
The study of comparative analgesic activity of Lidocaine and Ropivacaine on albino rats

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Abstract: Analgesics are the drugs which possess significant pain relieving properties by acting on the CNS or peripheral pain receptors without significantly affecting consciousness. Lidocaine and Ropivacaine are well studied individually; but there are conflicting reports of the comparison of actions between these two drugs both in experimental and clinical trials. Total of 30 rats were taken, they were divided into six groups each containing 5 rats. The analgesic activity of drugs was studied by measuring drug-induced changes in the sensitivity of the pre-screened mice to heat stress applied to their tails (reaction time: 2-4 sec). With increasing the dose of the analgesics from 6.25 to 25µg/kg the analgesic action occurred earlier. A clinical significance is that Lidocaine has its some better analgesic effect than Ropivacaine. As known, the dose of Lidocaine for local anesthetic action is < 7mgs/kg body weight, and of Ropivacaine it is <8mgs/kg body weight. But in our study a dose of the analgesics was low, up to 25µg/kg only. Because of this low dose, the mechanism of analgesic action of the drugs is different, and it is discussed in this paper.

Keywords: Lidocaine, Ropivacaine, Analgesics, Albino Rats

1. Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. It is not a disease by itself in fact it is a warning signal of noxious stimulus. Pain is a subjective experience, it occurs only in consciousness, in the mind. Pain can be experienced in response to both external perceived events and can sometimes follow from nociception. Pain is believed to be the earliest sign of morbidity by which a person judges the existence of disease in him that makes the person to consult the doctor. When the cause of pain cannot be removed, then drugs are generally used to relieve it. Sensation of the pain or awareness of pain is called nociception, which is mediated by nerve ending receptors in peripheral tissues and transmitted to the CNS by primary afferent fibers' and relayed by secondary afferent fibers' to the brain. So the awareness of pain can be blocked by drugs that act in the periphery as well as centrally by analgesics and anesthetics. The nerve impulse transmission can be reduced by drugs acting on several neurotransmitter receptors. Impulse can

be completely prevented by blocking the sodium channels through which conduction of nerve impulse takes places.

Analgesics are the drugs which possess significant pain relieving properties by acting in the CNS or on peripheral pain receptors without significantly affecting consciousness. When applied locally to nerve tissue in appropriate concentration local anaesthetics can act on any part of nervous system and on every type of nerve fibers'. Local anesthetics can effectively and reversibly block impulse conduction along axons that uses sodium channels for the primary action potential generation. Though the pharmacological effects of Lidocaine and Ropivacaine are well established individually, there are conflicting reports of the comparison of actions between these two drugs both experimentally and clinically^[2]. While Lidocaine is a well established local anesthetic, Ropivacaine is a new amide local anesthetic agent with a greater margin of safety than other local anesthetics for cardiovascular and central nervous systems^{[3][4]}. It is known that Lidocaine has analgesic activity not in conjunction to its anesthetic activity because the analgesic dose is lower than anesthetic

dose [5, 6, and 7]. Ropivacaine is also being studied for its analgesic activity in different literatures [8, 9, 10]. Whether it is having any merits or demerits over Lidocaine is to be studied. So in this study the analgesic activities of Lidocaine and Ropivacaine were compared by using tail flick method on albino rats.

