The objective of this study was to investigate the perioperative analgesic effects of oral firocoxib following cauter disbudding in preweaned calves. Twenty Holstein calves approximately 5 weeks old were orally administered firocoxib, a non-steroidal anti-inflammatory, using a dose of 0.5 mg/kg (n=10) or placebo (whey protein) (n=10) in a randomized clinical trial. All animals received a cornual nerve block using a local anesthetic prior to disbudding. Pain biomarkers including ocular temperature, mechanical nociception threshold, and heart rate were evaluated following cauter disbudding at 2, 4, 7, 8, and 24 hrs. Blood samples were collected over 96 hours and analyzed for plasma cortisol and substance P concentrations by radioimmune assay. Additionally, ex-vivo prostaglandin E2 (PGE2) concentrations were determined over the same 96 hour study period using an enzyme immunoassay. Data were analyzed using a linear mixed effects model with repeated measures. An attenuation of the integrated cortisol response (mean±SEM) as calculated as area under the effect curve tended to be greater in placebo treated calves (1611.1±249 nmol.h/L vs. 1114.2±181 nmol.h/L) (p=0.058). A significant decrease in cortisol concentrations (mean±SEM) was observed in firocoxib treated animals at approximately 48 hrs after disbudding (11.3±1.9 nmol/L vs. 22.8±2.8 nmol/L) (p=0.0013). Additionally, a significant inhibition (p<0.01) of ex-vivo PGE2 concentration was observed from 12 to 48 hrs following disbudding in calves treated with firocoxib. These data support the potential for firocoxib to be used to provide analgesia after cautery disbudding in calves; however, further investigation of its perioperative analgesic effects is warranted.