General Surgery



ROLE OF HYOSCINE N-BUTYLBROMIDE (HBB) AS MONOTHERAPY IN THE MANAGEMENT OF ACUTE URETERAL COLIC

| Dr Mukesh Suvera | Associate Professor, Department of General Surgery, Smt Shardaben General Hospital, Saraspur, Ahmedabad -380018 |
|-----------------------|--|
| Dr Sachi Sankhala* | M.S, 3 rd Year Resident, Department of General Surgery, Smt Shardaben General Hospital, Saraspur, Ahmedabad -380018 *Corresponding Author |
| Dr Swapnil Sharma | M.S, 3 rd Year Resident, Department of General Surgery, Smt Shardaben General Hospital, Saraspur, Ahmedabad -380018 |
| Dr Bhimsi Bhadarka | M.S, 3 rd Year Resident, Department of General Surgery, Smt Shardaben General Hospital, Saraspur, Ahmedabad -380018 |

ABSTRACT INTRODUCTION: HBB is used regularly in some countries to treat a variety of urological conditions, by virtue of its spasmolytic effect on the smooth musculature of the urinary tract. Its role as a monotherapy in the management of the acute ureteric colic is still debatable. Even if HBB does not appear to have the same effect as NSAIDs, it has less cardiac and nephrologic side effects.

AIMS AND OBJECTIVE: To determine the efficacy of HBB as a monotherapy in the management of acute ureteric colic.

MATERIALS AND METHODS: A prospective randomized control study was conducted in smt Sharadaben general hospital from December 2016 to July 2017. 150 outdoor patients were selected, both females and males with diagnosis of acute ureteric colic.

RESULTS: All the patients were treated with HBB. Out of 150 patients, 110 patients were benefited with HBB alone but effect of analgesia as compared to combined analgesic therapy was found to be low.

CONCLUSION: HBB is effective in the management of acute ureteric pain. However its role as a monotherapy in the management is still unclear as no advantage when used as monotherapy over established forms of analgesia.

KEYWORDS : Hyoscine N-butylbromide, Ureteral colic, Spasmolytic, Analgesia

INTRODUCTION

The management of pain from acute urinary obstruction continues to be an expanding field of research. Pharmacological intervention is the mainstay of initial management. Various categories of medication have been studied during clinical trials, alone or in combination, in order to identify the most efficient first-line treatment of pain due to obstruction by a calculus. Renal colic is generated by hyperperistalsis of the obstructed ureter. Peristalsis is modulated by alpha- receptors (contraction), beta-receptors (relaxation) and prostaglandins (PG F2alpha: contraction; PG E1/E2: relaxation). Increases in collecting system pressure and ureteral wall tension are also proposed mechanisms of renal colic ^[1]. Primate models reveal that distentionmediated activation of renal pelvis mechanoreceptors results in spinothalamic (pain pathway) C fiber excitation. The mean threshold pressure to elicit this primate response was 32 mm Hg. This is similar to the 30 mm Hg proposed threshold for evoking pain in humans^[2]. This effect is augmented by the resulting inflammation and edema caused by stone impaction and by increasing ureteral peristalsis as a direct consequence of the obstructing calculus. All these changes constitute the pharmacological targets of the various medications used in the treatment of acute renal colic. HBB is used regularly in some countries to treat a variety of urological conditions, by virtue of its spasmolytic effect on the smooth musculature of the urinary tract ^[3] Also described as scopolamine butylbromide or butylscopolamine, it is available both as a prescription drug and as an over-the-counter medicine worldwide. It is also used in many fields of medicine, especially in gastroenterology, anesthesia and chronic pain management; yet, the evidence for its specific use in the management of acute ureteric colic is limited. HBB is a quaternary ammonium compound with anticholinergic properties. It exhibits high affinity for muscarinic receptors and also binds to nicotinic receptors. Inhibition of cholinergic transmission in the abdominal and pelvic parasympathetic ganglia produces the spasmolytic effect in the smooth muscle of gastrointestinal, biliary, urinary tract and female genital organs [4]. It is usually administered parenterally, as oral bioavailability is low. In many countries, HBB is often prescribed for treatment of renal and ureteric colic, usually as adjuvant therapy to NSAIDs and/or opioids 15 . Even if HBB does not appear to have the same effect as NSAIDs^[6], it has less cardiac and nephrologic side effects. This could become even more important as diclofenac (and other NSAIDs too) is getting more and more controversially discussed in cardiac- impaired patients since

