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Evaluation the antinociception effect of chronic use of buspirone and effect of that in tolerance to morphine analgesia in mice

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Received: 2006/11/27 , Accepted: 2007/4/18

Objectives: Several studies indicate that central serotonergic neurons have important role in morphine analgesia and tolerance. The aim of this study was to investigate possible role of 5-HT_{1A} receptors by chronic administration of buspirone (partial agonist of 5-HT_{1A} receptors) in producing analgesic effect and on development of tolerance to analgesic effect of morphine using hot plate test. **Methods:** Experiments were performed on adult male mice weighing between 20 and 25 g. The control mice (n=8) had daily i.p. injection of morphine (5mg/kg/day). In the vehicle and test groups before injection of morphine (5mg/kg/day, i.p.), we injected vehicle of buspirone (saline normal: 0.5 ml/kg/day, i.p.) and buspirone (5, 7.5 and 10 mg/kg/day, i.p.) respectively and the hot-plate test just before and 30 minutes after the morphine injection performed once every 5 days. Experiments were continued for 5 days after the attainment of tolerance to analgesic effect of morphine. In the another three groups, we injected only buspirone (5, 7.5 and 10 mg/kg/day, i.p.) and the hot-plate test just before and 30 minutes after the buspirone injection performed once every 5 days for the evaluation of the analgesic effect of buspirone in chronic uses. **Results:** Chronic injection of buspirone (5, 7.5 and 10 mg/kg/day, i.p.) significantly delayed tolerance to morphine analgesia (p<0.05). In addition, chronic administration of buspirone (5, 7.5 and 10 mg/kg/day, i.p.) produce significant analgesic effect (p<0.05). **Conclusion:** The results confirmed the important role of 5-HT_{1A} receptors in analgesia and the development of tolerance to morphine and may dissolve clinical problems due to long duration of opioides administration. However, the exact mechanism of interaction between serotonergic and opioidergic systems is not clear and remains to be elucidated.

Key words: Buspirone, 5-HT_{1A} receptors, D₂ receptors, Morphine, Tolerance, Analgesia.

(n=8) (5-HT_{1A}) 5-HT_{1A}
 (mg/kg/day) (mg/kg/day)
 (/ mg/kg/day) (/ ml/kg/day)
 (/ mg/kg/day)
 (p<0.05) (/ mg/kg/day) :
 (p<0.05) (/ mg/kg/day)
 5-HT_{1A}
 D2 5-HT_{1A}

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() 5-HT_{1A}
 α_2 D₂

()

()
(°C ±)
)

()

()

(

()

()

() (TEMAD CO., Tehran, Iran)
(% /)

5-HT_{1A}

5-HT_{1A}

()

(/ ml/kg/day, i.p.)

(1-PP)

()

(mg/kg/day, i.p.)

()

α_2

(/ mg/kg/day, i.p.)

1-PP

D₂

5-HT_{1A}

()

CNS

± /

α_2 5-HT_{1A}

(cut-off time)

)

()

()

()

:

()

Tukey

one way ANOVA

P<0.05

() ()
()

()

(p<0.05)

()

(/ mg/kg

(Latency Time)

: %MPE

$$\%MPE = [(TL-BL)/Time_{cut-off} - BL] \times 100$$

MPE = Maximum Possible Effect

TL= Test Latency time

BL= Base Latency time

()

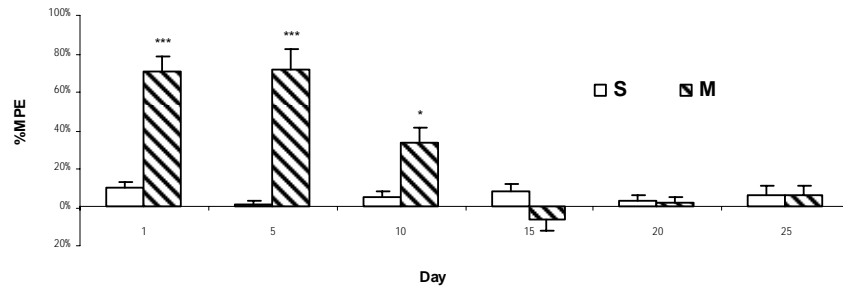
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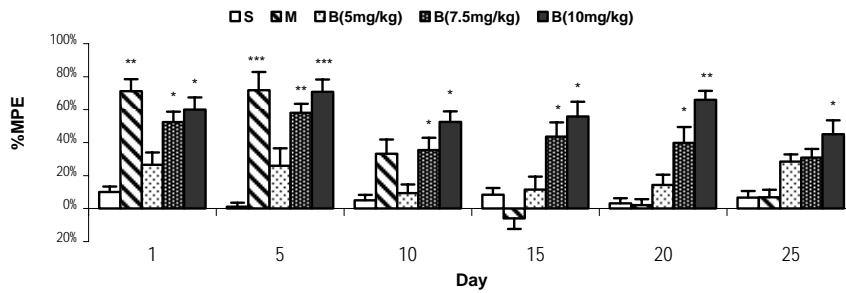
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(%MPE)