2. Materials and Methods: Tail Flick Method (Rat)

Male albino rats are selected for the experiments. Animals are weighed with the help of weighing machine. The animals weighing 150 gms on average are selected for the experiment. Total of 30 rats were taken, they were divided into six groups each containing 5 rats. (i.e., group I, II, III, IV, V and VI respectively). The analgesic activity of drugs were studied by measuring drug-induced changes in the sensitivity of the pre-screened (reaction time: 2-4 sec) mice to heat stress applied to their tails by using a Medicaft Analgesiometer Mask-N (D'Amour and Smith, 1941) [11]. Briefly, the current intensity passing through the naked macramé wire was maintained at 5 ampere. The distance between the heat source and the tail skin was 1.5 cm and cut-off reaction time was fixed at 10 second to avoid any tissue damage. The first, second, and third groups were administered 6.25µg, 12.5µg, and 25µg of Lidocaine per kg/body weight subcutaneously, respectively. The fourth, fifth, and sixth groups were administered 6.25µg, 12.5µg, and 25µg of Ropivacaine per kg/body weight subcutaneously, respectively. The analgesic effect was studied by noting the tail retaining time on the analgesiometer, i.e., the absence of tail-flick was taken as the start of analgesic effect. Each animal was tested for the tail-flick before administering the test drugs, which served as the control. The duration of action was noted as the tail-flick was regained. The time taken for the flicking the tail was measured at 15, 30, 60, 90 and 120 min after the administration of samples. The evaluation Using the analgesia as a parameter, after injecting different doses of Lidocaine and Ropivacaine, dose – response were established, further more duration of activity was evaluated and statically analysis of data done using student's unpaired t-test by using Excel and SPSS software. The results are tabulated.

3. Results

For this comparative study of analgesic effect of Lidocaine and Ropivacaine on albino rats by tail flick method 30 rats were selected as their tails are long thin and easy to elicit the analgesic effect by the tail flick method (by applying radiant heat) and are divided into six groups each containing 5 rats (i.e., group I, II, III, IV, V and VI respectively). The weight and normal time of tail flick latency in each rat is recorded before injecting the drug.

The rats group I (dose of 6.25µg of Lidocaine per kg)

showed onset of action of 7 ± 2.73 minutes; while the rats group IV (dose 6.25 µg of Ropivacaine per kg) showed onset of action at a mean of 12 ± 2.73 minutes (Table 1 and Fig.1). The group II (dose 12.5µg of Lidocaine per kg) showed onset of action at a mean of 6 ± 2.23 minutes; and the group V (dose 12.5 µg of Ropivacaine per kg) showed onset of action at a mean of 11 ± 2.23 minutes. The group III (dose 25µg of Lidocaine per kg) showed onset of action at a mean of 5 ± 1.58 minutes; and the group VI (dose 25 µg of Ropivacaine per kg) showed onset of action at a mean of 9 ± 1.58 minutes.

In rats group I (dose 6.25µg of Lidocaine per kg) a mean duration of action was of 93 ± 12.54 minutes; and in rats group IV (dose 6.25 µg of Ropivacaine per kg) it was of 138 ± 12.54 minutes (Table 2 and Fig.2). The group II (dose 12.5µg of Lidocaine per kg) showed a mean duration of action of 117 ± 15 minutes; and the group V (dose 12.5 µg of Ropivacaine per kg) showed duration of action of 234 ± 15 minutes. In group III (dose 25µg of Lidocaine per kg) a mean duration of action was of 162.6 ± 11.06 minutes; and in group VI (dose 25 µg of Ropivacaine per kg) it was of 288 ± 11.06 minutes.

The standard error of the onset of action between Lidocaine and Ropivacaine at a dose of 6.25 µg/kg is obtained as 1.71, with t value of 2.92 and $p < 0.02$, which is significant as shown in Table I. The standard error of the onset of action between Lidocaine and Ropivacaine at a dose of 12.5 µg/kg is obtained as 1.408, with t value of 3.55 and $p < 0.01$, which is highly significant. The standard error of the onset of action between Lidocaine and Ropivacaine at a dose of 25 µg/kg is obtained as 0.995, with t value of 4.018 and $p < 0.01$, which is highly significant. The standard error of the duration of action between Lidocaine and Ropivacaine at a dose of 6.25 µg/kg is obtained as 7.9, with t value of 5.6 and $p < 0.001$, which is highly significant as shown in Table 2. The standard error of the duration of action between Lidocaine and Ropivacaine at a dose of 12.5 µg/kg is obtained as 9.45, with t value of 12.38 and $p < 0.001$, which is highly significant. The standard error of the duration of action between Lidocaine and Ropivacaine at a dose of 25 µg/kg is obtained as 6.97, with t value of 18.26 and $p < 0.001$, which is also highly significant.

