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上尿路腔内手术中降低肾盂压力机制与方法的研究进展*

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摘要:1983年, Wickham教授首先提出微创外科(minimally invasive surgery), 此后, 微创泌尿外科逐渐成外具有科学意义上的微创外科学的一个重要的分支学科。上尿路的腔内手术, 包括PNL (Percutaneous nephrolithotomy)、URS(Ureteroscopic)、f-URS (Flexible ureteroscope)等。与传统手术相比, 上尿路的腔内手术具有创伤小、时间短、恢复快、并发症少, 并且可以直视下进行手术操作, 临床应用较广泛。在腔内操作时, 为保证术中手术视野的清晰度, 手术多采用生理盐水(NS)进行灌注, 进而导致肾盂压力升高, 引起各项潜在的危害。因此如何在上尿路腔内手术中降低肾盂压力成为一个研究的热点。近些年, 腔内器械的改进, 包括镜体灌注通道入路与出路的分开设计、回流鞘的设计、压力泵的改进, 在一定程度上降低了肾盂压力。灌注液体中加入相应浓度的药物, 抑制上尿路平滑肌的蠕动与收缩, 也在一定程度上降低了肾盂压力。本文介绍了上尿路腔内手术中肾盂压力的影响因素, 回顾了肾盂压力升高后的危害, 分析了肾盂压力升高机制, 总结了肾盂压力降低的各种方案以及将来的应用前景。

关键词:上尿路; 腔内; 肾盂压力

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The Research Progress of Reducing Pelvic Pressure in Endoluminal Operation of Upper Urinary Tract*

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ABSTRACT: In 1983, Professor Wickham was the first to propose "Minimally Invasive Surg". Then Minimally Invasive Urology became an important branch of Minimally Invasive Surg. Endoluminal operation of upper urinary tract includes PNL (Percutaneous Nephrolithotomy), URS (Ureteroscopic), f-URS (Flexible ureteroscope), etc. Compared with conventional surgery, endoluminal operation, has advantages of shorter time, quicker recovery, fewer complications and under direct vision, and thus is applied widely in clinic. In order to ensure the clarity of the operative vision, taking isotonic saline (NS) solution as irrigation fluid increases pelvic pressure, which may causes potential hazards. Therefore, how to reduce pelvic pressure during endoluminal operation becomes a hot topic. In recent years, endoluminal operative devices improvements, including newly developed continuous-flow ureterorenoscope, ureteral access sheaths and pressure pump, have reduced pelvic pressure in a certain degree. Adding drug into the irrigation liquid, inhibits peristalsis and contraction of smooth muscle and reduces the pelvic pressure. This article focuses on the factors affecting intrapelvic pressure, analyzes the renal pelvic pressure elevated mechanism and hazards, and summarizes various schemes to reduce pelvic pressure and future prospects.

Key words: Upper urinary tract; Endoluminal irrigation; Pelvic pressure

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1983年, Wickham教授首先提出微创外科(minimally invasive surgery), 此后, 微创泌尿外科逐渐成外具有科学意义上的微创外科学的一个重要的分支学科。近些年, 随着泌尿外科理念、技术、设备的改善提高, 微创泌尿外科得到迅猛发展。泌尿系统存在尿路这一生理腔道, 从上到下依次为肾盂、输尿管、膀胱、尿道, 为腔内技术的开展提供了场所及优势。近些年来, 随着光学及电子技术的发展, 上尿路的腔镜与成像设备、

操作设备、激光设备相结合, 已可进行多项检查及治疗, 成为腔内泌尿外科的一种基础技术。

上尿路的腔内手术, 包括PNL(Percutaneous nephrolithotomy)、URS(Ureteroscopic)、f-URS(Flexible ureteroscope)等。与传统手术相比, 上尿路的腔内手术具有创伤小、时间短、恢复快、并发症少等优点, 临床应用较广泛。在腔内操作时, 为保证术中手术视野的清晰度, 手术多采用生理盐水(NS)进行灌注。NS

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灌注虽能扩张腔镜操作通道、压迫血管止血、保持视野清晰,但同时会造成肾盂内压力升高。本文介绍了上尿路腔内手术中肾盂压力的影响因素,回顾了肾盂压力升高后的危害,分析了肾盂压力升高机制,总结了肾盂压力降低的各种方案以及将来的应用前景。

1 腔内手术肾盂压力的影响因素

正常人体肾盂容积为 5-12 mL,肾盂节律性蠕动收缩,正常的肾盂压力 5-15 mmHg。肾盂纤细而非薄,内部的压力较易受到多种因素影响。

1.1 腔内生理解剖

肾盂上面与肾盏相连通,下面与输尿管相连通,任何腔内段先天性、后天性的生理解剖异常,都会影响到肾盂压力。任何造成上尿路变窄的病因,因影响灌注液体的流出,造成灌注液体在上尿路滞留,进而引起肾盂压力升高。最常见的病因,如肾盂畸形、肾盂输尿管连接处(UPJ)狭窄、输尿管占位、输尿管畸形等。

