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Efficacy of Atropine to Blunt Unopposed Vagal Activity in Prevention of Hypotension in Parturients Undergoing Spinal Caesarean Section

Muhammad Salman Maqbool, Shumaila Ashfaq

ABSTRACT:

Objective: To determine efficacy of prophylactic atropine to blunt un-opposed vagal activity in prevention of hypotension associated with caesarean spinal block in first 15 minutes.

Study Design & Setting: Randomized controlled interventional study (purposive sampling method) done at Islam Teaching Hospital, Sialkot from 03-3-2021 to 11-8-2021

Methodology: Chairman Ethics Review Board, Islam Medical College, Sialkot vide letter No.2021-04/A, dated 03-3-2021, consented for study. G-power statistics v3.1.9.2, employing chi-square goodness of fit test value of 11.07, total sample was 144 bunched into two prophylactic treatment groups by using computer generated numbers (group-A, Inj. atropine 0.5mg and group-B, Inj. Placebo (control) planned for elective caesarean spinal delivery. Primary study variable being hemodynamic stability (pulse, blood pressure) in first 15 minutes after placing block. Independent-Samples Kruskal-Wallis Test used to compare systolic blood pressures between groups for association. Chi- square hypothesis test, was done with P-value <0.05 considered as statistically significant. SPSS analysis was done with v.21

Results: In Atropine group-A, there was rather a 11% increase in mean heart rate at 15 minutes mark (statistically significant) than the mean baseline value while in group-B (placebo)similar values parameter showed a 4.7% decline in mean heart rate value. In group-A, mean systolic blood pressure value declined only by 12.2% at 15 minutes mark from baseline value whereas in group-B, a decline of 13.2% was noted.

Conclusion: Prophylactic bolus of atropine against un-opposed vagal activity provided stable hemodynamic values in cesarean spinal delivery.

Key words: Atropine, Co-load, hypotension, Obstetric anaesthesia, Subarachnoid Anaesthesia.

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INTRODUCTION

The spinal block is the widely practiced anaesthesia technique due to its wide safety margin.[1] It is also currently the method of choice for elective caesarean section, because it avoids risks linked with general anesthesia, such as full stomach (risk of acid aspiration syndrome), mask ventilation / intubation difficulties and general anesthesia drugs causing fetal depression, secondly it has the advantages of reducing maternal mortality, low dose of local anesthetic agent, maternal-fetal bonding, complete dense block, including decreased blood loss, and excellent postoperative pain control compared to general anesthesia etc.[2,3] It is an invasive procedure that could be associated with hypotension (33%) and bradycardia (33%) with an incidence of up to 75% of spinal hypotension in parturient who receive spinal anesthesia.[4,5] The cardio-vascular physiological response following spinal anesthesia results either from extent of sympathectomy or un-opposed parasympathetic tone. The systemic vasodilation induced by sympathetic blockade after sub-arachnoid block, results in venous pooling of blood and reduction in the systemic vascular resistance, has been regarded as the predominant mechanism for hypotension. The sympathetic block extent is related to the cranial spread of the local anesthetic within the subarachnoid space, narrowing of the sub-arachnoid spaces due to compression effect of uterus along with the aorto-caval compression and due to higher sensitivity to local anesthetics are main reasons for higher incidence of hypotension in parturient, in comparison to non-obstetric patients. In different studies, it was postulated that in the setting of spinal anesthesia, reduced venous return along-with unopposed vagal tone

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results in variable degree of hypotension and bradycardia,[6] with blockade of cardioaccelerator fibers (sympathetic nerve fibers from T1 to T4,), and possibly due to reversal of the Bainbridge reflex (may result in cardiac arrest).[7]

Currently various techniques have been adopted to overcome the degree of hypotension and bradycardia administration of vasoactive medication, pre or co-loading of intravenous fluids, other methods such as right pelvic wedge placement, and calf compression devices.[7,8]