With increasing of doses of Lidocaine and Ropivacaine the onset of analgesic action is early, but when Lidocaine is compared to Ropivacaine the onset is early with Lidocaine and late with Ropivacaine (Table I and Fig.1). With increasing doses of Lidocaine and Ropivacaine the duration of analgesic action is long, but when Lidocaine is compared to Ropivacaine the duration is long with Ropivacaine and short with Lidocaine (Table 2 and Fig. 2).

4. Conclusions

In the present study in rats treated with Lidocaine and Ropivacaine with the increase in dose from 6.25 to 25µg/kg the onset of action was early. Male albino rats (150 Gms)

were selected for the study divided into six groups, five rats in each group. First group of rats were treated with 6.25µg/kg, second group with 12.5µg/kg and third group with 25µg/kg of Lidocaine. Fourth group of rats were treated with 6.25µg/kg, fifth group with 12.5µg/kg and sixth group with 25µg/kg of Ropivacaine. Analgesic property was assessed by using digital analgesiometer. Tail flick latency was considered as reaction time. In rats treated with Lidocaine with increase in dose the duration of action was increased but is less in comparison to rats treated with Ropivacaine, which was increased with the increase of dose. In the work done by Karunakar Kota, S Jhon Premendaran, T. Jayasree^[13] on comparative study of analgesic action of Lidocaine and Ropivacaine on albino rats with Lidocaine with the increase of dose (6.25, 12.5 and 25µg/kg) the onset of action was early where as in rats treated with Ropivacaine the onset of action was uniformly the same for all the three doses. In rats treated with Lidocaine with increase of dose the duration of action was increased; but it is less in comparison to rats treated with Ropivacaine duration of action, which was increased with the increase of dose. So from the present study it was clear that both drugs have an analgesic action.

The local anesthetic doses of Lidocaine is <7mgs/kg body weight and for Ropivacaine it is <8mgs/kg body weight. But in this study the maximum dose was 25µg/kg. Because of low dose, the mechanism of the analgesic

action should be different from that of local anesthetic action. The increasing of doses leads to early onset of the analgesic action. When Lidocaine is compared to Ropivacaine, the onset at the same dose is early for Lidocaine and late for Ropivacaine. Most probably, the increase of concentration of neurotransmitter acetylcholine in CSF, which would exacerbate the inhibitory descending pain pathways resulting in analgesia by binding of the drug to muscarinic receptor M3, inhibition of glycine receptor and release of endogenous opioids. The nerve impulse transmission can be reduced by drugs acting on several neurotransmitter receptors. Impulse can be completely prevented by blocking the sodium channels through which conduction of nerve impulse takes places.

The analgesic action of Lidocaine and Ropivacaine on rats by tail flick reaction was studied. In albino rats treated with Lidocaine, the increase of dose caused enhance of the duration of action; but this effect was less in comparison with rats treated with Ropivacaine. The extra potent and longer analgesic action of Ropivacaine was proved in comparison with Lidocaine. It was found that Ropivacaine increased the duration of action in both low and high dose [14]; the similar observations have made also at experiments in humans. Due to expressed analgesic effect these drugs are being used clinically in Neuropathic pain conditions. But whether they can be used in inflammatory pain conditions that have to be studied.