it affects platelet aggregation, which in turn might increase blood loss ^[7,8]. For renal insufficiency and cardiac patients it is an alternative to opioids, as long as it is given intravenously and in a systematic fashion. It is also used in protocols to treat bladder spasm, to aid stone expulsion through ureteric relaxation and perioperatively to facilitate ureteroscopy and other endourological procedures such as stent insertion^[5,9].

AIMS AND OBJECTIVES: This study determines the use and role of HBB as monotherapy in the management of pain resulting from an acutely obstructing ureteral stone.

MATERIALS AND METHODS: A prospective randomized control study was conducted in smt Sharadaben general hospital from December 2016 to July 2017. 150 outdoor patients were selected, both females and males with diagnosis of acute ureteric colic. All the patients were treated with injection buscopan and relief of pain after giving HBB, duration of pain relief was recorded. The results were compared with other analgesics like injection diclofenac sodium, NSAIDS and tramadol. Exclusion criteria were pregnant females, patients who came with retention of urine. All patients were followed up on outdoor basis.

Observation and discussion: Out of 150 patients, majority of the patients (110) were found to be benefited by effects of HBB. Early pain relief and duration of pain free period was found to be longer compared to injection diclofenac and NSAIDS alone. In rest of the patients in addition to HBB other analgesics were needed for pain relief. In 40 patients, who were treated with combined therapy for pain relief had better and longer analgesia as compared with HBB alone.

Table-1: Pain relief

| No of patients | Pain relief with HBB only | Pain relief after |
|----------------|---------------------------|-------------------|
| | | combined therapy |
| Total =150 | 110 | 40 |

However, the stone explusion after giving HBB alone on follow up was low as compared with combined therapy .In a study by Gurbuz et al. ^[10], 140 patients with stones in the distal ureter were treated with HBB compared to three different alpha 1-adrenergic blockers (doxazosin, terazosin and alfuzosin). The stone expulsion rate was

76

higher in the groups of patients treated with different doses of alpha 1adrenergic blockers than in the groups that received HBB. In vitro, HBB is not effective in relaxing isolated human ureteric smooth muscle^(3, 11, 12). The drug had virtually no lasting effect on the ureter nor did it help the passing of stones by reducing friction in vivo in a rabbit model ^[15,14]. Patient-controlled analgesic consumption during shock wave lithotripsy was comparable between HBB and placebo^[15]. HBB as an Analgesic Antimuscarinics are often used in the management of ureteral colic, most commonly in combination with conventional analgesia or as part of the analgesic ladder. HBB as a monotherapy was proven responsible for a 33% reduction in VAS score, in contrast to 96% with 2.5 mg diclofenac sodium as a monotherapy. The timedependent relation to painreduction following parenteral administration was demonstrated and HBB was found to be equally effective as 100 mg i.v. tramadol both 30 and 50 min after delivery When patients' perception of pain was evaluated, the responses showed a notable difference. About two-thirds of patients (73%) treated with HBB experienced long-lasting pain reduction (of at least 10 mm on the VAS) and as many as 90% rated their treatment as good to very good. It is unclear, however, whether this long-lasting effect was influenced by the natural, gradual decrease of intensity of renal colic with time.

CONCLUSION HBB is often used in the management of urological conditions where urinary tract smooth muscle spasm is thought to be part of the pathophysiological process. According to our results HBB is effective in the management of acute ureteric pain. However its role as a monotherapy in the management is still unclear as no advantage when used as monotherapy over established forms of analgesia. When compared with NSAIDs, the onset of and duration of analgesia with NSAIDs is superior to that of HBB alone. There appears to be a timedependent relation to pain reduction following parenteral administration, but this needs to be confirmed by more prospective randomized cohorts.

