟烷吸入全身麻醉相比，丙泊酚静脉麻醉降低了患者苏醒期呛咳的发生率，这与拔管时麻醉药物的残留浓度有关，可能是因为拔管时七氟烷的残余浓度低，而同样条件下，丙泊酚组在拔管时具有更深的残余麻醉效应，且瑞芬太尼的残余浓度高[23]。

3.2. 拔管呛咳的不良影响

大约 40%的患者在全麻苏醒后拔管时会咳嗽[1] [2]。随着麻醉效果的消退，咳嗽随之而来，并使外周和中枢神经系统对气管插管刺激气管的感觉增强[24]。除了不舒服之外，咳嗽还有重要的生理后果：胸腔内压力增加，右心房静脉回流减少，腹腔内压力增加、功能残气量降低和血压升高[12]。虽然大多数患者没有明显的后遗症，但在某些情况下，应强调尽量减少出现时的咳嗽。呼吸功能较差的患者群体，如功能储备能力下降的肥胖患者，可能会发展为继发于痉挛后肺不张的低氧血症。特殊的手术也应该“平稳拔管”，咳嗽最少，以避免并发症：甲状腺切除术(手术出血) [25]、剖腹手术或疝修补术(伤口裂开) [26]、颈动脉内膜切除术(颈部血肿)和颅内手术(脑出血) [27]。

4. 利多卡因预防呛咳的机制

利多卡因是一种钠通道阻滞剂，通过抑制交感神经－肾上腺系统功能，作用于交感神经细胞膜上的 Na^+通道，使 Na^+通道功能失活，抑制神经细胞动作电位产生，抑制神经信号传导，从而抑制气管机械性刺激黏膜上交感神经感受器的功能[28]，减轻拔管时的血流动力学波动。同时，利多卡因也是一种直接的心脏抑制剂和外周血管扩张剂。利多卡因有几种有益的作用，如镇痛、抗痛觉过敏和抗炎[29] [30]。此外，利多卡因可抑制有髓 A 和无髓 C 神经纤维的棘突活性、振幅和传导时间[31]。几项研究表明，利多卡因可以通过不同的方法降低麻醉出现时咳嗽的发生率和严重程度，包括插管内、导管润滑、气管内滴注和诱导前静脉推注[7] [32] [33] [34]。静脉给药抑制中枢脑干网状结构的心血管中枢，间接抑制气管黏膜表面丰富的神经丛传递活动[35] [36]。经气管内给药可直接抑制气管黏膜表面丰富的神经丛，从源头上抑制患者的应激反应[37]，可发挥以下作用：(1) 气管滴注可局部麻醉气管黏膜，阻断气管黏膜上迷走神经感受器对拔管机械性刺激的传入；(2) 可经黏膜毛细血管吸收入血，与静脉注射使用具有相同的麻醉效果。

5. 利多卡因的临床应用

5.1. 给药时机及方式

目前关于利多卡因给药时机的研究主要包括插管前导管润滑、气管内或缓慢静脉推注、雾化、气管导管套囊内用药，术中气管内或静脉持续泵注、滴注直至手术结束，拔管前单次静脉或气管内注射。龙云[38]等人研究指出插管前及拔管前 5 min 左右按 1.5 mg/kg 标准缓慢滴注或气管导管内注入 2%利多卡因均可减轻血流波动，降低插管时、拔管时呛咳反应发生率。Hu 等[39]研究表明，对接受甲状腺手术的患者麻醉诱导前 10 分钟内分别静脉滴注 1.5 mg/kg 利多卡因(2%)，剂量为 20 ml 生理盐水和 20 ml 生理盐，

然后每小时连续静脉滴注 1.5 mg/kg 利多卡因，剂量为 20 ml 和 20 ml 生理盐水，直到手术结束前 30 分钟，咳嗽发生率(28.3%)显著低于对照组组(66.7%)，能够减少术后出血量，并提供更好的术后镇痛效果。Jee 和 Park [33]研究显示，气管拔管前 5 min，在气管导管内喷洒 2%利多卡因 1 mg/kg 可以减少呛咳的发生、减弱血流动力学的剧烈波动，使患者平稳地度过围术期。而在 Lee 等[40]静脉注射利多卡因 1.5 mg/kg 抑制拔管呛咳的研究中，拔管呛咳的发生率高达 72.7%，认为拔管期静注利多卡因并不能抑制呛咳的发生。