Anticholinergic (atropine) is an ester of aromatic acid in combination with organic base. The ester linkage is essential for effective binding of the anticholinergics to the acetylcholine receptors. This competitively blocks binding by acetylcholine and thus prevents receptor activation. Atropine being a tertiary amine, the naturally occurring (laevorotatory form) is active, but the commercial mixture is racemic. Its intravenous administration, demonstrates a pattern of increase in heart rate and systolic blood pressure and lower diastolic pressure resulting in slightly increase cardiac output and decrease central venous pressure.[9] The prophylactic atropine averts blunted Bain-bridge reflex effect, the net effect being increased heart rate and improved cardiac output after sympathetic spinal block.[7] In another study employing parturient positioning with table tilt (along with wedge under right hip) to prevent the effect of aorto-caval compression, atropine was given prophylactic atropine in caesarean section as a combination technique to prevent sympathetic block hypotension.[8]

The efficiency of prophylactic atropine in the elderly population has been researched, but inadequate information is there regarding its use in parturients planned for caesarean section under intra-thecal block.[10] Therefore a study was designed to evaluate the efficacy of atropine in prevention of hypotension in parturient undergoing spinal caesarean section in first 15 minutes after spinal injection.

METHODOLOGY:

This randomized controlled interventional study (purposive sampling method) was conducted whereby, term parturient due for elective caesarean spinal delivery were enrolled at Department of Anaesthesia & Intensive Care, Islam Medical & Dental College, Islam Teaching Hospital, Pasroor Road, Sialkot from 03-3-2021 to 11-8-2021. The Chairman Ethics Review Board, Islam Medical & Dental College, Sialkot vide letter No.2021-04/A, dated 03-3-2021, consented for this study. Sample size was considered by G-power statistics v3.1.9.2, taking effective size w-value of 0.3, á-error of 0.05 and 80% power to detect a true effect with Df value 5 and employing chi-square goodness of fit test value of 11.07, the total sample came out to be 144 cases. Pre-anesthesia evaluation and informed written consent was taken in all cases. Using the sequence of elective surgery schedules subjects were randomly bunched into two prophylactic treatment groups by using computer generated numbers into (group-A, Inj. atropine 0.5mg and group-B, Inj. Placebo (control) both constituted to make a 3ml solution, with 72 cases (computer generated) for this randomized controlled interventional study. Parturient were not aware to which group they were allocated. Inclusion criteria was ASA I or II, term parturient age between 18-40-year for elective Pfannenstiel incision surgery under sub-arachnoid block, baseline heart rate between 80-90/minute. Exclusion criteria was coagulation disorder, preeclampsia, arrhythmias such as atrial fibrillation, tachycardia (heart rate baseline value above 100-110/ minute), HELLP syndrome, sepsis at the site of injection, indeterminate neurologic disease, raised intracranial pressure, allergy to anesthetics, discopathy, and fixed cardiac output state e.g., aortic stenosis. All Patients fasted and were pre-medicated with (ranitidine 150 mg at night before the operation) according to ASA guidelines. Per-operatively,18G intravenous lines were placed, baseline vitals (blood pressure, heart rate, and oxygen saturation) noted and all patients received crystalloid isotonic fluid as co-load. Spinal anesthesia with bupivacaine spinal 0.75% hyperbaric (12mg) in sub-arachnoid space over a period of 15 seconds was managed by consultant anesthesiologist employing standard aseptic technique with 25g quincke needle at L3-4 level in left lateral position and placed supine after block. The anesthetist was blinded to prophylactic medication (given by nurse anesthetist at time of giving sub-arachnoid block injection) provided by fellow consultant anesthetist in sealed labelled syringes and both were part of study team with fixed roles. The block was evaluated by pin prick in midline(sensory), modified bromage scale(motor) at 3 minutes, while the autonomic block was checked by spirit dipped swabs to check for cold and warm sensation. Pulse, systolic and diastolic blood pressure was monitored at 1,3,5,7,9,11,13 and 15 minutes interval following administration of prophylactic medication for hemodynamic stability (the primary outcome variables of the study). The primary study variable being hemodynamic stability (pulse, blood pressure) in first 15 minutes after placing block. The notable secondary outcome variables being need of vasopressors, anticholinergic drugs and adverse effects. Hypotension was defined in study as a decrease in mean blood pressure of less than 12% from the baseline value or systolic blood pressure < 90mmHg) and treated with intra-venous bolus of vasopressors. Inj. atropine was given for heart rate < 60 beats/minute or 35% decrease from baseline value. Hemodynamic parameters were compared with baseline values among the groups. Independent-Samples Kruskal-Wallis Test was applied to compare systolic blood pressures between group-A(atropine) and group-B(placebo) for association. Chi- square hypothesis test, was done to determine if there is a statistically significant difference between expected and observed frequencies with P-value <0.05 considered as statistically significant. SPSS analysis was done with v.21. Null hypothesis i.e., a claim we want