1.2 腔内上尿路感染

上尿路伴有感染时,细菌侵及肾盂及输尿管黏膜,产生炎症因子,抑制肾盂及输尿管蠕动,使平滑肌细胞收缩力受损,引起肾盂压力升高。上尿路梗阻合并感染时,肾盂压力比单纯梗阻时升高的幅度更大^[1]。

1.3 腹腔内压力

肾盂及输尿管是肌性器官,无骨骼支撑保护。腹内压力变化时,在一定程度上会直接压迫肾盂及输尿管,引起肾盂内压力变化。输尿管的长度越长,柔韧性越好,就越能承载腹内压力的变化,从而阻碍灌注液体的流出,导致肾盂压力的升高^[2]。瞬时腹内压升高,可能影响到肾盂压力升高,而引起肾盂自发性破裂^[3]。长时间的肾盂高压,可能导致肾盂积水^[4]。

1.4 腔镜通道

上尿路的腔镜通道,包括经皮肾通道和经输尿管逆行通道。经皮肾通道,灌注液体除能从穿刺通道流出部分外,还能从输尿管逆行流入膀胱,与输尿管镜相比,肾盂压力升高幅度较小。PNL 术中,肾盂内压力一般不超过 20 mmHg^[5]。对于不同大小的 PNL 通道,肾盂压力无明显变化^[6]。PNL 术中多通道时,由于增加了灌注液体流出路径,肾盂压力升高的幅度明显降低^[7]。URS 过程中,手术灌注位置距肾盂越近,肾盂压力升高越明显^[8]。

1.5 灌注液体流速

肾盂每分钟收缩约 4 次,相当于肾盂每分钟将 1-2 mL 的尿液输送到输尿管^[9]。灌注速度超过 2 mL/min 时,液体滞积在肾盂,引起肾盂压力的升高。Mortensen J 等人根据灌注速度对肾盂压力的影响,将肾盂压力升高分为四个阶段。第一阶段,当灌注速度 0-2 mL/min 时,由于输尿管代偿性蠕动频率增加,肾盂压力轻微增加;第二阶段,当灌注速度 2-4 mL/min 时,蠕动频率加快而使输尿管充盈下降,肾盂压力迅速增加;第三阶段,当灌注速度 4-6 mL/min,由于尿团之间的渗聚,肾盂压力增加幅度变小;第四阶段,灌注速度大小 6 mL/min 时,输尿管成柱状开放,肾盂压力与灌注速度成线性相关^[10-12]。

1.6 手术器材及设备

上尿路腔镜手术时,腔镜的直径会对肾盂压力产生影响。PNL 术中,相同直径的肾镜在不同粗细的经皮肾通道进行手术时,通道直径越粗,灌注液体外流越快,对肾盂压力影响越小^[7]。

2 肾盂压力升高的生理病理影响

2.1 生理影响

先前研究已证实当肾盂压力达到 30-35 mmHg 时,会发生肾盂-静脉、肾盂-肾小管、肾盂-淋巴、肾盂-间质返流^[13]。返流过程中,细菌、内毒素随灌注液体进入肾皮质及循环系统,可能引发术后脓毒血症发生^[14,15]。

2.2 病理影响

肾盂压力升高时,肾髓质、肾皮质依次感应压力变化。与肾小球相比,肾小管距离肾盂较近,首先感应到压力变化。肾小管上皮细胞首先出现细胞内空泡,可见绒毛脱落及细胞溶解。压力超过一定限度,肾小管上皮细胞内线粒体、溶酶体扩张,细胞裂解,肾间质水肿,继而引起肾小球、肾小囊肿胀,炎症细胞浸润,肾小球内皮细胞裂解、脱落^[16]。

3 肾盂压力升高的危害

泌尿外科腔内手术现已广泛开展,灌注也随之普遍存在。因液体灌注而引起的肾盂高压,给机体带来了近期及远期损害。

3.1 近期损害

肾盂压力升高,导致灌注液体、细菌、内毒素等吸收入血,引发一系列并发症。术后发热是上尿路腔内手术最常见的并发症,文献报道发生约 20%^[17,18]。脓毒血症发生率为 1%-2%^[19]。肾盂压力短期升高,会引起肾功能一过性下降^[20]。肾盂高压导致的返流,可能导致肾盂及输尿管肿瘤的扩散转移^[21]。