5.2. 使用剂量

关于利多卡因剂量的研究，较多关注单次静脉注射和气管内滴注的剂量，包括麻醉诱导前后及拔管前后。有研究表明，全身麻醉过程中抑制咳嗽反射所需的利多卡因的血浆浓度在 2.3~3 ug/ml [41]，通过推注给药很难及时达到该浓度；然而，可以通过延长静脉输注时间来获得目标浓度。Beford [42]等人研究表明在静脉推注 1.5 mg/kg 利多卡因后 90 秒，血浆水平可以达到 3.2 ± 0.6 ug/ml，Erb [43]等研究表明，静注利多卡因 1.5~2.0 mg/kg 可有效抑制气道反应。利多卡因会根据给药方式和剂量导致血药浓度变化，当被用于气管内表面麻醉时起效时间约为 20 s，持续 30 min [43]。静脉注射利多卡因的血药浓度通常高于气管内注射。呼吸系统中主要分布于肺泡壁与支气管壁上的 C 型无髓鞘神经，主要功能为感受疼痛与反射。利多卡因经气管导管给予时可以抑制气道 C-纤维感受器的兴奋，有效地抑制神经信号传递，抑制血流动力学波动及咳嗽反应[44]，而并非达到血药浓度从而抑制呛咳的发生。由此可以推断，全麻诱导期及拔管期行 2%利多卡因气管内表面麻醉相比于静脉注射的相同剂量方式，可以有效的抑制呛咳反应的发生，且起效时间更快。

6. 小结

综上所述，全麻时应用利多卡因能有效预防严重呛咳的发生，其机制可能是作用于交感神经细胞膜上的 Na^+通道，使 Na^+通道功能失活，抑制神经细胞动作电位产生，对神经信号传导具有抑制作用，从而抑制气管机械性刺激黏膜上交感神经感受器的功能。虽然它可能会造成心率下降、苏醒延迟，但只要合理用药(剂量及时机)，仍然能发挥其优势。目前的研究对利多卡因的临床效果已有了确切认识，但对小儿、老人、特殊疾病的病人的呛咳效果仍然有待探索，以使不同的病人都能平稳的度过苏醒期，达到舒适化医疗的要求。

参考文献

[1] Estebe, J.P., Gentili, M., Le Corre, P., Gi Dollo., Chevanne, F. and Ecoffey, C. (2005) Alkalinization of Intracuff Lidocaine: Efficacy and Safety. *Anesthesia & Analgesia*, **101**, 1536-1541. https://doi.org/10.1213/01.ANE.0000180995.24211.89

[2] Fagan, C., Frizelle, H.P., Laffey, J., Hannon, V. and Carey, M. (2000) The Effects of Intracuff Lidocaine on Endotracheal-Tube-Induced Emergence Phenomena after General Anesthesia. *Anesthesia & Analgesia*, **91**, 201-205. https://doi.org/10.1213/00000539-200007000-00038

[3] Kim, E.S. and Bishop, M.J. (1998) Cough during Emergence from Isoflurane Anesthesia. *Anesthesia & Analgesia*, **87**, 1170-1174. https://doi.org/10.1213/00000539-199811000-00036

[4] Soh, S., Park, W.K., Kang, S.W., *et al.* (2014) Sex Differences in Remifentanil Requirements for Preventing Cough during Anesthetic Emergence. *Yonsei Medical Journal*, **55**, 807-814. https://doi.org/10.3349/ymj.2014.55.3.807

[5] Tung, A., Ferguson, Na., Ng, N., Hu, V., Dormuth, C. and Griesdale, D.E.G. (2020) Medications to Reduce Emergence Coughing after General Anaesthesia with Tracheal Intubation: A Systematic Review and Network Meta-Analysis. *British Journal of Anaesthesia*, **124**, 480-495. https://doi.org/10.1016/j.bja.2019.12.041