to test is, H_0: Atropine prophylactic use for hemodynamic stability in cesarean section under spinal anesthesia do have any clinically significant effect, while alternate hypothesis, H_a: Atropine prophylactic use for hemodynamic stability in cesarean section under spinal anesthesia do not have a clinically significant effect, were the hypothesis of the study.

RESULTS:

The mean age(years) in group-A(atropine) & B(placebo) in study being 26.59(SD of 4.22) and 26.72(SD of 3.22) respectively. Pulse variation and systolic blood pressure readings in both groups are depicted in table-1 and 2 respectively. The mean baseline and at 15 minutes diastolic blood pressure(mmHg) in group-A, being 85.01(SD of 12.48) and 64.97(SD of 14.39) whereas similar readings in group-B, being 88.61(SD of 15.38) and 67.56(SD of 14.37) respectively and showed no marked statistical difference. The heart rate variations of both groups are shown in graphical way in graph-1.

The distribution and analysis done by Independent-Samples Kruskal-Wallis Test of systolic blood pressure (mmHg) is the same across all categories in (Atropine group-A and Placebo group-B) sig. value was .478(significance level was .050) and we retain the null hypothesis. Pearson correlation coefficient value of 0.439 & 0.446 in group A & B, of study was also significant statistically at 0.05 & 0.01 level (2–tailed) as regard to heart rate variation from baseline value respectively. On application of Pearson Chi-square test 0.015 value was calculated in group-A data, the output resulted concludes interpretation of the P-value of 0.975 at df-2(degree of freedom) which indicates that there is insufficient evidence to reject the null hypothesis. In placebo group-B, high chi-square computed was .501 due to which expected and observed were not close and the model was a poor fit to the systolic blood pressure readings in comparison to baseline value data and cannot reject null hypothesis. The systolic blood pressure variations of both groups A and B are depicted in graph-2.

DISCUSSION:

Bradycardia is a presentation of cardio-vascular collapse after neuraxial block anaesthesia. A wide number of etiological factors are postulated such as the sudden shift of cardiac autonomic balance, myocardial pacemaker cells reflex arc activation, Bainbridge reflex, hypoxia and respiratory apnoea, triggering of cardioinhibitory receptor and the pacemaker-stretch reflex i.e., decreased stretch is evident as bradycardia, paradoxical response of stretch receptors in sinus node (bezold jarisch reflex) and baroreceptor mediated activation of vagal reflex arc. No supportive data exists as to whether cardio-inhibitory receptors or bezold jarisch reflex is solely responsible for the event.[11] Cardiac accelerator fibres T_1-T_4 blockade modifies autonomic nervous system cardiac input leading to un-opposed parasympathetic activity (at Sino-atrial and atrioventricular node) may manifest as bradycardia and asystole and the "reverse" Bainbridge reflex explains decreases in heart rate noticed under condition of decreased venous return e.g., in intra-thecal block.[12,13] In another study it was backed to practice a rationale for cardio-vascular changes (bradycardia and hypotension) following intra-thecal block by treating bradycardia immediately with anti-cholinergic agent, if hypotension persists it is managed by appropriate vasopressors.[13] Similar practice was implemented in our study by using prophylactic atropine intra-venously at time of spinal block.

Hypotension associated with neuraxial block is secondary due to sympathetic block. The systemic vascular resistance decreases, peripheral vasodilation with redistribution of the central blood volume to splanchnic circulation and lower limbs along with decrease in myocardial contractility. The cause of bradycardia is however less clear, but there is a shift towards vagal predominance with sub-arachnoid anaesthesia. There is evidence that cardiac afferent fibre activation helps to preserve diastolic filling time during relative decrease in venous return and that bradycardia is associated with echocardiographic evidence of small left ventricular chamber size.[14]