3.2 远期损害

近些年,上尿路腔内手术远期并发症的研究及报道较少。若肾盂压力持续升高,可造成肾盂积水,远期肾功能受损,甚至肾衰竭、肾无功能、尿毒症等。术中肾盂压力过高,有可能启动 TGF- β 1-NF- κ B 肾纤维化途径,引起远期肾萎缩。

4 降低肾盂压力的方法

上尿路腔内手术中,肾盂压力升高带来各种损害。科研上已进行多种降低肾盂方法的研究,不少已进入到 1 期临床应用。

4.1 灌注液体中加入药物

肾盂及输尿管粘膜表面均有 α -受体、 β -受体、M 型受体分布,若在灌注液体中加入相应药物,可以降低肾盂及输尿管的蠕动及收缩,从而使肾盂压力下降。灌注药物是属于局部用药,在降低肾盂压力同时,未大量进入循环系统,避免了药物引起的全身反应。Selmy GI 等人在 1994 就证实了灌注液中加入维拉帕米、PGF2- α 、去氧肾上腺素、去甲肾上腺素等对肾盂压力的影响^[22]。

灌注液中加入乙酰胆碱,激活肾盂及输尿管粘膜表面的 M 受体,使上尿路平滑肌舒张,同时降低蠕动频率,从而降低肾盂压力^[23]。

在灌注液中加入吡啶美辛,抑制环氧合酶活性,使前列腺

素脱氢酶活性升高,使前列腺素合成减少,从而使肾盂、输尿管平滑肌直接舒张,降低了肾盂压力^[24]。

灌注液中加入异丙肾上腺素,降低了肾盂及输尿管的收缩频率,抑制了上尿路平滑肌的收缩,从而使肾盂压力降低。Jung H 等人通过在 f-URS 时灌注液中加入异丙肾上腺素,进行的临床随机对照实验(RCT),发现异丙肾上腺素能明显降低肾盂压力,而不会引起全身副反应^[25]。

4.2 腔内手术设备的改进

近些年的 URS 设备,通过将灌注液体的灌注通道与回流通道分开,效率比传统单通道灌注回流提高 100 倍,却不引起肾盂压力的明显升高^[26]。在 f-URS 手术中,回流鞘(UAS),提供了灌注液体的回流通道,明显降低了术中的肾盂压力^[27-30]。Brian DM 等人开发出新型脚控式连续灌注泵,不仅使双手从压力泵的手动控制上解放出来,而且灌注效率比常规压力泵提高 3-6 倍,进一步的实验证实与常规灌注泵相比,这种脚动式灌注泵并不引起肾盂压力的升高^[31]。

5 降低肾盂压力的临床应用及前景

输尿管镜技术、PNL 技术分别在 20 世纪 60 年代、80 年代被引入临床。由于此类腔内手术技术创伤小、恢复快、并发症少,并且可以直视下进行手术操作,因此在泌尿外科中逐渐得到推广应用。

肾盂压力升高后,灌注液体在压力作用下被过量吸收入血,增加心脏负荷,可能导致心衰。据报道,在输尿管镜手术中,病人平均吸收灌注液体 54 mL,最大甚至吸收 137 毫升^[32]。肾盂压力升高以及引起的发热、脓毒血症等并发症,是上尿路腔内手术不可忽视的问题。

肾盂压力升高,可能导致各项潜在的危害。因此如何在上尿路腔内手术中降低肾盂压力成为一个研究的热点。近些年,腔内器械的改进,包括镜体灌注通道入路与出路的分开设计、回流鞘的设计、压力泵的改进,在一定程度上降低了肾盂压力。灌注液体中加入相应浓度的药物,抑制上尿路平滑肌的蠕动与收缩,也在一定程度上降低了肾盂压力。

腔内器械的改进,包括器械的各种创新与设计,反复的测试与磨合,动物实验的验证与应用,临床上小规模应用与检测,以及大规模的临床应用与远期随访。一旦临床意义得到论证,改进后的设备将带来巨大的经济效益与临床意义。

灌注液中加入相应药物,除了需进行大规模的药理学研究、动物实验研究,还需要进行临床上的研究。灌注过程中能明显降低肾盂压力并且不会引起局部或系统副反应,是药物实验的根本出发点和立足点。

目前,上尿路腔内手术中肾盂压力的基础研究仍较少,例如压力引起炎症因子受体的表达机制、压力相关性肾纤维化的发生机制、压力返流机制、压力引起脓毒血症机制,还需要较深入基础层面的研究。近期,药物灌注尚缺乏远期随访研究,能否取得较好的远期疗效,尚需要更长随访时间临床资料的支持。因此,如何在上尿路腔内手术中进一步降低肾盂压力,需要越来越多研究人员的关注和研究,也需要更进一步的寻找创新点与突破点。

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