[6] Yukioka, H., Hayashi, M., Terai, T. and Fujimori, M. (1993) Intravenous Lidocaine as a Suppressant of Coughing during Tracheal Intubation in Elderly Patients. *Anesthesia & Analgesia*, **77**, 309-312. https://doi.org/10.1213/00000539-199308000-00016

[7] Souissi, H., Frechette, Y., Murza, A., *et al.* (2016) Intracuff 160 Mg Alkalinized Lidocaine Reduces Cough Upon Emer-

gence from N2O-Free General Anesthesia: A Randomized Controlled Trial. *Canadian Journal of Anesthesia/Journal canadien d'anesthésie*, **63**, 862-870. https://doi.org/10.1007/s12630-016-0652-8

[8] Minogue, S.C. and Ralph, J. (2004) Laryngotracheal Topicalization with Lidocaine before Intubation Decreases the Incidence of Coughing on Emergence from General Anesthesia. *Anesthesia & Analgesia*, **99**, 1253-1257. https://doi.org/10.1213/01.ANE.0000132779.27085.52

[9] Liu, H., Zhou, C. and Ji, J. (2016) Effects of Using Different Dose of Dexmedetomidine during Tracheal Extubation for Patients with Parotidectomy after General Anesthesia. *Shanghai Journal of Stomatology*, **25**, 368-372.

[10] Inoue, Y., Koga, K., Sata, T. and Shigematsu, A. (2005) Effects of Fentanyl on Emergence Characteristics from Anesthesia in Adultcervical Spine Surgery: A Comparison of Fentanyl-Based and Sevoflurane-Based Anesthesia. *Journal of Anesthesia*, **19**, 12-16. https://doi.org/10.1007/s00540-004-0278-9

[11] Cho, H., Kim, H., Baek, S. and Jung, K. (2008) The Effect of Remifentanil Infusion on Coughing during Emergence from General Anesthesia with Desflurane. *Korean Journal of Anesthesiology*, **55**, 670-674. https://doi.org/10.4097/kjae.2008.55.6.670

[12] Miller, K.A., Harkin, C.P. and Bailey, P.L. (1995) Postoperative Tracheal Extubation. *Anesthesia & Analgesia*, **80**, 149-172. https://doi.org/10.1213/00000539-199501000-00025

[13] Jubb, A. and Ford, P. (2009) Extubation after Anaesthesia: A Systematic Review. *Update in Anaesthesia*, **25**, 30-36.

[14] 王志, 董源洪, 陈振毅, 等. 地佐辛、利多卡因、麻黄碱对芬太尼呛咳反应抑制作用的比较[J]. 药学实践杂志, 2016, 34(5): 463-465.

[15] Lee, J.H., Choi, S.H., Choi, Y.S., *et al.* (2014) Does the Type of Anesthetic Agent Affect Remifentanil Effect-Site Concentration for Preventing Endotracheal Tube-Induced Cough during Anesthetic Emergence? Comparison of Propofol, Sevoflurane, and Desflurane. *Journal of Clinical Anesthesia*, **26**, 466-474. https://doi.org/10.1016/j.jclinane.2014.02.002

[16] Reynolds, S.M., Mackenzie, A.J., Spina, D., *et al.* (2004) The Pharmacology of Cough. *Trends in Pharmacological Sciences*, **25**, 569-576. https://doi.org/10.1016/j.tips.2004.09.009

[17] Berninger, M.T., Friederichs, J., Leidinger, W., *et al.* (2018) Effect of Local Infiltration Analgesia, Peripheral Nerve Blocks, General and Spinal Anesthesia on Early Functional Recovery and Pain Control in Total Knee Arthroplasty. *BMC Musculoskeletal Disorders*, **19**, Article No. 232. https://doi.org/10.1186/s12891-018-2154-z

[18] 陶嘉斌, 苏喆, 王艳, 等. 全凭静脉麻醉对腔镜下甲状腺手术的苏醒躁动及术后镇痛效果的影响[J]. 现代生物医学进展, 2018, 18(9): 1679-1682.