In the group-A of study, there was rather 11% increase in mean heart rate at 15 minutes mark (statistically significant) than the mean baseline value (91.25 vs 100.85) as in only 17(23.6%) of cases repeat bolus dose of atropine was given while in 55(76.4%) cases no atropine was needed. In Placebo group-B, in 30(41.7%) cases repeat atropine bolus intra-venously was used, while no atropine was used in 42(58.3%) of cases, while there was 4.7% decline in mean heart rate value at 15 minutes in comparison to baseline value (105.58 vs 101.93) respectively. In the Atropine group-A, mean systolic blood pressure value declined only by 12.2% at 15 minutes (chi-square value of .015) from baseline value (131.51 vs 115.45) whereas in Placebo group-B there was a decline of 13.2% in mean systolic blood pressure (chi-square value of .501) at value 15 minutes from baseline value (135.51 vs 118.666) respectively. Therefore group-A, showed better hemodynamic (heart rate and systolic blood pressure) stability and so we cannot reject null hypothesis in our study. In group-A & B the mean decrease in diastolic blood pressure at 15 minutes from baseline value was 24.7% and 23.9% respectively which was statistically insignificant.

In group-A & B vasopressor was given in 36(50%) of cases and not used in 36(50%) cases whereas, similar values in group-B, being 38(52.78%) and in 34(47.2%) of cases respectively. In 4(5.6%) cases in group-B, severe hypotension occurred requiring colloids and measures to increase venous return. In group-A, colloid fluid was administered in 1 case only (0.69%). A single case was of late post-partum hemorrhage (placenta previa) where intra-venous fluids were rushed along with bolus doses of vasopressor agents.

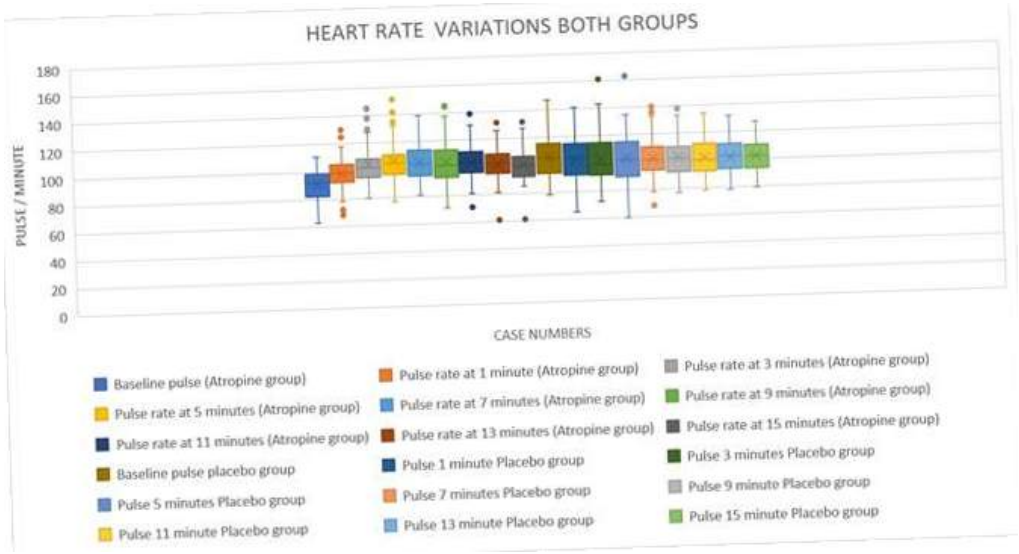
Table-1: Pulse variations in both groups A and B. (n=72)

	Minimum	Maximum	Mean	Std Deviation
Baseline pulse / minute (Atropine / Placebo) group A & B	63 / 78	111 / 147	91.25 / 105.58	10.476 / 15.422
Pulse at 01-minute (Atropine / Placebo) group A & B	68 / 65	130 / 141	98.06 / 102.99	11.640 / 15.756
Pulse at 03-minute (Atropine / Placebo) group A & B	80 / 72	147 / 161	105.00 / 102.83	13.905 / 17.082
Pulse at 05-minute (Atropine / Placebo) group A & B	77 / 60	151 / 163	106.21 / 103.10	14.918 / 17.189
Pulse at 07-minute (Atropine / Placebo) group A & B	81 / 68	139 / 140	104.67 / 102.49	12.635 / 15.054
Pulse at 09-minute (Atropine / Placebo) group A & B	71 / 77	145 / 138	104.46 / 102.67	14.213 / 13.346
Pulse at 11-minute (Atropine / Placebo) group A & B	71 / 78	139 / 134	103.67 / 101.99	12.450 / 12.540
Pulse at 13-minute (Atropine / Placebo) group A & B	61 / 78	132 / 132	101.76 / 101.89	11.746 / 11.556
Pulse at 15-minute (Atropine / Placebo) group A & B	61 / 79	132 / 127	100.85 / 101.93	11.494 / 11.636