Table 1. Comparative study of onset of action (minutes) of analgesic effect of lidocaine and ropivacaine

No	N	Drug	Dose (µg/kg)	Mean ± SD	SE	t value	p value
1.	10	Lidocaine	6.25	7±2.73	1.71	2.92	< 0.02
		Ropivacaine		12±2.73			
2.	10	Lidocaine	12.5	6±2.23	1.408	3.55	< 0.01
		Ropivacaine		11±2.23			
3.	10	Lidocaine	25	5±1.58	0.995	4.018	< 0.01
		Ropivacaine		9±1.58			

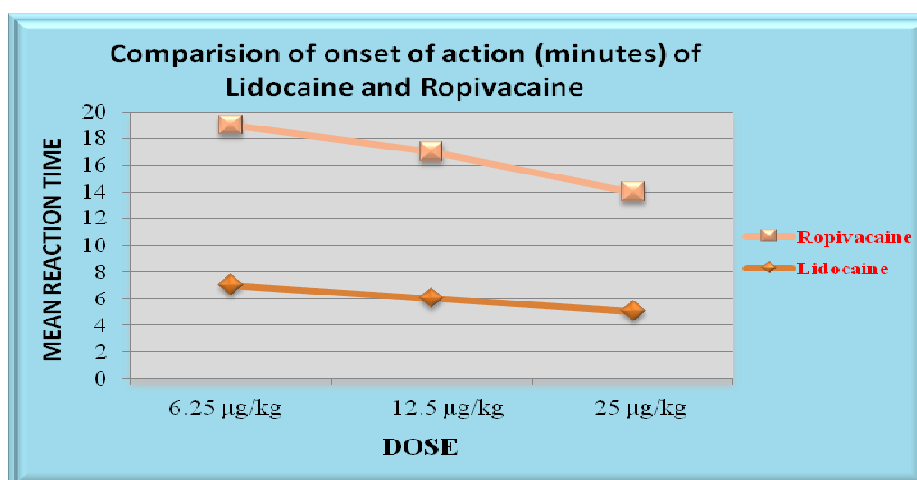
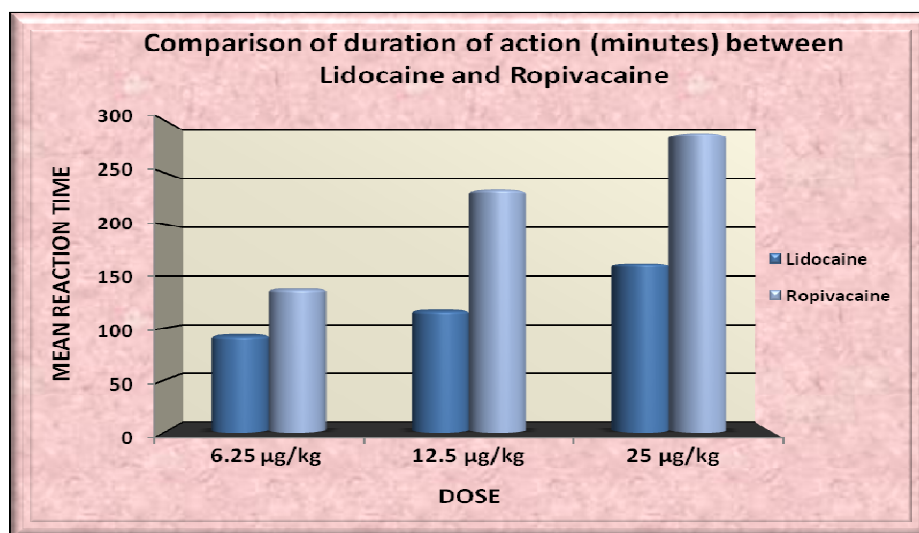


Figure 1. Comparison of onset of action (minutes) of lidocaine and ropivacaine

Table 2. Comparative study of duration of action (minutes) of analgesic effect of Lidocaine and Ropivacaine

No	N	Drug	Dose (µg/kg)	Mean±SD	SE	t value	p value
1.	10	Lidocaine	6.25	93±12.54	7.9	5.6	< 0.001
		Ropivacaine		138±12.54			
2.	10	Lidocaine	12.5	117±15	9.45	12.38	< 0.001
		Ropivacaine		234±15			
3.	10	Lidocaine	25	162.6±11.06	6.97	18.26	< 0.001
		Ropivacaine		288±11.06			

**Figure 2.** Comparison of duration of action (minutes) between lidocaine and ropivacaine

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