[19] Xie, S., Ma, W., Shen, M., *et al.* (2018) Clinical and Pharmacogenetics Associated with Recovery Time from General Anesthesia. *Pharmacogenomics*, **19**, 1111-1123. https://doi.org/10.2217/pgs-2018-0085

[20] Thenuwara, K.N., Yoshimura, T., Nakata, Y., *et al.* (2018) Time to Recovery after General Anesthesia at Hospitals with and without a Phase I Post-Anesthesia Care Unit: A Historical Cohort Study. *Canadian Journal of Anesthesia/Journal canadien d'anesthésie*, **65**, 1296-1302. https://doi.org/10.1007/s12630-018-1220-1

[21] Sitilci, T., Demirgan, S., Akcay, C., *et al.* (2017) Comparison of Patients with and without Intellectual Disability under General Anesthesia: A Retrospective Study. *Nigerian Journal of Clinical Practice*, **20**, 438-444. https://doi.org/10.4103/1119-3077.204372

[22] Zhang, Y., Shan, G.J., Zhang, Y.X., *et al.* (2018) Propofol Compared with Sevoflurane General Anaesthesia Is Associated with Decreased Delayed Neurocognitive Recovery in Older Adults. *British Journal of Anaesthesia*, **121**, 595-604. https://doi.org/10.1016/j.bja.2018.05.059

[23] Hans, P., Marechal, H. and Bonhomme, V. (2008) Effect of Propofol and Sevoflurane on Coughing in Smokers and Non-Smokers Awakening from General Anaesthesia at the End of a Cervical Spine Surgery. *British Journal of Anaesthesia*, **101**, 731-737. https://doi.org/10.1093/bja/aen271

[24] Canning, B.J. (2006) Anatomy and Neurophysiology of the Cough Reflex ACCPevidence-Based Clinical Practice Guidelines. *Chest*, **129**, 33S-47S. https://doi.org/10.1378/chest.129.1_suppl.33S

[25] Rosato, L., Avenia, N., Bernante, P., Palma, M., Gulino, G., Nasi, P.G., *et al*. (2004) Complications of Thyroid Surgery: Analysis of a Multicentric Study on 14, 934 Patients Operated on in Italy Over 5 Years. *World Journal of Surgery*, **28**, 271-276. https://doi.org/10.1007/s00268-003-6903-1

[26] van Ramshorst, G.H., Nieuwenhuizen, J., Jeekel, J., Lange, J.F., *et al*. (2010) Abdominal Wound Dehiscence in Adults: Development and Validation of a Risk Model. *World Journal of Surgery*, **34**, 20-27. https://doi.org/10.1007/s00268-009-0277-y

[27] Drummond, J.C., Patel, P.M. and Lemkuil, B.P. (2015) Anesthesia for Neurologic Surgery. In: Miller, R.D., Ed., *Miller's Anesthesia* (8*th Edition*), Elsevier, Philadelphia, 2158-2199.

[28] 陈卫, 井发强, 谭金明, 等. 利多卡因对 AMI 动物模型星状神经节内心交感神经元电活动的影响[J]. 重庆医学,

2015, 44(17): 2327-2329, 2332.

[29] Hollmann, M.W. and Durieux, M.E. (2000) Local Anesthetics and the Inflammatory Response: A New Therapeutic Indication? *Anesthesiology*, **93**, 858-875. https://doi.org/10.1097/00000542-200009000-00038

[30] Koppert, W., Ostermeier, N., Sittl, R., Weidner, C. and Schmelz, M. (2000) Low-Dose Lidocaine Reduces Secondary Hyperalgesia by a Central Mode of Action. *Pain*, **85**, 217-224. https://doi.org/10.1016/S0304-3959(99)00268-7

[31] Wu, C.T., Borel, C.O., Lee, M.S., Yu, J.C., Liou, H.S., Yi, H.D., *et al.* (2005) The Interaction Effect of Perioperative Cotreatment with Dextromethorphan and Intravenous Lidocaine on Pain Relief and Recovery of Bowel Function after Laparoscopic Cholecystectomy. *Anesthesia & Analgesia*, **100**, 448-453. https://doi.org/10.1213/01.ANE.0000142551.92340.CC

[32] Thapa, P., Shrestha, R.R., Shrestha, S. and Bajracharya, G.R. (2017) Betamethasone Gel Compared with Lidocaine Jelly to Reduce Tracheal Tube Related Postoperative Airway Symptoms: A Randomized Controlled Trial. *BMC Research Notes*, **10**, Article No. 361. https://doi.org/10.1186/s13104-017-2694-6