Table-2: Systolic blood pressure in mmHg (SBP) variations both groups A and B. (n=72)

	Minimum	Maximum	Mean	Std Deviation
SBP Baseline (Atropine / Placebo) group A & B A B	104 / 96	187 / 200	131.51 / 135.74	15.260 / 18.603
SBP at, 1-minute (Atropine / Placebo) group A & B	97 / 64	180 / 182	128.62 / 131.81	18.018 / 19.703
SBP at, 3- minute (Atropine / Placebo) group A & B	87 / 65	184 / 175	123.45 / 126.16	20.082 / 22.633
SBP, at 5- minute (Atropine / Placebo) group A & B	77 / 53	188 / 166	122.75 / 120.38	24.109 / 23.381
SBP at, 7- minute (Atropine / Placebo) group A & B	91 / 55	173 / 171	123.30 / 119.40	17.834 / 22.848
SBP at, 9- minute (Atropine / Placebo) group A & B	76 / 61	165 / 174	120.51 / 119.40	18.598 / 21.734
SBP at, 11-minute (Atropine / Placebo) group A & B	80 / 72	165 / 157	117.69 / 117.90	17.703 / 18.105
SBP at,13- minute (Atropine / Placebo) group A & B	60 / 75	157 / 146	116.11 / 117.66	17.835 / 14.805
SBP at,15-minute (Atropine / Placebo) group A & B	74 / 85	158 / 148	115.45 / 118.66	15.067 / 14.733

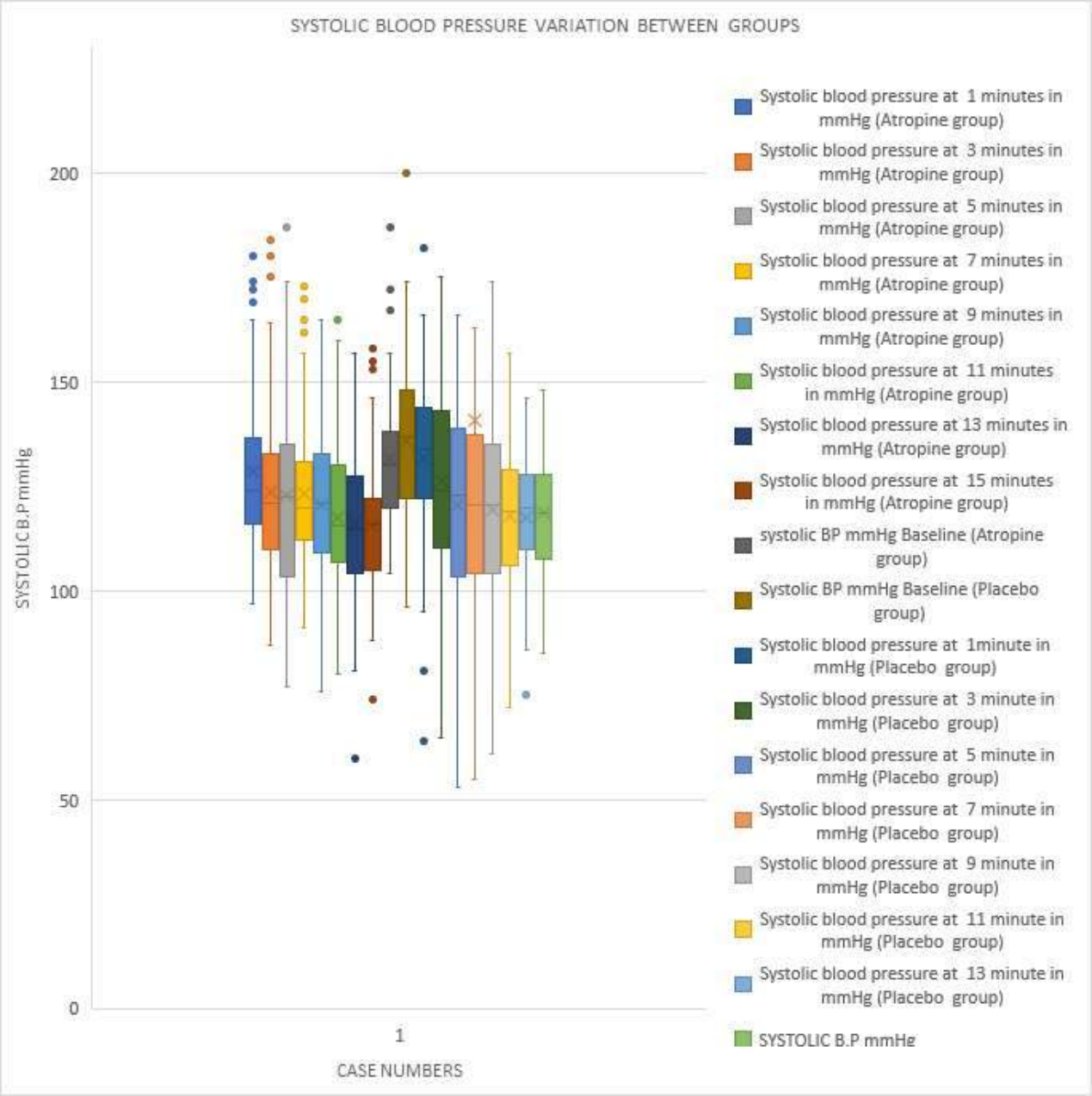
Graph-1: Pulse variations in both groups (n=72)