REFERENCES

- Holmlund D: The pathophysiology of ureteral colic. Scand J Urol Nephrol Suppl 1983; 75:25-27
- Ammons WS: Bowditch Lecture. Renal afferent inputs to ascending spinal pathways. 2 Am J Physiol 1992;262(2 Pt 2):R165-R176.
- 3. Tytgat GN: Hyoscine butylbromide: a review of its use in the treatment of abdominal cramping and pain. Drugs 2007;67:1343-1357. Dellabella M, Milanese G, Muzzonigro G: Efficacy of tamsulosin in the medical
- 4. management of juxtavesical ureteral stones. J Urol 2003;170(6 Pt 1):2202–2205. Tytgat GN: Hyoscine butylbromide – a review on its parenteral use in acute abdominal 5.
- spasm and as an aid in abdominal diagnostic and therapeutic procedures. Curr Med Res Opin 2008:24:3159-3173.
- Holdgate A, Pollock T: Nonsteroidal anti-inflammatory drugs (NSAIDs) versus opioids for acute renal colic. Cochrane Database Syst Rev 2005;2:CD004137. Schmit A, Björkman S, Åkeson J: Preoperative rectal diclofenac versus paracetamol for 6.
- 7. 8.
- Schmitz, Ejorkhan S, Arkson J Hoffeldav Feeda Marka Versa Brackenhol to tonsillectomy: effects on pain and blood loss. Acta Anaesthesiol Scand 2001;45:48–52. Sostres C, Gargallo CJ, Arroyo MT, Lanas A: Adverse effects of non-steroidal anti-inflammatory drugs (NSAIDs, aspirin and coxibs) on upper gastrointestinal tract. Best Pract Res Clin Gastroenterol 2010;24:121–132. 9.
- Weiser T, Just S: Hyoscine butylbromide potently blocks human nicotinic acetylcholine receptors in SH-SY5Y cells. Neurosci Lett 2009;450:258-261. Gurbuz MC, Polat H, Canat L, Kilic M, Caskurlu T: Efficacy of three different alpha 1-10
- adrenergic blockers and hyoscine N-butylbromide for distal ureteral stones. Int Braz J Urol 2011; 37: 195–200; discussion 201–202.
- Gratzke C, Uckert S, Kedia G, Reich O, Schlenker B, Seitz M, Becker AJ, Stief CG: In 11. vitro effects of PDE5 inhibitors sildenafil, vardenafil and tadalafil on isolated human
- vito enecus of PDE2 minotors sidenain, varientian and tadatani of solated numan ureteral smooth muscle: a basic research approach. Urol Res 2007;35:49–54. Wanajo I, Tomiyama Y, Tadachi M, Kobayashi M, Yamazaki Y, Kojima M, Shibata N: The potency of KUL-7211, a selective ureteral relaxant, in isolated canine ureter: 12
- The policity of UD-1211, a solucity encoded relation to a solution of the encoded relation of the specific phosphodiesterase-IV-inhibitor rolipram on the ureteral peristalsis of the rabbit in vitro and in vivo. JUrol 1998;160(3 Pt 1):920–925. 13.
- Miyatake R, Tomiyama Y, Murakami M, Park YC, Kurita T: Effects of isoproterenol and 14 butylscopolamine on the friction between an artificial stone and the intraureteral wall in anesthetized rabbits. J Urol 2001; 166:1083–1087.
- 15. Wixforth J, Grond S, Lehmann KA: Ketorolac and butylscopolamine in combination with alfentanil for renal lithotripsy (in German). Schmerz 1998;12:396–399.
- Stankov G, Schmieder G, Zerle G, Schinzel S, Brune K: Double-blind study with
- Hofstetter AG, Kriegmair M: Treatment of ureteral colic with glycerol trinitrate (in 17. German). Fortschr Med 1993;111:286-288.