[33] Jee, D. and Park, S.Y. (2003) Lidocaine Sprayed Down the Endotracheal Tube Attenuates the Airway-Circulatory Reflexes by Local Anesthesia during Emergence and Extubation. *Anesthesia & Analgesia*, **96**, 293-297. https://doi.org/10.1213/00000539-200301000-00058

[34] Saghaei, M., Reisinejad, A. and Soltani, H. (2005) Prophylactic versus Therapeutic Administration of Intravenous Lidocaine for Suppression of Post-Extubation Cough Following Cataract Surgery: A Randomized Double-Blind Placebo Controlled Clinical Trial. *Acta Anaesthesiologica Taiwanica*, **43**, 205-209.

[35] Couceiro, T.C., Lima, L.C., Burle, L.M., *et al.* (2015) Lidocaína intravenosa no tratamento da dor pós-mastectomia: ensaio clínico aleatório encoberto placebo controlado [Intravenous Lidocaine for Post-Mastectomy Pain Treatment: Randomized, Blind, Placebo Controlled Clinical Trial]. *Brazilian Journal of Anesthesiology*, **65**, 207-212. https://doi.org/10.1016/j.bjan.2014.05.016

[36] 夏道林, 柴小明, 徐敏, 等. 利多卡因静脉输注对静脉麻醉丙泊酚用量和气管拔管期心血管不良反应的影响[J]. 江苏医药, 2019, 45(7): 710-712.

[37] 杨育英, 贺定辉, 张丽蓓, 等. 气道内持续输注利多卡因预防腭咽成形术后患者带管期应激反应的效果[J]. 河北医药, 2018, 40(10): 1537-1539.

[38] 龙云, 李茜, 王浩, 等. 利多卡因经气管内给药和静脉给药对全麻苏醒期患者镇静镇痛效果、血流动力学和呛咳反应的影响[J]. 现代生物医学进展, 2020, 20(23): 4526-4529, 4575. https://doi.org/10.13241/j.cnki.pmb.2020.23.027

[39] Hu, S., Li, Y., Wang, S., Xu, S., Ju, X. and Ma, L. (2019) Effects of Intravenous Infusion of Lidocaine and Dexmedetomidine on Inhibiting Cough during the Tracheal Extubation Period after Thyroid Surgery. *BMC Anesthesiology*, **19**, Article No. 66. https://doi.org/10.1186/s12871-019-0739-1

[40] Lee, J.H., Koo, .BN., Jeong, J.J., *et al.* (2011) Differential Effects of Lidocaine and Remifentanil on Response to the Tracheal Tube during Emergence from General Anaesthesia. *British Journal of Anaesthesia*, **106**, 410-415. https://doi.org/10.1093/bja/aeq396

[41] George, S.E., Singh, G., Mathew, B.S., Fleming, D. and Korula, G. (2013) Comparison of the Effect of Lignocaine Instilled through the Endotracheal Tube and Intravenous Lignocaine on the Extubation Response in Patients Undergoing Craniotomy with Skull Pins: A Randomized Double-Blind Clinical Trial. *Journal of Anaesthesiology Clinical Pharmacology*, **29**, 168-172. https://doi.org/10.4103/0970-9185.111668

[42] Bromage, P.R. and Robson, J.G. (1961) Concentrations of Lignocaine in the Blood after Intravenous, Intramuscular Epidural and Endotracheal Administration. *Anaesthesia*, **16**, 461-478. https://doi.org/10.1111/j.1365-2044.1961.tb13426.x

[43] Erb, T.O., Ungern-Sternberg, B.S, von Keller, K., *et al.* (2013) The Effect of Intravenous Lidocaine on Laryngeal and Respiratory Reflex Responses in Anaesthetised Children. *Anaesthesia*, **68**, 13-20. https://doi.org/10.1111/j.1365-2044.2012.07295.x

[44] 顾竹劼, 马钰, 汪建胜. 不同利多卡因给药方式对于拔管呛咳及心率血压的影响[J]. 中国医药指南, 2020, 18(18): 74-75.