A study showed using crystalloid infusion of atropine in spinal anesthesia can increase heart rate in the initial few minutes and lowers incidence of hypotension after sub-arachnoid block.[15] In another study, pinal anesthesia-induced hypotension (resulting from arterial and venous vasodilatation resulting due to the sympathetic block along with a paradoxical cardioinhibitory receptors activation) occurs frequently, particularly in the elderly and in patients undergoing caesarean spinal delivery, though several strategies have been advocated, but no one measure has been sufficiently effective and they stated that bradycardia after spinal block must be urgently treated.[16]

In another study atropine in (dose of 0.6mg) was administered one minute after placing intra-thecal block in elderly surgical

Graph-2: Systolic blood pressure variation both groups A and B (n=72)



patients and was noted to be helpful in lowering the incidence of hypotension and bradycardia.[17] In study done atropine prophylactic was administered in parturient undergoing cesarean section in a teaching hospital set-up and they supported the regimen, keeping in view better hemodynamic values noted after spinal block.[18] The results support our study inference. In look for better and newer agents, a study was done employing prophylactic nor-epinephrine along with its rescue use as required in cesarean spinal delivery and depicted promising results with prophylactic use needing less atropine and vasopressors.[19]

In study by Aweke Z and colleagues, it was rationalized to treat bradycardia and hypotension after subarachnoid block by administering atropine initially followed by if needed vasopressor agents.[20] In another study, it was concluded that atropine given prophylactically in spinal caesarean delivery had better and stable haemodynamic (pulse and blood pressure) parameters.[21] In another study, it was concluded that methoxamine along with atropine bolus administration in caesarean section under spinal anaesthesia had augmented hemodynamic effect with few adverse effects, in comparison to when methoxamine was given separately.[22]

Limitation of the study was that invasive blood pressure technique was not used, we relied on non-invasive blood

pressure readings, it was multi-centered study, emergency cases and those parturient with co-morbid diseases were not extrapolated. More randomized, case-controlled studies are required to further validate our findings.

CONCLUSION:

Prophylactic bolus of atropine against blunt unopposed vagal activity provided stable hemodynamic (pulse and systolic blood pressure) values in caesarean section at time of spinal block.

Authors Contribution:
Muhammad Salman Maqbool: Concept & Design Study, Drafting, Revisiting Critically, Final approval of version
Shumaila Ashfaq: Concept & Design Study, Drafting, Revisiting Critically, Data Analysis

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