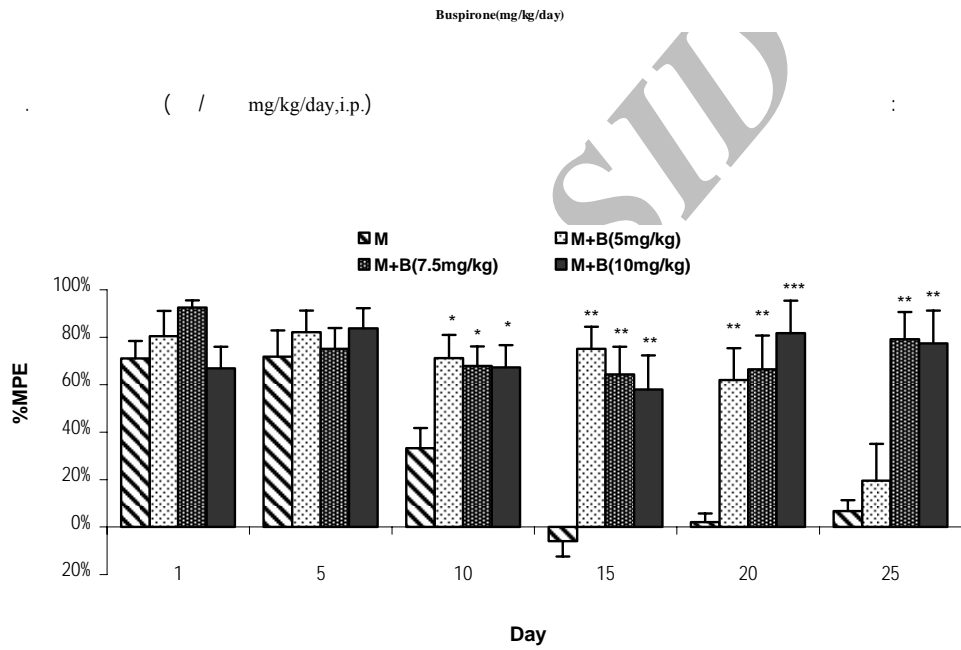
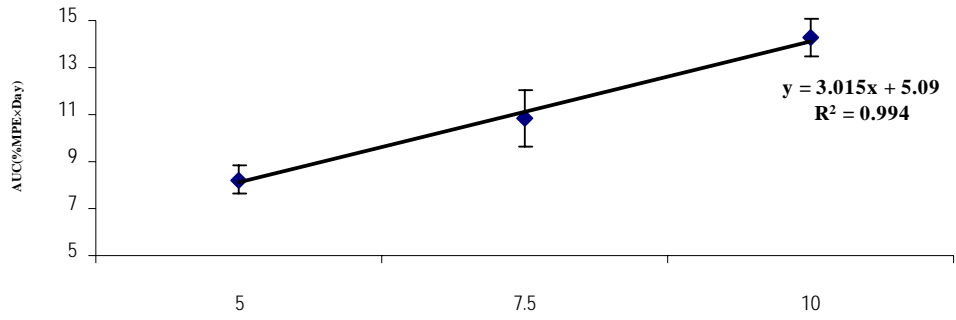
mean + S.E.M



(n=7-8) (mean+S.E.M.) %MPE (± /)
 (***)P<0.001 *P<0.05 (S) (mg/kg/day,i.p.) (/ ml/kg/day,i.p.)
 M=Morphine, S=Saline, MPE=Maximum Possible Effect



(mg/kg/day,i.p.) (/ mg/kg/day,i.p.)
 (S) (n=7-8) mean+S.E.M. (%MPE) (n=7-8)
 M=Morphine, S=Saline, MPE=Maximum Possible Effect. (***)p< / **p< / *p< /)



(/ mg/kg/day,i.p.)
 (n=7-8) mean+S.E.M. (%MPE)
 M=Morphine, MPE=Maximum Possible Effect (/ mg/kg/day,i.p.)
 (***)p< / (**p< /) (M)

Acad

SID

()

(8-OH-DPAT) 5-HT_{1A}

()

α₂ ()

(D₂)

()

(/ mg/kg)

- μ

() ()

() () 8-OH-DPAT ()

()

()

()

()

5-HT_{1A}

() μ ()

() 5-HT_{1A}

5-HT_{1A} (down-regulation) 5-HT_{2A/2C} (down-regulation)

()

() D₂

()

()

α₂ (1-PP)

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